Hazy memories

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The impact of drugs on false memory formation from a legal-psychopharmacological perspective

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Cover design: Jackson Tupper (hello@jacksontupper.com)

Typesetting: Lilian Kloft

ISBN: 978-94-6419-236-0

Printing: Gildeprint, the Netherlands

Maastricht University

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DISSERTATION

To obtain the degree of Doctor at Maastricht University, on the
authority of Rector Magnificus, prof. dr. Rianne M. Letschert,
in accordance with the decision of the Board of Deans,
to be defended in public on Wednesday,
23rd of June 2021 at 10:00 hours in Maastricht
by

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The laboratory research in this dissertation was conducted at the Department of Neuropsychology and Psychopharmacology, Maastricht University, The Netherlands, as well as at The Langton Center, Sydney, in collaboration with The University of Sydney, Australia. The field research in this dissertation was conducted in cannabis coffeeshops, cafes, and buildings of Maastricht University, as well as the Lowlands festival 2018, Biddinghuizen, The Netherlands.

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Chapter 1

General introduction and outline

A Case of Hazy Memories

On the night of Halloween, 2001, a man was found strangled to death in a parking lot in Columbia, Missouri (Possley, 2017). Witnesses described two white males at the scene. They helped police devise a composite sketch. However, the murder went unsolved for two years. In 2003, after viewing media coverage of the case and seeing the composite sketch, 19-year-old Charles Erickson began to wonder whether he had been involved with the crime. He and high school classmate Ryan Ferguson, both 17 at the time, had been out partying in the area near the crime scene during the night of the murder. Erickson, having used alcohol, cocaine, and Adderall® had blacked out that night, but later developed "dream-like" memories of committing the murder (Fischer, 2014). He underwent a lengthy police interrogation in which he was coerced to confess to the crime, implicating both him and Ferguson[1] (Fischer, 2014; Greathouse, 2020). Based on Erickson's questionable testimony and that of two other witnesses, Erickson and Ferguson were convicted of murder and given a 25- and 40-year sentence, respectively. Their conviction, however, ignored evidence that showed Erickson had already arrived home by the time of the murder and that the DNA evidence from the crime did not match either suspect. All testimonies were later recanted and multiple persecutorial violations, including coercion of witnesses to lie under oath, were revealed. Ferguson was exonerated in 2013 after having spent nearly a decade in prison. However, Erickson remains imprisoned, still battling his conviction until this day, and the case remains unsolved (see appeal in casu *Erickson v. Ehlers*, Greathouse, 2020).

This case highlights a myriad of troubling issues. Of central relevance to this thesis is that it provides a real-life example of how alcohol and drug influence can blur and distort memory and consequently play a key role in wrongful convictions. It is likely that the suspect had a blackout due to alcohol and other drug intoxication and could not recollect what he did during that night, making him more susceptible to suggestion. This case illustrates the potential adverse consequences of drug-induced memory errors or false memories from both the role of a suspect and a witness since Erickson both incriminated himself and gave unreliable eyewitness testimony. Indeed, eyewitnesses, victims, and suspects in legal cases are frequently intoxicated with alcohol

1 See e.g.: http://www.freecharleserickson.org for comprehensive case information (case files, interrogation tapes)

and other drugs during the crime, during questioning, or both (Evans et al., 2009; F. T. Palmer et al., 2013). However, how such intoxication may affect their statements is not always considered. To prevent miscarriages of justice, such as in the case of Ferguson and Erickson, knowledge about how drugs might contaminate memory is needed in court. Therefore, the current thesis addresses key issues of false memory formation after drug use from a legal-psychopharmacological perspective.

Background

Already in 1914, the scholar van Geuns wrote about the interplay between intoxicants and testimonial accuracy in his dissertation on eyewitness testimony (1914). Van Geuns discussed how the consequences of acute and chronic drug abuse[2], such as psychotic states, heightened suggestibility, and decreased memory ability, might affect the fitness to give testimony. In writing this dissertation, van Geuns introduced two important premises. First, courts rely on evidence that comprises the memory and reports of a witness, such as testimonies and identifications of a suspect. Second, the occurrence of eyewitness intoxication may lead to opportunities in which their memory, and thus the evidence they give, is vulnerable to contamination.

Memory formation is a dynamic and malleable process that is sensitive to disruption by factors such as the passage of time, aging, or sleep deprivation (e.g., Diekelmann et al., 2008; Norman & Schacter, 1997; Wixted, 2004). Rather than resembling a Netflix episode that we can revisit, the retrieval of an event from memory is always a reconstruction of the original experience. When initially forming a memory, it must undergo the transference from short-term memory into long-term memory, a process termed *consolidation*, in which the synaptic connections between neurons are strengthened (Dudai, 2009). During retrieval, however, memory traces are reactivated and enter a labile state again in which they can be revised and updated with new information before being *reconsolidated* (Dudai, 2009). Presumably, memory's function is to adapt and adjust humans to new circumstances, and therefore does not always accurately reproduce reality (e.g., Howe, 2011; Ofengenden, 2014). As a consequence, memories cannot only be forgotten, they can also be misremembered.

[2] Van Geuns mentioned opiates, cocaine, cannabis, tobacco, and alcohol in this context.

More specifically, memories of events or details that were not experienced are referred to as *false memories* (Loftus & Palmer, 1974; Otgaar, Howe, et al., 2016). They frequently occur spontaneously but can also be elicited through external influence (e.g., suggestive pressure). False memories are every-day phenomena that can pertain to benign details, such as remembering that one put their keys in their bag, while in reality they left them on the kitchen counter. They may become problematic, however, when entering the legal realm, where reliable testimonies of remembered events are of the utmost importance. Legal cases such as the one described here have illustrated that eyewitnesses and innocent suspects can falsely remember to have seen non-existing details of a crime or falsely confess to have committed a crime due to suggestive interrogation tactics of the police (Howe & Knott, 2015). Such false memories can lead to wrongful convictions of the innocent (e.g., Innocence Project, 2020).

One of the earliest accounts of false memory formation dates back to 1884, when Hippolyte Bernheim was the first to recognize *suggestibility* as a general phenomenon in which a powerful party (e.g., therapist) could impose beliefs upon a weaker one (Weitzenhoffer, 1978). Specifically, he warned that persistent pressure could induce memories of scenes that never occurred (Crews, 2017). Bernheim's experiments on post-hypnotic suggestion later proved highly influential, giving rise to Sigmund Freud's psychoanalytic theory and the concept of the unconscious. Subsequently, in the late 19th and throughout the 20th century, several approaches were taken to study memory distortion, revealing the reconstructive and associative nature of memory (e.g, Bartlett & Burt, 1933; Deese, 1959; for a historical review see Oliveira et al., 2018). However, it was not until the 1990's that the term 'false memory' was first cited in the cognitive research literature after it was coined by Elizabeth Loftus in the context of suggestively implanted false memories for childhood sexual abuse (Pezdek & Lam, 2007). The research into the formation of false memories was predominantly fueled by the so-called 'memory wars' in which legal cases were put forward of people who falsely remembered that they had been sexually abused (e.g., Otgaar, Howe, Patihis, et al., 2019). Loftus and colleagues' landmark studies (1974; 1975) had previously highlighted that exposure to misleading information can profoundly contaminate memory for an event. Since then, the field of cognitive psychology has seen an explosive growth of false memory research, along with a wave of methodological research paradigms.

Born out of these historical research traditions was a key distinction still frequently adopted today: false memories can on the one hand arise from internal cognitive processes, such as the natural effort to extract meaning from experiences or the activation of associated knowledge. On the other hand, they may result from a range of external influences, such as the suggestion of false information by an outside source (e.g., misleading questions by an interviewer, Reyna et al., 2002; Reyna & Lloyd, 1997). While internal and external mechanisms can certainly blend together when a false memory is formed, false memories resulting from the former are generally referred to as *spontaneous*, or *naturally-occurring*, while those arising from the latter are termed *suggestion-induced* false memories (Mazzoni, 2002). These two major types are reflected in two separate research methodologies. Spontaneous false memories are regularly studied using the *Deese-Roediger/McDermott*, or short *DRM*, method, in which individuals study lists of associatively related words (e.g., hot, snow, warm, winter, ice), which are centred around an unpresented concept (the *critical lure*, in this case, cold, Deese, 1959; Roediger & McDermott, 1995). Decades of research have robustly shown that in a memory test, people display high rates of false recall or false recognition of the critical lure (e.g., Gallo, 2010). Theories have attempted to account for this phenomenon in terms of associative strength between words and their activation within one's mental knowledge base, monitoring failures when trying to identify the source of the information, as well as proposed dualistic memory processes as underlying cognitive mechanisms (Brainerd et al., 2008; Howe et al., 2009; Roediger, Balota, et al., 2001; see Chapter 2 for more detail).

The chief research method to induce suggestion-based false memory is the *misinformation paradigm* (Loftus, 2005). This is a three-stage procedure in which subjects first are exposed to an event (e.g., staged crime or video), followed by some false misleading information about the event (e.g., the perpetrator wore a black coat, when in reality it was a grey jacket), and finally a memory test about the event. When questioned about the events, participants often report the misinformation (e.g., reporting that the perpetrator wore a black coat) – a memory phenomenon termed the *misinformation effect*. Of close resemblance to this method are measures of *suggestibility*, in which misinformation is not presented separately between encoding (i.e., experiencing an event) and retrieval (i.e., the memory test), but rather is part of the memory test. For example, responses in a memory test could be suggested as ostensibly correct to the participant through, for example, leading questions (e.g., "Did you see the attacker's black coat?", van Oorsouw et al., 2015), negative experimenter feedback (Gudjonsson, 1997), or pre-selected

response options by another alleged participant (Evans et al., 2019). Theoretical accounts explaining the misinformation effect have focused on the memory strength and retrievability of the original event and the misinformation, as well as the ability to attribute a memory to the sources of this information (Ayers & Reder, 1998; Johnson et al., 1993).

Despite the early academic mentions of false memory susceptibility and the possibility of heightened suggestibility due to intoxication by van Geuns (1914), research has largely overlooked how intoxication might lead to the formation of false memories. A substantial amount of contemporary research has been conducted on the impact of alcohol on crucial eyewitness memory variables, such as event recall and face identification (e.g., Jores et al., 2019; Monds, Kloft, et al., 2019). Only a handful of studies however exist with research methodologies specifically aimed at inducing and testing false memories and suggestibility (see Chapter 2). Recently, researchers have turned to studying cannabis in an eyewitness memory context (Pezdek et al., 2020; Vredeveldt et al., 2018; with one early exception by Yuille et al., 1998), but studies on false memory are scarce. Moreover, false memory effects on other substances are mostly unexplored. This knowledge gap is striking as recreational drug use is widespread, and eyewitnesses and suspects are often under influence of drugs such as alcohol, cannabis, and ecstasy (e.g., Evans et al., 2009; Nordfjaern, 2017).

Memory and Drug Use

The use of psychoactive drugs to alter reality dates back even further into our past than the study of false memory. For example, archaeological evidence shows that humans were taking opium, cannabis, hallucinogenic cacti, and psychedelic mushrooms as far back as 10,000 years ago (Guerra-Doce, 2015). Nowadays, modern society is characterized by various applications of the use of both legal and illegal substances. To illustrate, caffeine is used to increase alertness, productivity, and concentration, and alcohol to relax and socialize (Franke et al., 2011; Kuntsche et al., 2005). Cannabis has various uses, from increasing appetite, pleasure, and relieving boredom, to coping with stress, alleviating pain, and inducing tiredness (Hecimovic et al., 2014). Taking *microdoses* (sub-perceptual doses) of the psychedelic substance LSD has emerged as a major trend to hack creativity and ameliorate overall life-quality (Hutten et al., 2019). What many of the effects that people seek when using drugs have in common is that they seem to alter cognitive functioning.

Recent research has begun to shed light on how certain illicit substances may be used as tools to improve treatment of a variety of medical and psychiatric conditions. For example, a growing body of scientific literature now indicates the potential of the two major cannabinoids Δ9-tetrahydrocannabinol (THC) and cannabidiol (CBD) to treat severe forms of epilepsy, multiple sclerosis, chronic pain, and muscle spasms (Maccarrone et al., 2017). Although the main psychoactive compound of ecstasy, 3,4-methylenedioxymethamphetamine (MDMA) is widely known as a club drug, it has proven a promising avenue for management of treatment-resistant posttraumatic stress disorder (Mithoefer et al., 2019). However, these substances do not come without side effects, and often, cognitive functioning is vulnerable to their impact. Psychopharmacological agents therefore present a double-edged sword, alleviating certain ailments but creating disturbances elsewhere.

A cognitive domain that is especially sensitive to effects of psychoactive substances is that of memory. Alcohol, for example, is notorious for causing blackouts, and its effects on cognition have been compared to those of a sledgehammer (White, 2003). Likewise, THC and MDMA have been linked to memory impairments, reducing declarative memory (memory for information that can be explicitly stored and retrieved) for experienced events – in other words, increasing the chance of forgetting (Broyd et al., 2016; Kuypers & Ramaekers, 2005). These drugs have the potential to induce temporary amnesia, but may also cause persistent memory issues with continued use (Carbia et al., 2017; Lovell et al., 2020; Rogers et al., 2009).

Although it is known that these drugs of abuse can decrease memory for true events, their effects on false memory formation are less clearly elucidated. Several indications however warrant that the link between drug use and false memory formation is worth investigating. For example, chronic alcohol abuse is widely known to induce *confabulations*, the formation of false memories to fill in memory gaps (van Oorsouw & Ramaekers, 2010). A recent study (Riba et al., 2015) also found that abstinent cannabis users were more prone to spontaneous false memory production and displayed reduced activation in brain areas associated with memory processing, compared to healthy controls. Knowledge on whether an individual's acutely drugged state increases susceptibility to spontaneous or suggestion-based false memories is however still scarce, even though courts need this information to evaluate the reliability of a testimony. Examining false memory effects specifically resulting from the aforementioned drugs is particularly relevant as

alcohol, cannabis, and MDMA are the most often recreationally-used drugs on a global scale (Winstock, 2019). Additionally, in light of the recent therapeutic and legal developments with cannabis and MDMA (e.g., Urits et al., 2019; van Amsterdam et al., 2020), evaluating the impact of these substances on false memory susceptibility and suggestibility is a pressing need.

Aim and Methods of the Dissertation

The core aim of the current thesis is to examine the effects of drugs of abuse on false memory formation in a legal-psychopharmacological context. Across one literature review and four experimental studies, it was assessed whether acute and residual drug intoxication can increase the susceptibility to spontaneous and suggestion-induced false memories. The main experimental focus of the research was on the two drugs cannabis and MDMA (**Chapters 3, 4, and 5**), but other substances (e.g., alcohol) have been reviewed (**Chapter 2**) and studied to some extent as well (**Chapter 6**). The thesis presents interdisciplinary research that can be placed at the intersection of the fields of psychopharmacology, forensic, and legal psychology. Hence, a multi-method approach to investigating drug effects on memory was employed, combining psychopharmacological with legal-forensic psychological methods. Two laboratory-based studies in this thesis were randomized double-blind placebo-controlled trials, representing the psychopharmacological gold standard to isolate the effects of a substance (**Chapter 4: cannabis, Chapter 5: MDMA**). Additionally, two field experiments were conducted in order to capture effects of naturally occurring (i.e., self-administered) mono- and multi-drug use (**Chapter 3: cannabis, Chapter 6: multiple substances**). Furthermore, the research combined basic memory measures of high internal validity and reliability (word list tasks) and innovative methods of real-world applicability (e.g., virtual reality to simulate crime scenarios from the viewpoints of eyewitnesses and perpetrators). With this approach I sought to elucidate intoxication effects on false memory formation from both a fundamental and an applied memory perspective.

Outline of the Dissertation

Chapter 2: This chapter represents a detailed introduction to the topic of false memories and intoxication. It consists of three parts: a) a review of the prevalence of legal cases that involved substance intoxication on the part of an eyewitness, victim, or suspect in order to illustrate the practical importance of this issue; b) a background of the scientific study of false memories; and c) a review of the current state of the scientific literature regarding the effects of substance intoxication on false memory formation and suggestibility.

Chapter 3: This chapter is a field study on the effects of acute and residual cannabis intoxication on spontaneous false memory formation. Memory performance is compared between three groups: acutely intoxicated regular cannabis users, sober but regular cannabis users (recruited from coffee shops in Maastricht), and sober controls (recruited in University buildings).

Chapter 4: This chapter is a randomized double-blind placebo-controlled study examining the effects of THC on immediate and delayed spontaneous and suggestion-based false memory formation. Participants are healthy occasional cannabis-users.

Chapter 5: Akin to chapter 4, this chapter presents a randomized double-blind placebo-controlled study examining the effects of MDMA on immediate and delayed spontaneous and suggestion-based false memory formation. Participants are healthy volunteers with prior experience with MDMA.

Chapter 6: This final study is a field experiment assessing effects of naturally occurring drug intoxication and naturally occurring sleep restriction on false memory susceptibility in response to various suggestive manipulations. Participants are visitors of a large music festival.

Chapter 7: This final chapter is an overview of the main findings in this dissertation; furthermore, directions for future research and implications are provided.

Chapter 2

Hazy memories in the courtroom: a review of alcohol and other drug effects on false memory and suggestibility

This chapter is an extended version of the following publication:

Kloft, L., Monds, L. A., Blokland, A., Ramaekers, J. G., & Otgaar, H. (2021). Hazy memories in the courtroom: A review of alcohol and other drug effects on false memory and suggestibility. *Neuroscience & Biobehavioral Reviews, 124*, 291-307. https://doi.org/https://doi.org/10.1016/j.neubiorev.2021.02.012

Abstract

Alcohol and other psychoactive drugs are oftentimes implicated in legal cases. A pertinent question herein is whether such substances might adversely affect testimonies of victims, eyewitnesses, or suspects by propelling the formation of false memory and increasing susceptibility to suggestion. In the current review, we amassed all available evidence on the effects of intoxication on false memory formation and suggestibility, including the substances alcohol, benzodiazepines, cannabis, stimulants, hallucinogens, and antipsychotics. Our review indicated that alcohol and cannabis under certain conditions increased the susceptibility to false memories and/or suggestion with effect sizes ranging from medium to large. When intoxicated during an event, alcohol is most likely to increase this susceptibility at high intoxication levels or after a delay, whereas cannabis exerts detrimental effects during acute intoxication but not necessarily once sober. For other substances, ecologically valid research separating different memory phases is needed. Overall, differences between substances regarding false memory effects exist, suggesting that a nuanced approach is needed when dealing with intoxicated individuals in a legal context.

Introduction

Human memory does not operate like a video camera. That is, memories are not exact replicas of the original event but are reconstructions of past experiences (Conway & Pleydell-Pearce, 2000; Johnson & Raye, 1998). During such reconstructions, errors can occur, resulting in false memories. False memories can refer to people remembering events that never happened or remembering them differently from the way they happened (Roediger & McDermott, 1995). Research has shown that people can be led to have false memories of even highly implausible events, traumatic experiences, or bizarre actions (Otgaar et al., 2009; Porter et al., 1999; Thomas & Loftus, 2002). However, the seriousness of such false memories becomes evident when they appear in legal cases (Howe & Knott, 2015). Of importance here is the fact that the lion share of false memory studies have been conducted on participants in a sober state of mind while in many legal cases, witnesses, victims, or suspects might be under the influence of drugs (e.g., alcohol, cannabis). Strikingly, research on the impact of alcohol and other drug intoxication on false memory formation and susceptibility to suggestion is still relatively scarce, aside from perhaps alcohol and cannabis effects on false memory proneness (e.g., Evans et al., 2019; Kloft et al., 2020). The main aim of this article is to review findings on alcohol and other drug effects on false memory production and interrogative suggestibility. In order to examine the problem and demonstrate the relevance of these drug effects, we will also provide a review of the prevalence of intoxicated witnesses, victims and suspects.

Testimonies play a critical role in advancing a criminal investigation and securing a conviction. In many criminal trials, testimonies are the sole piece of evidence available and are strongly relied on by triers of fact in the courtroom (Howe et al., 2017). Therefore, the validity of these testimonies is of utmost importance. A factor that may influence the validity of statements is the level of alcohol and/or other drug intoxication. Eyewitnesses, victims, and suspects might be intoxicated during the criminal event or when giving a statement, or both (Evans et al., 2009). Intoxication during an event may lead to perceptions of reduced credibility in legal professionals (e.g., Kassin et al., 2001) and jurors (Evans & Schreiber Compo, 2010), thus reducing the likelihood of a conviction. Equally relevant, however, is the question whether intoxication might impact false memory creation and suggestibility in individuals involved in crime. It is imperative to understand how intoxication during the crime and/or during questioning may affect testimonial accuracy. To examine this, we will first present an outline of the prevalence of legal cases that

involved substance intoxication in several selected countries with accessible data. The latter is important because it can show how large the problem of intoxicated witnesses, victims and suspects can be in legal cases. This will be followed by an explanation of key methods and theoretical accounts of false memory formation in general as well as linked to substance effects. We will end with a discussion on the effects of several commonly used drugs/drug classes on false memories and suggestibility.

Prevalence of Legal Cases involving Alcohol and Drug Influence across Countries

Before reviewing the literature of the effects of intoxication on false memory and suggestibility, we will first address the question of how often in legal or criminal cases it generally happens that one of the involved is intoxicated with alcohol or another substance. Hence, we will review the prevalence of intoxicated witnesses, victims, and suspects in several countries across the globe. The purpose of this is to help illustrate the importance and magnitude of this issue. Official national statistics on the number of cases where suspects, witnesses or victims were intoxicated with alcohol and other drugs at the time of the crime or at the time of their interview are not always available, since this information is not consistently assessed or documented in police files and reports (van Laar & van Gestel, 2018; Yuille & Tollestrup, 1990). Therefore, we will review a number of relevant findings collated from numerous sources in order to elucidate the problem from different angles and provide an overview of the prevalence with which legal cases and intoxication co-occur.

Although it is already well documented that alcohol use and crime are closely related (e.g., Martin, 2001), people frequently combine alcohol with other substances (e.g., Winstock et al., 2017) which makes it difficult to separate alcohol from other drug use. Hence, our review was aimed at identifying data on the prevalence of substance use (including alcohol and other drugs, alone or in combination) in crime. The search focus was on several Western countries and nations (Australia, the Netherlands, England and Wales, United States [US]) but also included Indonesia. This selection occurred for practical reasons, such as one of the authors being fluent in these countries' native language, as well as data being readily accessible or available. First, databases containing legal case judgments per country (England and Wales: "British and Irish Legal

Information Institute", Australia and US: "LexisNexis" accessed through Nexis Uni, Netherlands: "Rechtspraak", Indonesia: "Direktori Putusan") were searched for official national statistics on court case decisions of offenses involving alcohol or drug influence (either by searching for categorized offenses or by keyword search). This was to identify an overall proportion of legal cases involving substance use. Additionally, governmental criminological resources monitoring crime and drug use were consulted.

Second, a literature search was performed in PsycINFO, using *intoxication*, *witnesses, suspects, and victims* as keywords (intox* AND DE "Witnesses" OR DE "Suspects" OR DE "Victims"; search date March 24, 2020). This search was performed primarily as a guide rather than an exhaustive summary, and as a starting point to identify other relevant papers and findings. The selection criteria were that the study was published in English, and only journal articles and dissertations were included. This search resulted in 30 search hits, which led to identification of further 9 relevant articles. In order to illustrate the timely situation, we focused on recent references only (years 2000-2020). In contrast to the numbers obtained from governmental legal databases, information from these sources more often focused on a specific subset of cases (e.g., violent crime). Table 1 (see end of chapter) integrates results from both searches, presenting an overview of the described prevalence findings by country in alphabetical order.

England and Wales

The British and Irish Legal Information Institute (BAILII) is an online database that provides access to court rulings. A case law search of all England and Wales court rulings in the time range from January 1, 2010 up until April 1, 2020 using the search terms *"influence of alcohol"*, "*influence o*f *drugs",* and *intoxication* resulted in a sum of 822 case rulings. This represents ~2.4% of all case law rulings from England and Wales courts in the database (N = 35,055, accessed April 2, 2020, see case summaries for total numbers).

The Crime Survey for England and Wales (CSEW) records data on violent crime and sexual offences. Around 70% of violent incidents that took place in public places between 2012 and 2014 were alcohol related (Office for National Statistics, 2015). More specifically, according to the year 2016, victims indicated that the offender(s) were under the influence of alcohol in 40%

of all violent incidents, and under the influence of drugs in one-fifth (19%; Office for National Statistics, 2017). With regard to police-recorded data on homicides, in the years 2013-2015, 39% of homicide suspects were reported by the police to have been under the influence of alcohol and/or drugs at the time of the homicide (Office for National Statistics, 2016). Overall, 25% of homicide suspects had been drinking alcohol, 4% had been taking an illegal drug, and 10% were under the influence of both. Concerning victims of homicide, a third (33%) was reported to have been under the influence of alcohol and/or illicit drugs at the time of the homicide: 24% had been drinking alcohol, 3% had been taking an illicit drug, and 7% were under the influence of both.

With specific regard to the prevalence of intoxicated witnesses, a recent study was conducted among England police officers to examine how frequently they come into contact with such individuals (Crossland et al., 2018). According to 82% of the participating officers (total N = 198), intoxicated witnesses are a common occurrence. Officers indicated that on average 44% of the interviews conducted each month were with witnesses who were intoxicated at the time of the crime. The types of crime that were most commonly associated with intoxicated witnesses were assault, rape, volume crimes, and robbery. However, this study exclusively referred to alcohol intoxication, so no findings about other substance intoxication are known.

The Netherlands

According to the Dutch national legal database called www.rechtspraak.nl, drug influence played a role in a total of 2600 cases that went to court and resulted in a verdict (keywords: *drugs invloed*) in the time between January 1, 2010 up until April 1, 2020. For alcohol influence, the database search resulted in a total of 4482 cases (keywords: *alcohol invloed*) for the same time range. Together this represents a total of 2.0% of all court cases that resulted in a verdict in the respective time range (N = 348,175). Moreover, according to information by the Centre for Criminal Prevention and Safety, 75% of the offenders who had been arrested for violence at nightlife parties were intoxicated at the time of their crimes, with 84% having ingested excessive amounts of alcohol and 14% a combination of alcohol and drugs (unknown sample size; CVV, 2011). This is in line with data from the National Drug Monitor (van Laar & van Gestel, 2018), according to which violent offenders have consumed alcohol relatively often (37% -78%). No data for intoxicated eyewitnesses or victims could be identified.

US

In the US there is a high prevalence of crime in connection with substance use, including both alcohol as well as illegal drugs. LexisNexis is a global online research database that provides access to a comprehensive collection of case law rulings, including US courts at the state, federal, and tribal level. A case search of all US court rulings in the time range from January 1, 2010 up until April 1, 2020 using the search terms *"influence of alcohol" or "influence of drugs" or intoxication* resulted in a sum of 92,213 case rulings. This represents ~2.1% of all case law rulings from US courts in the database (*N* = 4,308,048, accessed April 2, 2020).

Regarding governmental monitoring programs, according to the National Institute of Justice, illicit drug use is more prevalent among criminal arrestees than the general population, with drug type varying by region and offender characteristics. The Arrestee Drug Abuse Monitoring (ADAM) program conducted by the U.S. Department of Justice measures the prevalence of alcohol and illegal drug use among arrestees. The ADAM II report (Hunt et al., 2014) stated that the proportion of arrestees who tested positive for any of the 10 drugs[3] addressed by ADAM II ranged from 63-83% across jurisdictions. Arrestees testing positive for multiple drugs in their system ranged from 12-50%. Marijuana remained the most commonly detected drug in urine testing (34-50%).

To establish the prevalence of both intoxicated witnesses/victims and suspects, Evans and colleagues (2009) surveyed a total of 119 US and Canadian law enforcement officers about their encounters with both groups during their work. Seventy-three percent indicated that coming into contact with intoxicated witnesses was common or very common (83% said the same for suspects). Of those witnesses deemed under influence of any substance, officers estimated 59% to have consumed just alcohol, 18% to have used cannabis only, and 24% were estimated to have used multiple substances (Numbers when questioned about suspects: 55%, 18%, 23%, respectively). Officers also reported frequently interviewing witnesses and suspects who were intoxicated during the crime but sober during the interview (see Table 2 in Evans et al., 2009 for numbers), intoxicated during both crime and interview, and with a lesser frequency also individuals who were intoxicated during the interview only. With a similar goal, F. T. Palmer et al. (2013) conducted an archival

[3] Drugs assessed included marijuana, cocaine metabolites, opiates, amphetamine/methamphetamine (confirmation), barbiturates, benzodiazepine, buprenorphines, methadone, PCP, and oxycodone

analysis of court files from serious violent crimes (*N* = 1307 cases) and found that 13% of eyewitness testimonies and 28% of suspect testimonies heard in US courts stemmed from individuals under the influence of alcohol, another drug, or a combination of substances at the time of the crime. The majority had consumed alcohol only (witnesses 73%, suspects 63%), followed by substance combinations (witnesses 11%, suspects 16%), where alcohol combined with cannabis was the most common combination. It is also noteworthy that large proportions of adult and juvenile suspects reported having been intoxicated during interrogation (see Mindthoff et al., 2019).

Furthermore, there are multiple statistics on the prevalence of intoxicated victims of crime, suggesting that drinking and drug use increase the risk of victimization. For example, 63-74% college victims of violence had consumed alcohol and/or other drugs shortly before these incidents (Bureau of Justice Statistics, 2005). Other research also reports that approximately half of the sexual assaults reported by college students occur when the perpetrator, the victim, or both have been drinking alcohol (e.g., Abbey et al., 2014), although recent numbers suggest rates of up to 90% for alcohol and one third for alcohol combined with other drugs (Winstock, 2019). In a sample of college women, 72% of rape victims reported being alcohol-intoxicated during the assault (total N = 8,567; Mohler-Kuo et al., 2004). In line with this, toxicological analyses of 1000 suspected drug-facilitated sexual assault cases showed that 78% tested positive for one or more intoxicating substances (Fiorentin & Logan, 2019). Out of 101 detected different substances, alcohol was the most common (31%) followed by cannabinoids (29%), benzodiazepines (21%), amphetamine/methamphetamine (17%), and cocaine (10%). Also, in a toxicology analysis spanning the years 1990-98 among New York homicide victims (*N* = 12,573), alcohol was present in 30%, cocaine in 28%, cannabis in 19%, and opiates in 11% (any substance: 59%; Tardiff et al., 2005).

Australia

In Australia, a substantial number of violent crimes involve people who are intoxicated by one or more substances, including alcohol and illicit drugs (Monds et al., 2017). A search with LexisNexis using the same search strategy as for US cases resulted in a total of 7,286 case reports.

This represents ~4.3% of all case reports in the database in the set time frame (N = 168,872, accessed April 2, 2020).

As for governmental resources, the Drug Use Monitoring in Australia (DUMA) program is funded by the Australian Government and is the nation's longest-running ongoing survey of police detainees across the country. DUMA comprises two core components: a self-report survey on drug use, criminal justice history and demographic information; and voluntary urinalysis, which provides an objective measure for corroborating reported recent drug use. According to the most recent report, 75% of the 1,571 detainees who provided a urine sample tested positive to at least one type of drug and 40% tested positive to more than one drug type (Patterson et al., 2018). The most commonly detected drug was amphetamines (50%; mostly methamphetamine) followed by cannabis (44%), benzodiazepines (21%), opiates (17%), and cocaine. However, alcohol and cannabis were the most common substances detainees self-reported using in the 48 hours prior to detention. In 2016, detainees reported consuming an average of 20 standard drinks of alcohol in the 24 hours before committing the offence for which they were detained.

Moreover, the National Homicide Monitoring Program records nation-wide data on homicide offences. According to the most recent report (2012–13 to 2013–14), homicides in Australia were preceded by alcohol consumption, either by the victim or the offender (see Table 1 for more details), in over a third (39%) and by any illicit drug use in 33% of all 487 cases (Bryant & Bricknell, 2017). Compared to a report from preceding years (2008-2010), this represents a decrease of alcohol but increase of illicit drug use in homicide cases (47% and 20%, respectively; Chan & Payne, 2013). However, according to the report information on alcohol or other drug use is often missing, especially for offenders (>50%).

Other identified data of interest include, for example, one study investigating "king hit" fatalities (characterized by a single blow to the head; Pilgrim et al., 2014), which based on toxicology reports (N = 68) found that 79% of cases involved the use of alcohol or other drugs, alcohol being the most frequent substance, followed by cannabis. Toxicology analyses in New South Wales homicide victims during the period of 1996-2005 (N = 485) detected substance use in 62.6% and illicit drugs in 32.8% of cases (Darke & Duflou, 2008). Alcohol, cannabis, opioids, and psychostimulants were most commonly detected. Furthermore, a study on the prevalence and characteristics of alcohol-related incidents requiring police attendance in Queensland indicated that approximately one in four incidents attended by police involved alcohol, while 3% were drug-

related (31,090 total incidents; Palk et al., 2007). The most common incidents were vehicle/traffic matters, disturbances, offenses against property, and theft.

Finally, similar to the study by Evans et al., a recent study by Monds et al. (submitted) surveyed Australian Federal Police (AFP) officers (n = 151) about their interactions with intoxicated people. Sixty percent of officers indicated dealing with individuals intoxicated by any substance on either a daily or more than weekly (but less than daily) basis. The substances that AFP officers were most concerned about for the civilian and staff safety were amphetamines (99%), alcohol (92%), hallucinogens (66%), GHB (63%), ecstasy (57%), opioids (56%), and cocaine (51%).

Indonesia

The Indonesian national legal database "Direktori Putusan" (accessed on August 30 2019) contains a total of 52,339 entries of court rulings within the special crimes category "Narcotics and Psychotropics". This represents ~1.2% of all court rulings listed in the database (N = 4,086,662). As for other relevant data, the above-mentioned police survey by Monds et al. also included a sample of Indonesian police officers (n = 128). Compared with Australian police officers, Indonesian police reported less frequent interactions with intoxicated people: 24% reported this as a daily or more than weekly occurrence, but the majority (47%) reported this happening on a less than monthly basis.

Summary

The findings reviewed in this section stemmed from several resources, including official national statistics, governmental legal databases, police survey research, case file research, toxicology analysis, and victim surveys. Together, these findings demonstrate the frequent occurrence of intoxication within criminal cases. Legal cases or court rulings involving alcohol or other drug use were found to represent 1.2-4.3% of all court cases. These numbers were based on national as well as commercial legal databases, including a wide range of cases. Limitations here are that we cannot draw any inferences on how precisely substance use played a role (e.g., who

was intoxicated). However, they help provide a general estimate that seems consistent across countries (see Table 1 for details).

In contrast, the other resources reviewed more often focused on subsets of legal cases representing more serious types of crime (i.e., violent crime, homicide, sexual assault). In these violent crime cases, numbers for intoxicated potential perpetrators (i.e., suspects or people detained) were found to range from 25-78% for alcohol and from 10-83% for illicit drugs. For victims, numbers ranged from 24-72% for alcohol, and from 3-66% for other drugs. For eyewitnesses specifically, only one study gave a statistical finding that 13% were intoxicated with alcohol or other drugs, but law enforcement officers reported that they were frequent. Thus, we conclude that incidence of alcohol and drug use in violent crime cases is much higher than the ~1.2-4.3% of cases where substance use was involved.

The numbers reviewed vary of course substantially with the type of population surveyed and the type of crime in question. Another crucial reason for the varied results may be differences in methods of verifying substance use: while some of the reviewed resources were data from rather objective sources such as toxicological analysis, some relied on self-report (e.g., admissions from victims or suspects) or estimates (e.g., from victims or police staff). The latter two thus suffer from obvious drawbacks and actual numbers might be higher. Findings especially highlight the pervasive nature of alcohol across a range of criminal incidents, and that this substance is likely to be the most common substance used by witnesses, victims, and suspects. Other very commonly identified substances include cannabis (Fiorentin & Logan, 2019; F. T. Palmer et al., 2013), as well as stimulants such as amphetamines and cocaine. This reflects general global trends of substance use which show that alcohol, cannabis, and stimulants are by far the most widespread substances (Winstock et al., 2017). However, in the context of crime, substance use occurs at an even higher prevalence compared to daily population use patterns, increasing the risk of violent incidents, whether through direct drug effects or through violence surrounding substance use (Darke & Duflou, 2008).

Taken together, non-trivial percentages exist for intoxicated witnesses, victims, and suspects. These prevalence numbers underscore the importance of amassing the evidence on whether intoxication puts them at risk to produce false memories.

False Memories

When assessing drug effects on false memories in a laboratory setting several experimental paradigms have been applied. In general, the scientific literature distinguishes between two major types of false memories (Brainerd, 2013; Mazzoni, 2002): *spontaneous* and *suggestion-induced* false memories. When false memories arise without external suggestive influence or manipulation but are the result of endogenous mechanisms (e.g., spreading activation of items stored in memory, Roediger, Balota, et al., 2001) they are referred to as spontaneous false memories. Importantly, these are essentially memory errors due to normal associative and reconstructive memory processes (e.g., Gallo, 2010; Mazzoni, 2002). Spontaneous false memories are common in neurological and psychiatric conditions where they are often labeled confabulation (e.g., frontal lobe pathology, psychotic conditions, dissociative conditions; Kopelman, 1999), but are also a frequent occurrence in everyday life in healthy individuals (e.g., Schacter, 1999).

Spontaneous false memories are typically induced by using the Deese/Roediger-McDermott (DRM) paradigm, in which lists of associatively related words are presented during encoding (e.g., bed, dream, wake, rest, tired, etc.) with one prototypical exemplar of the word category (the *critical lure*: sleep) missing (Deese, 1959; Roediger & McDermott, 1995). When participants have to report which words they can still recollect, a significant proportion of subjects falsely recall or recognize the critical lure (Gallo, 2010). Some studies have also employed visual variants of these tasks, and sometimes included emotional on top of neutral stimuli (e.g., Guarnieri et al., 2016; Moritz et al., 2006).

Three major theories can account for the occurrence of spontaneous false memories: *Associative-Activation Theory* (AAT; Otgaar, Howe, et al., 2019a), *Activation/Monitoring Theory* (AMT; Roediger, Watson, et al., 2001) and *Fuzzy-Trace Theory* (FTT; Brainerd & Reyna, 2019). AAT is derived from spreading activation models and predicts the formation of false memories through spreading associative activation, where the processing of one word activates a corresponding node (i.e., concept) in one's knowledge base that may spill over to neighboring related but non-presented nodes, leading to formation of false memories. For example, processing a word such as *tired* might activate related concept nodes, such as *night*, *bed*, or *sleep*, increasing the chance that they will be remembered even though not presented. Also belonging to the family of spreading activation models and noteworthy in this context is Activation/Monitoring Theory

(AMT; Roediger, Watson, et al., 2001), which postulates that in addition to activation processes, monitoring (memory editing, e.g., deciding where the activated information originated) plays a role in DRM false memory too: while activation increases false memories, monitoring can reduce them (Gallo, 2010). Whereas AAT assumes that false memories are primarily evoked at encoding (Howe et al., 2009), AMT specifies that activation and monitoring processes occurring during both encoding and retrieval affect the probability of false memory in the DRM paradigm (Roediger, Watson, et al., 2001).

According to Fuzzy-Trace Theory (FTT), when experiencing an event, people process the surface information and the underlying meaning of an event, which they store as a separate *verbatim* (item-specific surface information) and *gist* (meaning-based information) memory traces. For example, in context of the DRM, verbatim refers to specific features of each word, such as word size or color, and gist to the theme of the list of words. Verbatim retrieval supports true memory but fades more rapidly compared to gist, whereas gist retrieval can support true memory as well as false memories of events that are consistent with the gist. Hence, false memories are thought to occur when people rely on the underlying meaning of an event, particularly when the verbatim trace has faded. In an eyewitness memory context, this can explain the occurrence of eyewitness misidentifications: verbatim information such as specific facial features fades quickly whereas gist information like age, race, gender, and body build remains ("The attacker was a muscular teenage Caucasian male"; Brainerd & Reyna, 2019).

In addition to measuring acceptance of critical lures that share many strong associative relations with the studied lists, studies with the DRM also typically employ a measure of baseline false responding to new and unrelated words. Whereas false alarms for critical or related items are seen as more likely to reflect underlying memory processes such as spreading activation, thus representing in fact false memories, false responding to unrelated items is frequently seen as an indication of response bias (i.e., the general tendency to respond to items in a systematic but potentially false direction, such as a yes-bias, Wright et al., 2008). The term *spontaneous* false memory oftentimes pertains to false memories elicited in the DRM paradigm. In contrast, the response criterion that an individual adopts for their memory decisions under conditions of uncertainty can be influenced by factors such as the experimental instructions given or feedback from an experimenter (Rotello & Macmillan, 2007; Verde & Rotello, 2007). However, it has been

critically noted that simply any false alarm on a recognition memory task is sometimes termed a false memory, despite that different cognitive mechanisms might underpin these false alarms (Pezdek & Lam, 2007).

Note that while the DRM paradigm is the chief method used in studies to induce spontaneous false memories, there are other methods to study naturally occurring false memories (e.g., Lindsay et al., 2004; see also Mazzoni, 2002). A particularly relevant example here comes from context-dependent false memories: While context reinstatement (explicitly matching environmental cues between encoding and retrieval) has been linked to improved memory retrieval (Smith & Vela, 2001) and is a commonly used interview technique to improve eyewitness memory (e.g., Geiselman et al., 1986), it can also lead to memory-undermining effects. When context reinstatement is employed (e.g., depicting the same visual scene at retrieval as at encoding) with different but perceptually similar lure objects as the ones presented in the study phase, this can distort memory and elevate the risk of false recollection (Doss, Picart, et al., 2018).

The formation of suggestion-induced false memory occurs due to external suggestive influence (coming from an outside source, e.g., a co-witness). Several methods exist to evoke suggestion-induced false memories with the misinformation and implantation method being perhaps the most studied and forensically relevant ones. In the *misinformation paradigm*, participants first witness an event, such as a staged crime, and are later exposed to erroneous information about the details of the event, such as the false detail that the perpetrator carried a gun (while in fact he did not have a weapon). In a later memory test, people often incorporate the suggestion and falsely report having seen the suggested detail (i.e., the gun). This phenomenon is called the *misinformation effect* (for a review see Loftus, 2005). Different studies have employed misinformation in various forms, most often consisting of narrative descriptions containing false statements. Such false memories are thought to arise in response to both internal (endogenous mechanisms, e.g., source confusion) and external (e.g., compliance) processes (Brainerd et al., 2008; Otgaar et al., 2012). Here, social factors play a major role in influencing the malleability of memory; for example, social interactions (whether containing misinformation or not) serve as a mechanism enabling the spread of a memory from one person to another, a process referred to as *social contagion* or *memory conformity* (e.g., Brown et al., 2012; Edelson et al., 2011).

Also important to mention in this context are measures of *interrogative suggestibility*, which has been defined as the extent to which an individual comes to accept information communicated during formal questioning within a closed social interaction (Gudjonsson, 1997). Most prominent here is the Gudjonsson Suggestibility Scale (GSS), which exposes participants to a narrative and, disguised as a memory test, measures how much they yield to suggestive questions and shift their responses under interrogative pressure from an examiner. Other suggestibility measures in the applied memory context have used misleading questions. Suggestibility and other suggestion-based measures, such as susceptibility to the misinformation effect, are terms that are often used interchangeably in the legal psychological context, even though they tend to be only weakly correlated (Bernstein et al., 2018). Other forms of suggestibility have been proposed, such as *primary suggestibility* (Eysenck & Furneaux, 1945), defined as the induction of thoughts or actions through suggestive procedures (e.g., imagination, see Carhart-Harris et al., 2015).

While false memories elicited in the misinformation paradigm focus on the formation of false memory for *details*, the implantation method (also called *lost-in-the-mall* technique) aims to plant entire autobiographical events that never occurred into a person's memory (Loftus & Pickrell, 1995; Wade et al., 2002). Typically, participants in this paradigm receive narratives of supposedly experienced events and are encouraged to recall these events over the course of multiple interviewing sessions. A myriad of suggestive techniques such as guided imagination, the help of family members, social pressure, and the use of fake photographs have been employed in such experiments to convince participants of remembering events that they never experienced. This suggestive manipulation causes an average of 30% of participants to partially or fully falsely remember entire rich complex events, such as a flight in a hot air balloon (Loftus, 2003; Otgaar et al., 2012; Scoboria et al., 2017).

An influential account to explain suggestion-dependent false memories is the *source monitoring framework* (SMF; Johnson et al., 1993), which is concerned with how people discriminate between memories from different sources (e.g., internally vs. externally generated). According to the SMF, false memories arise when information from one source is attributed to another (erroneous) source, which is then called *source misattribution*. For example, a witness might report details of a crime learned through discussion with a co-witness because they confuse the source of the information and attribute it to their own memory (Zaragoza & Lane, 1994). Memories from different sources are thought to differ in terms of perceptual characteristics (e.g.,

richness), and evaluation of these characteristics can help to distinguish between memories from different sources. According to the *discrepancy detection principle*, people are more prone to suggestive influences such as misinformation if their memory for the original event is poorer, as it becomes more difficult to distinguish truly encoded information from external, for example, suggested details (Schooler & Loftus, 1986; Tousignant et al., 1986).

The distinction of spontaneous, or naturally occurring, versus suggestion-induced false memories is not a mutually exclusive one, and in fact the boundaries are fuzzy and sometimes overlap (Mazzoni, 2002). Its function is to distinguish disparate research traditions as well as different underlying mechanisms of memory distortions; e.g., social psychological factors can play a prominent role in suggestion-based false memories, whereas basic cognitive processes are more likely to underlie spontaneous false memories. There are also some false memory paradigms that do not neatly fit into the dichotomy (e.g., boundary extension, Liu et al., 2016), or that blend elements from both (e.g., combining cognitive reconstructive mechanisms with misinformation to elicit memory errors, Doss et al., 2016).

For the current review, a critical question is whether susceptibility to spontaneous and suggestion-based false memories and suggestibility decreases or increases when suspects, eyewitnesses, or victims are under the influence of alcohol and/or other drugs. Similar to other vulnerable groups (e.g., children), intoxicated suspects and witnesses may show unique patterns of memory impairment that require special attention from law enforcement.

Intoxication Effects on False Memory and Interrogative Suggestibility

In the following sections, key findings from studies investigating effects of intoxication on false memory and suggestibility will be reviewed (see Table 2 for a summary, end of chapter). We included studies that made use of word list paradigms such as the DRM to assess false memory production, but also studies that were conducted using an eyewitness or perpetrator misinformation or suggestibility framework. Although studies that employed methods specifically designed to induce false memories were the primary focus of this review, some of the findings using these paradigms have also been demonstrated in other memory paradigms that did not necessarily focus on false memories. Thus, supportive data using non-false memory paradigms will be added where relevant. The sections are organized by substance or substance class, covering all those that have

been, to our knowledge, investigated in this context, i.e., alcohol, cannabis, stimulants (amphetamines, MDMA), benzodiazepines, antipsychotics, and hallucinogens.

An important distinction in psychopharmacological research is between *acute*, *residual*, and *persistent* (long-term) effects of a drug. Accordingly, there are studies looking into either one, testing effects of an acutely administered substance during its duration of action, versus testing effects of a substance sometime after its immediate drug effects have subsided, or both. Similarly, there can be methodological differences among memory studies, as memory is thought of as operating in different stages. According to basic memory models the three necessary stages in the learning and memory process are *encoding*, *storage*, and *retrieval* (White, 2003). Encoding is defined as the initial acquisition of information; storage refers to maintaining information over time; retrieval is the ability to access information when needed, such as in a memory test. Effects of substances on memory can be tested at each of these stages. Memory performance is measured using *recall* (involving reproduction of information) or *recognition* tests (involving the selection of correct from incorrect information). Memory studies distinguish between *true memory*, i.e., memory of an event that truly occurred, which can be measured in terms of completeness and accuracy (Evans & Fisher, 2011; Koriat et al., 2000), and on the other hand *false memory*. This review will primarily focus on studies that specifically manipulated false memory and interrogative suggestibility, the two often being used interchangeably in the context of eyewitness memory and both of major relevance to the legal field (e.g., Evans et al., 2019). Although possibly of legal relevance, studies on other forms of suggestibility (e.g., primary) have been conducted outside of the applied memory context and are beyond the scope of this review; however, they will briefly be pointed out. Similarly, results on true memory have been covered elsewhere but will briefly be touched upon for each substance.

Linking False Memory Theories to Substance Classes

Before reviewing the false memory findings for each substance or substance class, in this section the aim is to link the previously mentioned false memory theories to substances and arrive at specific predictions as to how false memory might be affected. At the broadest level, drugs can be classified in terms of *stimulants*, *depressants*, and *hallucinogens*, corresponding to their

respective effects on the central nervous system (CNS; e.g., Julien, 2013; Porath & Beirness, 2019). Stimulants (e.g., amphetamines, cocaine, caffeine) increase activity of the CNS, thereby invigorating mental and physical function, whereas depressants (e.g., alcohol, benzodiazepines, opioids, GHB) have the opposite effect, slowing down activity of the CNS and inducing effects ranging from increased relaxation to tiredness to coma. Hallucinogens encompass a wide range of substances that differ in and are classed by their pharmacological mechanism of action [e.g., serotonergic hallucinogens such as lysergic acid diethylamide (LSD), psilocybin, mescaline; N-methyl-D-aspartate (NMDA) antagonists, e.g., ketamine; anticholinergic agents, e.g., scopolamine, among others].They are characterized by their ability to elicit marked altered states of consciousness, including for example altered perception of self, time, space and one's surroundings, plus eyes-closed complex and vivid visual imagery (Nichols, 2004; Pallavicini et al., 2019). This is a simplistic classification and matters are more complicated as some substances fall into multiple categories; for example, MDMA is primarily a stimulant but has some hallucinogenic properties, whereas cannabinoids combine effects from all three categories.

In general, stimulants are thought to enhance cognition and memory processing whereas depressants are thought to interfere with it. Similarly, hallucinogens may interfere with cognition and produce memory loss (e.g., ketamine, Morgan & Curran, 2006). However, effects may be reversed, depending on the timing or, in other words, at which memory stage a drug is involved: to illustrate, alcohol as well as other pharmacologically similar sedatives (e.g., benzodiazepines) generally impair learning (encoding) but can facilitate memory for learned material if given after learning, a phenomenon known as *retrograde facilitation* (e.g., Fillmore et al., 2001; Reder et al., 2007; Wixted, 2004). Depending on memory stage and drug type, a substance might therefore facilitate or interfere with memory.

Because of the gamut of cognitive effects that certain drugs might have, it is challenging to come up with specific predictions on how each drug type might affect false memory creation and suggestibility. Nonetheless, our argument is that it is imperative to link existing false memory theories to drug effects on false memory and suggestibility as these links might fuel new research enterprises in this field. Applying theoretical accounts of false memory production to what effects substances might have in this regard leads us to a number of predictions. According to Associative-Activation Theory, Activation/Monitoring Theory, and Fuzzy-Trace-Theory, associative

activation and gist processing, respectively, support false memory. Drugs that impair encoding (i.e., produce amnesia) might reduce or prevent these mechanisms through reduced processing of to-be-encoded materials, resulting in reduced associative or gist-based false memory, whereas drugs that facilitate learning of new information might fuel false memory by enhancing associative activation and gist processing. However, it could also be argued that the reverse might be true, with cognition enhancers supporting verbatim encoding or successful monitoring, thus facilitating correct rejection of never encoded stimuli, and cognition-impairing drugs to induce more difficulty in discriminating between truly encoded and never presented stimuli (i.e., memory monitoring). Thus, it is difficult to make consistent predictions as for how spontaneous false memory might be affected.

Based on the source-monitoring framework, we use internal cues such as sensory or contextual details to help distinguish genuine memories from experiences that were only dreamed or imagined. In terms of suggestion-induced false memory and suggestibility, it could be the case that due to a poorer original memory from an amnesia-producing drug at encoding, people would be more lenient in the internal criteria they use to judge a memory's genuineness (Nash & Takarangi, 2011). That is, a weaker original memory might make it harder to rule out a suggestion as incorrect, therefore more likely incorporate a suggestion into their own memory to fill in the blanks. This is also consistent with the discrepancy detection principle, dictating that detecting discrepancies between suggestions and one's original memory becomes harder if the original memory is poor, which it could be due to an amnesia-producing drug (e.g., alcohol). Following this reasoning, we could predict that drugs that enhance true memory ability (e.g., amphetamines) might leave us less susceptible to external suggestion due to improved ability to correctly identify discrepancies and avoid source misattributions. More substance-specific theories (i.e., regarding alcohol) are added in the next section.

Depressants

Alcohol

Alcohol (ethanol) is the substance that has been investigated the most in terms of its influence on (false) memory and suggestibility. It facilitates activity at the $GABA_A$ receptor, therefore acting sedatively, but can also induce initial stimulatory effects (Doss, Weafer, Ruiz, et al., 2018; Hendler et al., 2013). Alcohol can produce partial (*fragmentary*) or full (*en bloc*) memory loss for new events (i.e., blackouts or alcohol-induced anterograde amnesia) owing to its disruptive effect of the brain's episodic memory network (i.e., fronto-hippocampal functioning, White, 2003). The general conclusion based on several studies and a recent meta-analysis from the applied memory context is that while alcohol consumption prior to the encoding of an event decreases the completeness of memory accounts when questioned immediately or after a sobering delay (i.e., fewer details recalled, moderate effect size g = 0.40), it does not appear to reduce accuracy or increase error rates (Altman, Schreiber Compo, Hagsand, et al., 2018; Altman, Schreiber Compo, McQuiston, et al., 2018; Crossland et al., 2016; Flowe et al., 2020; Flowe et al., 2016; Jores et al., 2019; van Oorsouw & Merckelbach, 2012). The effect was moderated by intoxication level, with highly intoxicated witnesses providing the least complete testimonies. Intoxicated witnesses have thus been designated as "better than their reputation" (Nadja Schreiber Compo et al., 2012, p. 77). Some evidence, however, suggests that under certain conditions, accuracy can also be negatively affected, but these conditions remain to be specified (see Altman, Schreiber Compo, Hagsand, et al., 2018).

To explain variations in how alcohol sometimes affects memory in individuals, three proposed mechanisms have been employed in the applied memory context: *State Dependent Retrieval*, *Alcohol Myopia*, and *Alcohol Hypervigilance*. Briefly, State-Dependent Retrieval occurs if a person is more accurate attempting to retrieve a memory is in a similar state to when they encoded that information (i.e., intoxicated at both time points) relative to if the person is not in the same state. However, the usually observed benefits of state-dependent retrieval do not seem to apply to intoxicated states, as memory has been shown to be most impaired when both encoding and retrieval take place when intoxicated and tested separately (e.g., see Schreiber Compo et al., 2017; Söderlund et al., 2005; Weissenborn & Duka, 2000). Alcohol Myopia Theory proposes that alcohol restricts the range of cues to which a person can attend while intoxicated and thus may

only report salient/central items (Steele & Josephs, 1990). The previously described meta-analysis found evidence for alcohol myopia, with intoxication during encoding being detrimental to the recall of peripheral but not central details (Jores et al., 2019; however, van Oorsouw et al., 2019 only found limited support). Alcohol hypervigilance suggests that people who are aware or expect that they have consumed alcohol may be expecting impairment and this can affect their performance over and above any actual alcohol effects (e.g., Evans et al., 2017), highlighting the importance of placebo-controlled studies. For example, Schreiber Compo and colleagues (2011) found more conservative reporting behavior in participants who received placebo compared to an alcoholic beverage. Taken together, these accounts can explain how some memory studies report no impairment during alcohol intoxication, while others report reduced completeness or increased errors.

In terms of DRM false memories, in one study participants received alcohol or placebo and encoded DRM lists (once vs. three times), followed by a sober test of both explicit (free recall) and implicit (stem completion task and post-hoc awareness measures) false memory 24h later (Garfinkel et al., 2006). Alcohol appeared to decrease associative activation leading to a reduction in both true recall and false recall of critical lures for lists presented once, but no statistical differences for repeated lists and implicit false memory were found (N = 32, between-subjects). In particular, it appears that increased learning with repetition, which increases the rejection of false memories under placebo, is reversed under alcohol leading to a decrease in rejection of critical lures. Furthermore, in a study by Milani and Curran (2000) a low dose of alcohol (0.26-0.28 g/kg) before encoding with retrieval shortly after exerted no effect on true and false recall or recognition rates of critical lures, but increased recollective experience of false recognition responses (increased level of remember vs. know judgments; N = 20, within-subjects; however, for recent evidence that alcohol impairs both recollection and familiarity of episodic memory see Doss, Weafer, Ruiz, et al., 2018). Finally, in Mintzer and Griffiths (2001b) it was found that neither a low or a moderate alcohol dose (0.27 and 0.60 g/kg, before encoding with retrieval shortly after) affected false recognition of critical lures (N = 18, within-subjects), although the high alcohol dose did reduce true recognition and induced a more conservative response bias. A more conservative response bias during acute alcohol intoxication has also been observed in other episodic memory tasks (see Mintzer, 2007)

In the two latter studies, both encoding and retrieval took place while intoxicated. Thus, these seemingly contradictory findings might stem from methodological differences in terms of the memory stage affected by alcohol, and since encoding and retrieval phases can be differentially affected by drugs that regularly impair true memory function, it is complicated to interpret findings from studies where these phases have not been separately tested (see also section on cannabis). Alternatively, it is possible that a substantial delay is needed in order to reveal the drastic effect of alcohol on both true and false memory, given that alcohol-induced memory impairments are not always detected when immediately tested (Carlyle et al., 2017) – a phenomenon that is also apparent in more applied studies as will be described in the following paragraphs.

With regard to misinformation/suggestibility studies, in one study, participants (N = 83, between-subjects) watched a crime film while sober, and then afterwards received alcohol, reverse placebo (received alcohol but were told it was non-alcoholic)[4], or control (told no alcohol and received no alcohol), before they were exposed to misinformation about the film (alcohol present during encoding of misinformation). The following day they completed a cued-recall test (sober). It was found that control participants were more likely to report misinformation compared to the alcohol and reverse placebo groups, showing that alcohol consumption after a criminal event can protect memory from misinformation, thus providing evidence that alcohol-induced retrograde facilitation can also be detected in a more applied paradigm (Gawrylowicz et al., 2017). The fact that both groups who had alcohol were less suggestible indicates that the facilitating memory effect was more likely due to pharmacological effects of alcohol, rather than due to alcohol-related beliefs. A study by Santtila et al. (1999) had previously found similar effects using the Gudjonsson Suggestibility Scales (N = 51, between-groups, alcohol conditions: high, medium, low, control). These studies are of forensic relevance, showing that alcohol can at times have beneficial effects on eyewitness memory by protecting against misleading post-event information.

In another lab study (Nadja Schreiber Compo et al., 2012), participants were assigned to an intoxication condition [dosed up to 0.08g/210L (= BrAC of 0.08%) vs placebo vs control, N = 93, between-subjects], after receiving their drink were exposed to a staged theft, received

[4] Many alcohol-memory studies control for alcohol expectancies by varying expectancy with intoxication condition, given that alcohol-outcome expectancies can influence different behaviors and cognitions (see e.g., Evans et al., 2019, or Jores et al., 2019, on the importance of this)

misinformation shortly after, and finally were interviewed about the crime. Intoxication was thus present during encoding of the event, the misinformation, and its retrieval, and had no impact on susceptibility to misinformation. However, both intoxicated and placebo participants had higher false recall rates for cued open-ended questions than controls (misinformation and control items combined). Importantly, as it is not always possible for police to immediately interview a witness after they have experienced the event, studies investigating the role of a delay on suggestibility are also necessary. To this end, in another study by this group (Evans et al., 2019), participants were assigned to the same intoxication conditions as above, but a further condition was included whereby some participants recalled the event immediately after encoding (while necessarily still in the same intoxication state as encoding), and others recalling after a delay of one week (at which point they were randomly assigned to be intoxicated, in a placebo group, or sober; intoxication state at encoding and retrieval were fully crossed in the delayed condition, BrAC 0.06-0.08%, N = 210). In this study, participants watched a film and misinformation was introduced via a forced-choice retrieval test with answers already circled (half were correct, half were incorrect), supposedly by a previous participant. It was found that although again following immediate recall there were no intoxication condition effects, intoxication was significantly related to increased suggestibility (acceptance of incorrect suggested answers) and decreased accuracy (correct responses divided by the total number of responses) a week later. Specifically, it was intoxication during encoding, combined with a delay before the first retrieval attempt that made participants less accurate and more likely to accept false suggested answers, while intoxication state at retrieval was unrelated to memory performance (see Schreiber Compo et al., 2017 for true memory results). This study provides important information about the timing of police interviews, particularly as in many jurisdictions the current recommendation is to avoid interviewing currently intoxicated people and await the 'sobering-up' of the witness prior to interview.

In Flowe et al. (2019) being questioned after a delay was also found to increase susceptibility to misinformation (recall and recognition), but this did not vary with having had alcohol during the encoding of a hypothetical rape case scenario (N = 80, between-subjects, mBAC = 0.06%, alcohol vs. sober with alcohol expectancy controlled). Here, misinformation was given after a delay in form of a post-event narrative of part of the scenario by an alleged past participant, but separately from retrieval. However, alcohol expectancy interacted with actual alcohol condition, with a mismatch in expectancy and beverage associated with higher levels of

confabulations (i.e., recalling details that were not in the actual scenario) in an interview. Although adding extra details could stem from the experimental instructions asking participants to imagine themselves in the scenario, a higher tendency to confabulate when having had alcohol without knowing so might be forensically relevant. As for true memory, alcohol during encoding was related to reduced completeness of accounts.

One common criticism of lab-based studies on intoxication and memory relate to the fact that, for ethical reasons, most lab studies only include participants who have blood alcohol concentrations around the legal driving limit (BAC 0.05–0.08%), but in real-life crime scenarios, higher intoxication levels are likely. So, several field studies have been conducted to combat this limitation and have recruited participants at elevated BAC levels. For example, in a field study by van Oorsouw et al. (2015), bar patrons (with blood alcohol concentrations ranging from 0.01-0.16) were instructed to commit a mock crime and then were immediately given a memory test that included misleading questions in a procedure akin to the Gudjonsson Suggestibility Scale. Memory was tested again 3-5 days later and it was found that severely intoxicated participants (BAC > 0.11%) displayed a greater tendency to go along with the suggestive cues compared with sober participants at both time points (N = 67, between-subjects). A drawback of this study is that the same memory tests were repeated at delayed test and therefore testing effects (i.e., retrieval practice, the improvement of long-term memory after retrieval, Roediger & Butler, 2011)might have played a role, although the authors argued that the findings cannot be explained solely based on practice effects.

In line with this, it has been demonstrated across two recent field studies (n = 86, BAC 0.00-0.16%, and n = 189, BAC 0.00-0.20%, mixed design with alcohol as continuous predictor) that overall, intoxication increased the acceptance of misinformation in response to suggestive questions (misinformation in the form of a combination of false alternative, affirmative, and leading questions) about a staged interaction (van Oorsouw et al., 2019). The misinformation effects were mediated by memory completeness, supporting the discrepancy detection principle. Findings regarding whether effects on misinformation acceptance were more detrimental at immediate intoxicated testing versus delayed sober testing were inconsistent; however, immediate intoxicated testing was superior to a delayed-only (sober) test. This study also evaluated the effects of repeated testing and found that only previously sober participants benefitted from this, whereas

previously severely intoxicated participants showed a reduction in peripheral memory accuracy (i.e., fabrication of new details or modifying details).

Overall, it is clear from the available research that it is important to study the dose–response effect of alcohol on memory. Most lab studies indicate no increased risk of false reporting when intoxicated and tested immediately (Evans et al., 2019; Milani & Curran, 2000; Mintzer & Griffiths, 2001b; Nadja Schreiber Compo et al., 2012), although at higher levels of intoxication this risk may increase (van Oorsouw et al., 2019; van Oorsouw et al., 2015). However, when witnesses were intoxicated during an event and questioned after a substantial delay, they may become more vulnerable to suggestion (Evans et al., 2019). For DRM false memory, despite scarcity of rigorous studies, findings point in the same direction, in that a delay is necessary to reveal more impairment. These results from both basic and applied memory literature suggest that alcohol affects encoding more drastically than retrieval, but some non-false memory studies also detected retrieval impairments under some conditions (e.g., during the ascending limb of the BAC curve, Söderlund et al., 2005) or that memory was most impaired when both encoding and retrieval occurred when alcohol was given during both phases (Söderlund et al., 2005; Weissenborn & Duka, 2000). The literature on alcohol effects on encoding, retrieval, and their interaction thus contains gaps and inconsistencies (e.g., Mintzer, 2007; Weissenborn & Duka, 2000) and additional research is required to further explore these promising findings.

Benzodiazepines

Benzodiazepines (e.g., Valium), like alcohol, are CNS depressants and $GABA_A$ positive allosteric modulators, and have been widely documented to produce transient anterograde amnesia, i.e., impairing encoding but not retrieval processes (Curran, 1991; Huron et al., 2001; Taylor & Tinklenberg, 1987). With regard to false memory, a handful of studies have been conducted on the effects of different benzodiazepines using the DRM procedure, producing mixed findings. In a placebo-controlled study by Huron et al. (2001), lorazepam and diazepam administered before encoding with retrieval shortly after both impaired true recognition but had no effects on false recognition of critical lures in healthy volunteers (n = 12 per group, between-subjects). However, lorazepam elevated false alarm rates of unrelated words. In contrast, across two studies encompassing three experiments, Mintzer and Griffiths (2000, 2001c) found that the benzodiazepine hypnotic triazolam (at encoding, retrieval shortly after) produced dose-related

decreases in both true recognition and false recognition of critical lures, despite producing increases in false recognition of unrelated words (N = 24, and N = 36, respectively, within-subjects).

Moreover, similar to results with alcohol by Garfinkel et al. (2006), studying lists twice versus once increased false recognition of critical lures in the triazolam condition, whereas it decreased false recognition in the placebo condition. These results were interpreted in light of Fuzzy-Trace Theory: whereas placebo participants benefited from repeated list presentation and were better able to discriminate between targets and lures, resulting in better verbatim (i.e., item-specific) memory, the opposite happened with triazolam, where intoxicated participants' verbatim processing seemed impaired, leading them to rely on gist-based memory. However, the findings from once-presented lists, indicate that normal memory functioning in the sense of semantic or gist extraction is impaired by triazolam. This is also in line with other studies reporting more global memory deficits of benzodiazepines and other $GABA_A$ positive allosteric modulators (Doss, Weafer, Ruiz, et al., 2018; Kamboj & Curran, 2006), and generally poor memory could also account for the increase in false alarms to unrelated lures that was detected with two of the tested benzodiazepines, as guessing might be increased. Triazolam also increased intrusions and false alarms in an episodic but non-false memory study (Mintzer & Griffiths, 2003b). It is interesting that despite their similar pharmacological effects, benzodiazepines seem to produce different memory patterns from alcohol: for instance, whereas the evidence thus far points to non-specific increases in false alarms under benzodiazepine influence, indicating more liberal responding, alcohol as well as alcohol placebo has often been found to increase conservative responding in memory tasks (Mintzer, 2007; Nadja Schreiber Compo et al., 2012). It has been put forward that benzodiazepines might be more sedative than alcohol and thus participants may also be less aware of the degree of drug effects (Mintzer & Griffiths, 2002; Roache et al., 1993). In contrast, conservative responding during alcohol and its placebo point to the importance of drug expectancies and compensating behaviors (M. A. Palmer et al., 2013), that might perhaps be more successful the more one is familiar with the substance in question, given that alcohol is usually what participants are most familiar with (Monds, Cullen, Kloft, van Golde, et al., 2020). In all of these studies, however, memory was tested shortly after encoding, so that intoxication was present during both encoding and retrieval and effects are not separable (however see Pernot-Marino et al., 2004 for a study on lorazepam on retrieval of autobiographical memories).

Cannabinoids

Δ-9-Tetrahydrocannabidiol

Cannabis can be classified as a depressant, hallucinogen, or stimulant. Its main psychoactive constituent Δ-9-Tetrahydrocannabidiol (THC) is a cannabinoid receptor agonist and well known for its memory-impairing effects (for a recent review see Broyd et al., 2016). However, the role of cannabis in relation to false memory production and suggestibility is less well elucidated. A handful of studies have investigated the link between DRM false memory and cannabis use. Ballard et al. (2012) administered THC (0. 7.5, and 15 mg) shortly before participants (N = 25, within-subjects) encoded DRM lists, whereas retrieval of the lists took place 48h later under sober conditions. Both true and false memory (the latter defined as false recognition of critical lures) were found to be statistically significantly reduced, but only when compared to a dextroamphetamine condition (a memory-enhancing drug, separate study thus between-subjects) and not the placebo condition. The inverse of this study design was employed by Doss, Weafer, Gallo, et al. (2018a), who had participants (N = 23, within-subjects) study DRM lists while sober and administered THC (15mg capsule) 48h later at retrieval. They found no statistically significant difference for correct recognition, but false alarms for both critical and unrelated lures were significantly increased compared to a placebo condition, indicating a cannabis-induced response bias. When hits and critical false alarms were adjusted for response bias, placebo participants outperformed intoxicated participants on true recognition, but adjusted false alarms did not differ between conditions. The fact that false alarms were also elevated in an emotional memory task, made with high confidence and increased subjective judgments of recollection, made the authors speculate that response bias alone does not account for the observed effects but that actual memory effects were at play. Together, these studies showed that different memory stages (encoding and retrieval) might be differentially affected by THC, and that people might be more vulnerable for false memories when intoxicated during retrieval rather than encoding.

In a recent field study conducted in Dutch coffeeshops (Kloft et al., 2019), three groups were subjected to the DRM procedure: intoxicated cannabis users, sober cannabis, and a non-using control group recruited at other public locations (N = 156, between-subjects). No differences between groups with regard to true recognition or false memory for critical lures was detected; however, both groups of cannabis users showed elevated susceptibility to false alarms in response

to new, semantically unrelated words. Although in this study retrieval took place shortly after encoding, it aligns well with findings by Doss et al. (2018), indicating that acute but also residual cannabis influence during retrieval elevates liberal responding. Using a modified DRM task version, Riba et al. (2015) also found increased susceptibility of abstinent but formerly heavy cannabis users to false memories in response to related lures, compared to healthy controls (n = 16 per group, between-subjects). Moreover, studies investigating acute effects of THC on word list tasks other than the DRM paradigm, with THC administered prior to encoding and retrieval shortly after, have detected an increase in intrusions (recalling non-presented items; e.g., Miller & Cornett, 1978; Miller et al., 1977; Pfefferbaum et al., 1977) and false alarms (recognition of non-presented items; e.g., Hart et al., 2010; Aaron B Ilan et al., 2004) in frequent as well as non-frequent users. Together, the evidence shows that THC at retrieval, not encoding, increases response or 'yes'-saying bias. The bias is most visible for unrelated items, thus is dependent on the strength of association between studied and tested items, and appears to be present not only with acute but also residual intoxication.

This interpretation of an association-dependent response bias was also supported by findings from a recent experimental study from our lab (Kloft et al., 2020). In a placebo-controlled study (N = 64, mixed design), cannabis was administered prior to encoding, with memory tested shortly thereafter while still intoxicated, and at a 1-week sober follow-up, using the DRM and misinformation paradigm. THC elevated the susceptibility to false memory in the DRM paradigm for related and unrelated lures, but did not affect critical lures or true recognition. At sober retrieval one week later, false memory for unrelated lures was still increased, while it was reduced for critical lures and true recognition. In the misinformation tasks, cannabis-intoxicated participants were more susceptible to false alarms in response to suggestive and non-suggestive questions about a virtual reality eyewitness scenario and virtual reality perpetrator scenario. The main effects observed in this study can be assumed to stem from THC affecting retrieval, and were not detected at 1-week follow-up, which has important implications for interviewing contexts. A drawback of this study is that the follow-up tests included some items that had previously been tested on the first memory test, thus potential testing effects (e.g., source confusion from initial memory test) cannot be differentiated from actual false memory effects.

A recent study also investigated the effects of THC given prior to encoding on context-dependent false memories, testing retrieval when sober 48 h later (N = 24, within-subjects, Doss et al., 2020). They found reductions in true memory for perceptual details of the objects studied, and that under some conditions, THC increased the context-based memory illusion. Specifically, when context was reinstated (e.g., visual beach scene) and was semantically congruent with the item (e.g., beach ball), THC increased false recognition of similar lure items (i.e., different beach ball). The reverse was however true when item and context were not congruent, in which case THC abolished context-based false memories. THC did not affect false recognition of dissimilar lures here, indicating that the response bias observed when tested sober in Kloft et al., (2019, 2020) may perhaps be specific to verbal stimuli.

In sum, there is evidence that acute cannabis but also residual use can increase false memory proneness and suggestibility, which seems to be driven largely by THC at retrieval elevating response bias but also increasing the potential for false memories when an event was experienced while intoxicated. For general studies on cannabis and eyewitness memory see Vredeveldt et al. (2018), Pezdek et al. (2020) and Yuille et al. (1998).

Stimulants

Moderate doses of stimulant drugs are known to enhance memory encoding and consolidation when present at the time of study (Ballard et al., 2015), but they may also fuel false memory formation in associative memory tasks such as the DRM. In the previously mentioned paper by Ballard et al. (2012), the stimulant dextroamphetamine when administered at encoding (n = 25, within-subjects) increased true recognition memory but also false memory for critical lures – although these effects were only apparent when compared to THC rather than a placebo condition. True and false memory in these analyses were corrected for response bias, and although analyses for how drug condition affected unrelated false alarms were not provided in the paper, it appears that dextroamphetamine at encoding numerically reduced response bias, while it did not consistently vary with THC (see Table 3 in Ballard et al., 2012). No other study has looked at effects of amphetamines or other classic stimulant drugs of abuse using a false memory task. However, in Ballard et al. (2014), dextroamphetamine administered at retrieval also increased false

recall and recognition rates in a word and a picture memory task, compared to placebo (N = 31, within-subjects). The increase in false recognition was accompanied by an increase in confidence in participants' responses, suggesting the presence of an actual memory illusion rather than a simple response bias. In addition, the world's most widely consumed CNS stimulant caffeine also increased both true recall and false recall of critical lures relative to placebo in the DRM paradigm, when administered prior to encoding with retrieval tested shortly after (N = 37, between-subjects; Capek & Guenther, 2009). Taken together these findings suggest that stimulants support both true and false memory, perhaps by supporting (healthy) associative activation or gist-based memory mechanisms.

3,4-methylenedioxymethamphetamine (MDMA) is a derivative of amphetamine and a potent indirect monoaminergic agonist, producing both release and reuptake inhibition of serotonin (5-HT) and to a lesser extent of dopamine (Vollenweider et al., 1998). It acts as both a stimulant and a hallucinogenic drug. In contrast to more traditional amphetamines, MDMA produces acute memory impairment, seemingly affecting both encoding and retrieval (Doss, Weafer, Gallo, et al., 2018b; Kuypers & Ramaekers, 2005), effects that seem to be mediated by its 5-HT_{2A} agonism (van Wel et al., 2011). Doss, Weafer, Gallo, et al. (2018b) administered MDMA (1mg/kg) either before encoding, retrieval, or placebo at both instances (n = 20 per group, between-subjects), to test effects in an emotional episodic memory picture task. MDMA at encoding did not affect hits but decreased recollection accuracy, indicating reduced encoding of salient visual details. They also reported a trend for MDMA at retrieval but not encoding to increase false rates alarm rates, especially for positive material (n = 20 per group, between-subjects).

The only study that tested how MDMA affects false memory formation using tasks specifically designed to induce false memories used the same design and method as the one by Kloft et al. with cannabis, described above (2020). In this study (Kloft, Otgaar, et al., submitted), MDMA reduced true recognition in the DRM, both when encoding and testing took place immediately during intoxication, as well as at 1-week sober follow-up. False memories for related lures, but not critical or unrelated lures, was increased by MDMA at the immediate test, providing some evidence of false memory susceptibility when MDMA affects retrieval. Similar to the authors' results with THC, MDMA slightly decreased false recognition of critical lures at the delayed test, likely due to their high similarity to studied items. In the two misinformation tasks,

MDMA did not reduce true memory or increase susceptibility to misinformation. Verbal memory tasks might be more sensitive to MDMA's memory-impairing effects than applied tasks, but more research on MDMA and suggestibility is warranted.

Hallucinogens

Dissociative drugs constitute a subclass of hallucinogens that distort sensory perception and induce feelings of detachment from the environment and self. Examples include ketamine (NMDA antagonist) and salvinorin A (a κ-opioid receptor agonist derived from the plant salvia divinorum), which have been found to interfere with true memory performance when administered before encoding (MacLean et al., 2013; Morgan & Curran, 2006). Similarly, the dissociative anaesthetic and NMDA antagonist nitrous oxide, better known as laughing gas, has been found to cause anterograde amnesia and heightened imaginative suggestibility during acute intoxication (Dwyer et al., 1992; Whalley & Brooks, 2009). Moreover, a study with the dissociative dextromethorphan (NMDA antagonist) and psilocybin (psychoactive ingredient of 'magic mushrooms/truffles', serotonin 2A receptor or 5-HT_{2A} agonist) indicated impairments of true memory (verbal recall) in response to both drugs (given before encoding and retrieval shortly after; Barrett et al., 2018). With the exception of the described substances, effects of hallucinogens on true memory ability as well as false memory and interrogative suggestibility are largely unexplored. However, several older studies as well as one recent study provide evidence that classic psychedelics (i.e., 5-HT_{2A} agonists), including lysergic acid diethylamide (LSD), psilocybin, and mescaline may induce heightened states of suggestibility, using tests of primary suggestibility such as imaginative procedures (Carhart-Harris et al., 2015; Middlefell, 1967; Sjoberg & Hollister, 1965). It is worth noting that classic psychedelics but also MDMA have been observed to increase mental visual imagery or vividness of memory (e.g., Carhart-Harris et al., 2012; Carhart-Harris et al., 2014; de Araujo et al., 2012). Mental imagery has been associated with enhanced false memory (e.g., Dobson & Markham, 1993; Hyman & Pentland, 1996; Roberts, 2002). Considering this together with the fact that psychedelic psychotherapy is currently experiencing a renaissance (e.g., Johnson et al., 2019), this gap in memory research is striking and both basic and applied studies on true and false memory are warranted.

Anticholinergic drugs ('deliriants') are muscarinic acetylcholine receptor antagonists, which also fall under hallucinogens. The anticholinergic scopolamine seems to produce similar patterns of true memory impairment as benzodiazepines (Mintzer & Griffiths, 2003a). In Mintzer and Griffiths (2001a), scopolamine produced dose-related decreases in both DRM true and critical false alarm rates, but had no effect on unrelated words (N = 18, within-subjects). These results were interpreted as scopolamine impairing both verbatim and gist memory, but not elevating response bias.

Antipsychotics

Antipsychotics do not fall under any of the previous major drug classifications but rather constitute a class in itself. Although not drugs of abuse, their effect on false memory formation might contribute to understanding mechanisms behind drugs and false memory. They tend to produce profound sedation and disrupt cognitive function, including memory (Ramaekers, 1998). One placebo-controlled study (N = 24, between-subjects) investigated effects of sulpiride, a dopamine D2-receptor antagonist and atypical antipsychotic, on true and false memory in a verbal and a visual DRM task, using both emotional and neutral stimuli (Guarnieri et al., 2016). Sulpiride (400 mg) was administered prior to encoding with memory tested shortly after (N = 24, between-subjects). The substance did not affect true memory but increased false recognition of related lures in both tasks and also increased false recognition of unrelated lures on the verbal DRM task. However, increased false recognition was only found for emotionally charged items (positive and negative) and not neutral ones. Similar results were found in a study with a different antipsychotic and D_2 antagonist – haloperidol (4 mg, N = 24, between-subjects, administration prior to encoding with memory tested shortly after; Guarnieri et al., 2017). True recognition was not affected by haloperidol but false recognition of related lures was increased, although in this study the DRM visual task only was employed, and the analyses did not distinguish between emotional and neutral content. These results suggest that a fully functional, D_2-mediated, dopaminergic system is important to enable correct discrimination between truly experienced events from similar, but novel, ones (Guarnieri et al., 2019); an effect that seems to go beyond simple elevation of a response bias. It should be noted that acute low doses of D_2 antagonists (e.g., as in Guarnieri et al., 2017) are assumed to preferably block presynaptic D_2-autoreceptors, leading to an increase in

phasic dopamine release [see also relevant work by Clos et al. (2019a, 2019b) on low-dose haloperidol and episodic memory and meta-cognition in non-false memory tasks].

Discussion

The reviewed studies indicate that in general, psychoactive drugs may influence false memory formation and suggestibility, but these effects vary with the studied substance and depend on which memory stage is in focus. The best-studied substances appear to be alcohol and cannabis, which seems promising because they are also the most widespread on a global scale (e.g., United Nations Office on Drugs and Crime, 2018). Using multiple false memory and suggestibility paradigms, the reviewed studies demonstrated that under certain circumstances, both alcohol and cannabis can impact the susceptibility to spontaneous and suggestion-based false memory or suggestibility, often exerting effects of medium or large size (see Table 2 for an overview). An important caveat here however is that often substances, especially cannabis, were also found to elevate response bias, which can result in inflated false memory rates, even though memory processes might not underlie these effects. For alcohol, moderate levels of intoxication during an event were not associated with increased spontaneous and suggestion-based false memory or suggestibility during an immediate memory test, but suggestibility was increased at higher levels (studies by van Oorsouw et al., 2015, 2019) and sometimes after a delay (Evans et al., 2019). In contrast, cannabis was most detrimental when memory was tested under intoxicated conditions, with cannabis during retrieval robustly increasing response bias (yes-saying, Doss et al., 2018b; Kloft et al., 2019, 2020). However, the evidence reviewed here on how specifically different substances affect false memory is characterized by substantial inconsistencies. This is most certainly due to the fact that in the vast majority of reviewed studies, participants were intoxicated during both encoding and retrieval, whereas some studies that separated these memory phases have shown that they might be differentially affected. Given that individuals involved in crime can be intoxicated either during the encoding of an event (e.g., witnessing a crime), retrieval (being questioned about the event), or both, the importance of studies investigating all of these possibilities is highlighted.

As for the theories introduced in this paper to account for false memory production, there is evidence that particularly the *discrepancy-detection principle* can help explain vulnerability to suggestion in response to alcohol (Evans et al., 2019; van Oorsouw et al., 2019). A poorer memory for an event experienced while alcohol-intoxicated, combined with a delay before questioning, elicits difficulties in detecting discrepancies between one's memory and suggested information,

making an individual more vulnerable to yield to suggestive cues. Apart from this, the presented studies do sometimes refer to but have not always explicitly tested these theoretical accounts (e.g., Ballard et al., 2012; Guarnieri et al., 2016; Kloft et al., 2019).

Interestingly, while cannabis and alcohol's effects were found to differ in terms of suggestion-based false memory/suggestibility, effects on DRM false memories were more comparable: in those studies where encoding took place while intoxicated but retrieval was sober, both alcohol and cannabis resulted in reduced false memory rates for critical lures (Ballard et al., 2012; Garfinkel et al., 2006; Kloft et al., 2020). This is in line with our prediction that amnesia-producing drugs might indirectly reduce associative activation or gist extraction during encoding, resulting in reduced associative/gist false memory later, thus providing partial support for AAT and FTT. An important point here is that alcohol appears to have no effect on automatic semantic activation (measured via a semantic priming task, Ray et al., 2004), and cannabis enhances semantic activation and fluency (Morgan et al., 2010; Schafer et al., 2012), thus perhaps leaving associative activation mechanisms intact (or even over-activated in case of cannabis). However, encoding of individual words is impaired by these substances and therefore also the conscious encoding of words they activate. In this respect it is also noteworthy that while alcohol has been observed as inducing a conservative response bias (Mintzer, 2007; Mintzer & Griffiths, 2001b), both acute and residual cannabis use has been linked to liberal responding perhaps stemming from loosened or irrelevant associations (Kloft et al., 2019, 2020; Riba et al., 2015). The fact that cannabis during retrieval induced the highest rates of false memories is difficult to reconcile by the main tenets of AAT and FTT, since both assume that false memories are primarily caused at encoding (e.g., Gallo, 2010). Although it is possible that during retrieval being confronted with targets might cause, for example, associative (re)activation of the lists, a framework with an explicit monitoring component such as the Activation/Monitoring Theory (AMT) might be better suited to account for the findings (e.g., Roediger, Watson, et al., 2001). Monitoring refers to the decision process that helps to determine the source of the activated information to discriminate studied from unstudied material, a process that is a direct reflection of conservative or liberal retrieval criteria, or in other words response bias. Furthermore from a theoretical perspective, as discussed above additional theories relating specifically to alcohol and memory have been developed; thus, it could be worth exploring whether *State-Dependent Retrieval,* substance *Myopia* or *Hypervigilance* accounts can inform understanding of the mechanisms behind any memory

effects for other substances. Exploring mechanisms and theoretical explanations thus is an important future direction for how drugs might impact memory errors.

Overall, substance effects on false memory have not been studied in sufficient depth. More sufficiently powered studies separating encoding and retrieval phases are needed, both on the substances reviewed here but also on other popular substances where false memory studies are entirely lacking (e.g., cocaine, hallucinogens, opioids). In addition, the types of information (e.g., scene, object, conceptual, perceptual) presented at both encoding and retrieval (and in between) matter if we are to further our understanding about the mechanisms underlying false memories, as well as which mechanisms drugs can affect. To move the field forward, tasks which carefully manipulate these types of information should be developed. Future research also needs to monitor societal drug trends, for example drug-drug combinations or microdosing psychedelics, which are prevalent (e.g., Hutten et al., 2019; Morley et al., 2015) but no false memory studies have investigated these trends and often, true memory has not been well-elucidated either. In light of recent advancements regarding therapeutic applications of hallucinogens (e.g., ketamine and classic psychedelics for treatment-resistant depression, addiction, end of life anxiety, MDMA for post-traumatic stress disorder, Johnson et al., 2019; Reiff et al., 2020), we stress that the potential to affect false memory and suggestibility is also a research topic worth pursuing from a clinical point of view.

Apart from alcohol and cannabis, the other substances were mostly studied using the DRM (verbal or visual) or other word list tasks. Though frequently criticized for its limited ecological validity, increased false memories on DRM measures have been linked to false childhood memories (Qin et al., 2008), memories of alien abductions (Clancy et al., 2002), and memories of past lives (Meyersburg et al., 2009) indicating that the task does bear some applied relevance. Nevertheless, it would be interesting to examine these substances with applied eyewitness and perpetrator memory tasks as well, particularly since DRM false memories are only weakly related to false memories on other tasks (e.g., Bernstein et al., 2018). A suggestion for a new direction to increase ecological validity of studies is to pursue virtual reality applications (e.g., Kloft et al., 2020). Virtual reality (VR) is a simulated experience that can be highly similar to the real world, incorporating auditory and visual feedback, but may also allow other types of sensory feedback through haptic technology. Benefits include a maximum of experimental control and thus internal

validity, combined with high degrees of realism (see also van Gelder et al., 2014). Moreover, participants report high degrees of telepresence, feeling fully immersed in the simulation. Technological advances in the VR field make this a fast-developing and attractive alternative to more traditional research methods such as case-vignettes or videos.

Another important factor to consider in terms of ecological validity is the fact that most crimes are distressing in nature, and memory for emotional events tends to be generally superior compared to neutral events (Hamann, 2001). Drugs can influence and selectively interact with mood and emotion (e.g., de Sousa Fernandes Perna et al., 2014), and emotion interacts with false memory (e.g., Chang et al., 2020), therefore drugs that affect emotion can modulate both true and false memory for emotional events (e.g., Ballard et al., 2013; Kamboj & Curran, 2006). Although not the main focus of this review, some of the described studies reported notable findings in this regard: for example, THC, dextroamphetamine, and MDMA all tended to disproportionately increase positive false memories (Ballard et al., 2014; Doss, Weafer, Gallo, et al., 2018a, 2018b). There may also be interactions between the substance consumed and the physiological stress response (e.g., norepinephrine, cortisol, heart rate variability) that could impact encoding and retrieval. How interactions between drug, emotional arousal, and stress might affect memory in a forensic context could be explored further in future studies. Finally, with the exception of three perpetrator memory studies (Kloft et al., 2020; Kloft, Otgaar, et al., submitted; van Oorsouw et al., 2015), applied research has focused on eyewitness memory perspectives. Knowing that psychoactive drugs can affect false memory and suggestibility, it appears pertinent to explore if this might also translate to increasing vulnerability to false confessions, a leading contributing cause to wrongful convictions (Leo, 2009).

Moreover, in the current review it was established through a combination of different sources of evidence that intoxication on part of the victim, witness or suspect is common. Whereas overall prevalence of legal cases involving substance use was found to range between 1.2-4.3%, the incidence in violent crime cases tended to be much higher. The prevalence of intoxicated suspects was found to range from 25-78% for alcohol and from 10-83% for illicit drugs, and for victims from 24-72% for alcohol and 3-66% for other drugs. Intoxicated eyewitnesses were also frequently reported by police officers, but specific numbers were mostly lacking (with the exception of F. T. Palmer et al., 2013). The fact that intoxication in criminal cases is frequent

entails several legal repercussions. As highlighted in this review, the validity and reliability of the intoxicated person might be at stake, due to potentially higher risk of memory distortion. To what extent this is the case still remains to be elucidated for multiple substances. An issue preceding the obtaining of a statement, however, is the initial detection of an intoxicated individual: while suspects of crime are regularly alcohol and/or drug tested (especially in situations involving driving), witnesses and victims of crime generally are not. As a consequence, unless this information is volunteered by the witness or victim, their intoxication status may not be known or recorded. The current research available suggests that in the absence of this admission, police may not always be able to accurately detect intoxication (see Monds, Quilter, et al., 2019 for a review). Therefore, further research is also required into improving police ability to determine whether a substance has been recently consumed that may impair the ability to provide an accurate testimony.

Second, although police officers might be aware of the risks of interviewing intoxicated witnesses, in many countries (e.g., UK, United States, Netherlands) there is no clear protocol on how to handle such situations, and when to interview an intoxicated witness (Crossland et al., 2018; Evans et al., 2019; Evans et al., 2009; van Oorsouw & Merckelbach, 2012). Evidence-based policies are required to inform and reform such practices. Research up to this point has already provided some preliminary indication that substances can distort memory, and that differences exist between substances in terms of how memory is specifically affected. Important to point out here is the difference between alcohol and cannabis with regard to timing of the interview: alcohol-intoxicated individuals might not provide less accurate information when interviewed in an intoxicated state, but if someone is intoxicated with cannabis they might be more prone to false reporting in an immediate interview (Evans et al., 2019; Kloft et al., 2020; van Oorsouw et al., 2019). Therefore, a nuanced approach is clearly needed in how to deal with intoxicated witnesses, victims, and suspects, taking into account factors such as the used substance, dose, and which memory phase was affected. Intoxicated individuals should be recognized and treated as a vulnerable group, for which extra caution should be taken, but they should not be lumped together.

Another important aspect is that of perceptions about the reliability of intoxicated individuals on the part of potential legal jurors and police officers. One study found that ninety percent of psychology and law experts agree that alcohol impairs eyewitness memory (Kassin et al., 2001). Other studies have found that potential jurors also agree with expert witness views

regarding alcohol and memory (Benton, Ross, Bradshaw, Thomas, & Bradshaw, 2006), and that they perceive intoxicated witnesses and suspects to be more cognitively impaired than sober ones (Evans & Schreiber Compo, 2010; Mindthoff et al., 2019). While these views are certainly correct with regard to alcohol's robust impairing effects of true memory when present during encoding, the literature reviewed here showed that these matters are highly nuanced and complicated when it comes to false memory and suggestibility. It is crucial to inform legal professionals about different substances' potential memory effects and to consult appropriate expert witnesses to aid during the legal decision-making process.

Some limitations should be mentioned. For the first part of our review, countries were selected for practical reasons, such as that their legal databases were relatively easily accessible. A drawback of the numbers obtained from official legal databases is that while substance use played a role in the offense, this might refer simply to the type of offense (e.g., drug possession), and does not mean that an involved person was actually intoxicated during the crime. However, it still provides an indication of the link between intoxication and crime. Relatedly, some of the numbers were based on estimates by police or witnesses. While an important first step in determining the prevalence of intoxicated victims and witnesses, the self-report nature of these estimates may be influenced by memory errors and biases. Finally, both review parts in this article are not meant to be exhaustive, but to provide a starting point. Thus, it is possible that other relevant data exists but has not been reported here.

To recap, the current paper aimed at a) establishing an overview of the prevalence of intoxicated individuals involved in legal cases, and b) a review of the current state of literature with regard to psychoactive substances and their effects on false memory production and suggestibility. Overall, intoxication and legal cases were found to frequently co-occur. Given the high prevalence identified in the first review part of this paper, it is evident that intoxication needs to be taken seriously as a factor that might affect testimony across the globe. Based on the second prong, there is emerging evidence that psychoactive substances can affect false memory and suggestibility in some circumstances, however the research is still in its infancy regarding the specific circumstances, especially for less commonly used substances.

Table 1

Intoxication and crime prevalence findings by country in alphabetical order

Country	Source/Type of data	Who was intoxicated	Findings/prevalence in %	Reference
Australia				
	Professional case law database "LexisNexis"	Unknown	2.1% of case reports involve alcohol/drug influence/intoxication	https://www.lexisnexis.com
	Drug use monitoring in Australia (DUMA) program - urinalysis	Police detainees	75% positive for at least one drug type, 40% for >1 drug type[a]	Patterson et al., 2018
	Toxicology reports	"King hit" fatality victims	79% positive for substances (73% alcohol, 15% other drug)	Pilgrim, Gerostamoulos, & Drummer, 2014
	Toxicology reports	Homicide victims	63% positive for substances (42% alcohol, 33% illicit drug, 25% multiple)	Darke & Duflou, 2008
	Police records and state coronial records[b]	Homicide victims	32% alcohol, 26% illicit drug use	Bryant & Bricknell, 2017
		Homicide offenders	28% alcohol, 16% illicit drug use	
	Police log data	Unknown (police-attended incidents)	23% alcohol-related, 2% drug related, 1% alcohol and drugs	Palk, Davey, & Freeman, 2007
	Police survey data	Person interacting with police	59% of police officers report daily/more than weekly interactions	Monds et al., submitted
Indonesia				
	National legal database	Unknown	1.2% of court rulings are drug related	https://putusan.mahkamahagung.go.id/
	Police survey data	Person interacting with police	24% of police officers report daily/more than weekly interactions	Monds et al., submitted

Netherlands				
	National legal database "De Rechtspraak"	Unknown	2.0% of court cases with a verdict involve alcohol or drug influence	https://www.rechtspraak.nl/
		Violent offenders	75% intoxicated with alcohol and/or drugs	CVV, 2011
		Violent offenders	37-78% intoxicated with alcohol	van Laar & van Gestel, 2018
England + Wales				
	National legal database "BAILII"	Unknown	2.4% of case law rulings involve alcohol or drug intoxication	https://www.bailii.org/
	Crime Survey for England and Wales (CSEW)			
	Police-recorded data	Homicide suspects	25% alcohol, 10% illicit drugs, 4% both	Office for National Statistics, 2016; 2017
		Homicide victims	24% alcohol, 3% illicit drugs, 7% both	
	Victim data	Offenders	40% alcohol, 19% drugs	
	Police survey data	Witnesses	82% of police officers say it is a common occurrence (alcohol)	Crossland, Kneller, & Wilcock, 2018
US				
	Professional case law database "LexisNexis"	Unknown	2.1% of case reports involve alcohol/drug influence/intoxication	https://www.lexisnexis.com
	Arrestee Drug Abuse Monitoring (ADAM)	Arrestees	63-83% drug positive across jurisdictions	Hunt et al., 2014
	Police survey data	Victims/witnesses	73% say it is common/very common	Evans, Schreiber Compo, & Russano, 2009
		Suspects	83% say it is common/very common	
	Archival court files (testimonies)	Eyewitnesses	13% intoxicated during crime with alcohol or other drug	Palmer et al., 2013

	Suspects	28% intoxicated during crime with alcohol or other drug	
Survey	Rape victims (college women)	72% alcohol-intoxicated during assault	Mohler-Kuo et al., 2004
Survey	Violence victims (college students)	63-74% consumed alcohol and/or other drugs	Bureau of Justice Statistics, 2005
Review	Sexual assault victims/perpetrators	~50% of cases occur when either or both drank alcohol	Abbey et al., 2014
Toxicology reports	Sexual assault victims[c]	78% positive for any substance (31% alcohol, 66% other drugs)	Fiorentin & Logan, 2019
Toxicology reports	Homicide victims	59% positive: 30% alcohol, 28% cocaine, 19% cannabis, 11% opiates	Tardiff et al., 2005

Note.

[a] Urine sample taken within 48h of detention.

[b]Data includes victim toxicology reports but usually lacks toxicological confirmation for offenders.

[c]Suspected drug-facilitated sexual assault cases only.

Table 2

Summary of reviewed false memory and suggestibility studies organized by substance

Sample size + design	Dose	Paradigm	Memory stage affected/tested	Primary finding regarding false memory/suggestibility	Effect size[a]		Reference
			Alcohol (depressant)				
N = 32, between-subjects	0.6 g/kg	DRM (implicit + explicit recall)	Alcohol/placebo at encoding, retrieval sober	Reduced false memory rates for once presented lists (false explicit recall); no effect on implicit false memory	d = 1.04[b]	(large)	Garfinkel, Dienes, & Duka, 2006
N = 20, within-subjects	0.26-0.28 g/kg	DRM (recall and recognition)	Alcohol/placebo at encoding + retrieval	No effect		–	Milani and Curran, 2000
N = 18, within-subjects	0.27 and 0.60 g/kg	DRM (recognition)	Alcohol/placebo at encoding + retrieval	No effect		–	Mintzer and Griffiths, 2001b
N = 83, between-subjects	*m*BAC 0.065%	Misinformation (presented via written narrative)	Encoding + retrieval while sober, alcohol/reverse placebo/control after encoding but before misinformation	Alcohol protected against misinformation (retrograde facilitation)	η^2_p = 0.09	(medium)	Gawrylowicz et al., 2017
N = 51, between-subjects	high: 1.32ml/kg, medium: .66ml/kg, low: .132ml/kg, placebo (using 95% alcohol)	Gudjonsson Suggestibility Scales	Encoding + immediate recall while sober, alcohol/ placebo before suggestive pressure and delayed recall	Alcohol decreased yielding to leading questions (potential retrograde facilitation) but had no effect on shifting responses after pressure	unknown		Santtila et al., 1999
N = 93, between-subjects	*m*BrAC 0.07%	Misinformation (presented via experimenter phone call)	Alcohol/placebo/control at encoding + retrieval	No effect		–	Schreiber Compo et al., 2012

N = 210, between-subjects	BrAC 0.06-0.08%	Misinformation (pre-circled answers by alleged co-witness)	Immediate: alcohol/placebo/control at encoding + retrieval Delayed: 3x3 counterbalanced conditions	Alcohol increased suggestibility in the delayed but not immediate condition; alcohol at encoding but not retrieval heightened suggestibility	η^2_p = 0.08, η^2_p = 0.13	(medium/ medium - large)	Evans et al., 2019
N = 80, between-subjects	*m*BAC 0.06%	Misinformation (narrative by alleged previous participant)	Alcohol/sober at encoding (counterbalanced with expectancy), misinformation + retrieval sober	No effect		–	Flowe et al., 2019
N = 67, between-subjects	*m*BAC 0.01-0.16%	Suggestive questioning	Alcohol (high/moderate/low) at encoding + immediate retrieval, delayed sober retrieval	High intoxication levels increased suggestibility at immediate and delayed retrieval	η^2_p = 0.12	(medium - large)	van Oorsouw, Merckelbach, & Smeets, 2015
n = 86 + *n* = 189, continuous design	BAC 0.00-0.16%, and BAC 0.00-0.20%	Misinformation (false alternative, leading, + affirmative questions)	Alcohol at encoding + immediate retrieval, delayed sober retrieval	Misinformation acceptance increased with rising intoxication levels but mixed findings regarding time of testing	unknown		van Oorsouw, Broers, & Sauerland, 2019
			THC (depressant/ stimulant/ hallucinogen)				
n = 25[c], within-subjects	0, 7.5, and 15 mg	DRM (recognition)	THC at encoding, retrieval sober 48h later	THC reduced false memory compared to dextroamphetamine but not placebo	η^2_p = 0.23	(large)	Ballard, Gallo, & de Wit, 2012
N = 23, within-subjects	0 and 15 mg	DRM (recognition)	Encoding sober, THC at retrieval 48h later	THC increased false memory compared to placebo	η^2_p = 0.36	(large)	Doss, Weafer, Gallo, & de Wit, 2018b
N = 156, between-subjects	self-determined (field study)	DRM (recognition)	Intoxicated/sober/control at encoding + retrieval	Higher false memory for unrelated but not critical lures in intoxicated and sober	η^2_p = 0.11	(medium - large)	Kloft et al., 2019

				cannabis users, compared to controls			
N = 32, between-subjects	–	DRM (modified; recognition)	Not applicable	Higher false memory rates in abstinent heavy users compared to controls	*d* = 0.79[b]	(medium - large)	Riba et al., 2015
N = 64, within-subjects	300 μg THC/kg	DRM (recognition)	THC at encoding + immediate retrieval, delayed retrieval sober	Immediate: THC increased false memory (related + unrelated); Delayed: THC increased unrelated but decreased critical lure false memory	*d* = 0.58 + 1.0; *d* = 0.38 + 0.27	(medium, large; small)	Kloft et al., 2020
N = 64, between-subjects		Misinformation (2 virtual reality scenarios, suggestive co-witness + suggestive questioning)		Immediate: THC increased several measures of false memory; Delayed: No effect	*d* = 0.54 - 0.86	(medium - large)	
N = 24, within-subjects	0 and 15 mg	Context reinstatement mnemonic similarity task (*MS-Doss*, recognition)	THC at encoding, retrieval sober 48h later	THC increased context-based false memories when item and context were semantically congruent	*d* = 1.34	(large)	Doss et al., 2020
			Stimulants				
n = 25[c], within-subjects	0, 10, and 20 mg dextroamphetamine (AMP)	DRM (recognition)	AMP at encoding, retrieval sober 48h later	AMP increased false memory compared to THC but not placebo	η^2_p = 0.23	(large)	Ballard, Gallo, & de Wit, 2012

N = 64, within-subjects	0 and 75 mg MDMA	DRM (recognition)	MDMA at encoding + immediate retrieval, delayed retrieval sober	Immediate: MDMA increased false memory (related lures only); Delayed: MDMA decreased critical lure false memory	*d* = 0.42; *d* = 0.30	(small)	Kloft et al., submitted
N = 64, between-subjects		Misinformation (2 virtual reality scenarios, suggestive co-witness + suggestive questioning)		Immediate: No effect; Delayed: reduced suggestion-based false memory in eyewitness condition	*d* = 0.77	(medium - large)	
			Benzodiazepines/ anticholinergics (depressants)				
N = 36, between-subjects	diazepam 0.3 mg/kg or lorazepam 0.038 mg/kg	DRM (recognition)	Diazepam/lorazepam/placebo at encoding + retrieval	Benzodiazepines had no effect on false memory of critical lures but lorazepam elevated fale memory of unrelated lures	unknown		Huron et al., 2001
N = 24, within-subjects	0.125 and 0.25 mg/70 kg	DRM (recognition)	Triazolam (high/low)/placebo at encoding + retrieval	Triazolam produced dose-related decreases in false memory of critical lures, but increased false memory of unrelated lures	unknown		Mintzer & Griffiths, 2000
n = 18 + *n* =18, within-subjects	0.25 mg/70 kg triazolam	DRM (recognition)	Triazolam/placebo at encoding + retrieval	Repeated lists increased false memory for triazolam but decreased for placebo; shorter lists reduced false memory in both conditions	unknown		Mintzer & Griffiths, 2001c
N = 24, within-subjects	0.3 and 0.6 mg/70 kg scopolamine	DRM (recognition)	Scopolamine (high/low)/placebo at encoding + retrieval	Scopolamine produced dose-related reductions in false memory (critical lures)	unknown		Mintzer & Griffiths, 2001a

Antipsychotics

N = 24, between-subjects	400 mg sulpiride	DRM (verbal + visual stimuli, recognition)	Sulpiride/placebo at encoding + retrieval	Sulpiride increased false memory of related and unrelated lures in the verbal DRM, and of related lures in the visual DRM	η^2_p = 0.16[d]	(medium - large)	Guarnieri et al., 2016
N = 24, between-subjects	4 mg haloperidol	DRM (visual, recognition)	Haloperidol/placebo at encoding + retrieval	Haloperidol increased false memory of related lures	$\eta 2$ = 0.38[b]	(large)	Guarnieri et al., 2017

Note.

[a] Original effect sizes included from articles where possible. Interpretation based on Lenhard and Lenhard (2016).

[b] Effect size calculated based on data in paper using Lenhard and Lenhard (2016).

[c] Separate studies but between-subjects analyses are reported so total *N* = 50.

[d] Effect size only available for verbal DRM (3-way interaction).

Chapter 3

False memory formation in cannabis users: A field study

Published as:

Kloft, L., Otgaar, H., Blokland, A., Garbaciak, A., Monds, L. A., & Ramaekers, J. G. (2019). False memory formation in cannabis users: a field study. *Psychopharmacology*, 1-12. doi:10.1007/s00213-019-05309-w

Abstract

Rationale: Cannabis use is widespread and has previously been associated with memory impairments. However, the role of cannabis in relation to false memory production, i.e., memories of events that were not experienced, is less well-understood.

Objective: The aim of the current field study was to examine the impact of cannabis use on false memory production.

Methods: The Deese/Roediger-McDermott (DRM) paradigm was used to induce false memories. In this paradigm, participants study word lists that are associatively related to a non-presented word, termed the *critical lure*. In a later memory test, true recognition rates and false alarm rates toward critical lures and unrelated items are assessed. Memory performance was compared between three groups: Regular cannabis consumers who were acutely intoxicated (n = 53), regular cannabis consumers who were sober (n = 50), and cannabis-naïve controls (n = 53). The participants were approached in Dutch coffeeshops (cannabis outlets) and cafes and asked to participate in our study. After collecting general information on their cannabis use, they were subjected to the DRM procedure.

Results: Although false memory rates for critical lures did not statistically differ between groups, both intoxicated and sober cannabis consumers falsely recognized more unrelated items than control participants. Also, individuals without a history of cannabis use demonstrated higher memory accuracy compared to the intoxicated group.

Conclusion: It is concluded that cannabis intoxication and history of cannabis use induce a liberal response criterion for newly presented words for which the level of association with previously learned words is low and uncertainty is high.

Introduction

Cannabis is the world's most widely used 'illicit' drug, with an estimated global prevalence of 2.7 - 4.9 percent and a lifetime-use of 78 percent (United Nation Office on Drugs and Crime, 2017; Winstock et al., 2017). Given the recent legalization of recreational (e.g., Canada; Denny & Shumaker, 2018) and medical (e.g., Australia; Thomsen, 2016) use of cannabis in several countries, as well as advances in technologies to deliver cannabis in less harmful ways, the way is being paved for increased cannabis consumption in the Western world. In comparison to alcohol and tobacco, cannabis has been ranked low on physical harm, dependency, and social harm (van Amsterdam et al., 2015). Although cannabis appears to have potential for medical use such as pain relief (Urits et al., 2019), cannabis may also induce cognitive impairment, particularly in the domain of memory (Broyd et al., 2016). A lack of knowledge exists, however, about the impact of cannabis on the formation of false memories (remembrance of events/details that were not experienced; Loftus, 2016; Otgaar, Howe, et al., 2016).

Cannabis use has been associated with memory impairments both during acute intoxication (Ranganathan & D'Souza, 2006) as well as during abstinence in long-term users (Solowij & Battisti, 2008). According to the majority of the research on this topic, cannabis use appears to primarily impair memory in the domains of verbal learning and declarative memory (Broyd et al., 2016; Schoeler & Bhattacharyya, 2013; Theunissen et al., 2015). That is, the primary active cannabinoid tetrahydrocannabidiol (THC) acutely elicits reliable, dose-dependent impairments in immediate and delayed verbal memory performance, most often measured using word list learning tasks testing both recall and recognition memory (although recognition memory is less consistently affected; e.g., Broyd et al., 2016; Hart et al., 2010).

Specifically, research has shown that acutely intoxicated participants recall fewer studied items compared to sober participants, a deficit which cannot be accounted for by cannabis induced disruption of attentional processes (Ranganathan & D'Souza, 2006). Such memory impairment has been found to persist in the unintoxicated state in long-term users, although some studies have also reported improvement or recovery of memory functioning after a period of abstinence (see Broyd et al., 2016). However, interpretation of findings is often complicated by confounding factors such as frequency and duration of use, and differences across studies in terms of route of administration, sample size, and variations in cannabis strains in terms of the percentage of THC and cannabidiol (CBD) content and dosage (e.g., Ranganathan & D'Souza, 2006).

While declarative memory impairments are a well-known consequence of cannabis use, an under-investigated avenue is the possibility of cannabis impacting false memory formation (memories for non-experienced events). A robust and reliable way to experimentally create false memories is by using the Deese/Roediger-McDermott (DRM) paradigm, in which lists of associatively related words are presented during encoding (e.g., *bed, dream, wake, rest, tired*) in which one highly related theme word (the "critical lure": *sleep*) is not presented (Deese, 1959; Roediger & McDermott, 1995). Research shows that critical lures are often incorrectly recalled or recognized as having been presented before, thereby forming false memories, and acceptance rates for critical lures are often as high as acceptance rates for presented items (Brainerd et al., 2008; Reyna & Lloyd, 1997).

Previous research on false memories and cannabis using the DRM paradigm is limited and has produced mixed results. Ballard and colleagues (2012) investigated effects of THC (0, 7.5, and 15 mg capsules) at encoding on DRM true and false recognition performance 48 h later and found that THC impaired true recognition memory at both doses. False memory was not affected compared to placebo but was reduced compared to a memory-enhancing drug (dextroamphetamine; AMP) condition. Moreover, drug effects on true and false memory were positively correlated. In contrast, in a more recent study from the same lab (Doss, Weafer, Gallo, et al., 2018a) encoding took place under sober conditions while retrieval 48 h later occurred during intoxication. They found that selectively administering THC (15mg capsule) during memory retrieval increased false recollection. Together these studies indicate that THC might affect encoding and retrieval differentially.

The relationship between cannabis and false memories was further investigated by Riba et al. (2015) in abstinent cannabis users. Daily cannabis consumers (n = 16), who were abstinent for 4 weeks, were compared to a matched cannabis-naïve control group. While no statistically significant difference between groups in true memory performance was found, abstinent cannabis users showed an increased susceptibility to false memory formation. However, these studies have limitations in that they do not provide any information on the acute effects of individually determined doses of smoked THC on false memory production.

Several studies investigating acute effects of THC on word list tasks other than the DRM paradigm have reported an increase in intrusions (recalling non-presented items; e.g., Miller & Cornett, 1978; Miller et al., 1977; Pfefferbaum et al., 1977) and false alarms (recognition of non-

presented items; e.g., Hart et al., 2010; A. B. Ilan et al., 2004) in frequent as well as non-frequent users. This indicates that intoxicated individuals might display an increased tendency to recall items that were never presented to them.

Investigating the possibility of cannabis use leading to false memories may be of particular relevance in legal or forensic contexts. Individuals who use cannabis may be involved in legal cases as witnesses or suspects where they have to provide accurate accounts of events. To date, two studies examining the acute effects of cannabis on eyewitness memory (e.g., memory for a crime film or staged crime) have been conducted (Vredeveldt et al., 2018; Yuille & Tollestrup, 1990). These studies did not find that cannabis intoxication led to a higher rate of incorrect recall. While both studies assessed the impact of cannabis on true memory recall, including a measure of incorrect details, neither study assessed the sensitivity of cannabis users for false memory production. A study that directly manipulates false memory such as through use of the DRM paradigm can better address the question whether cannabis use heightens the susceptibility to false memory.

The present study was designed to assess the impact of cannabis intoxication or recent use on false memory production with a classical DRM paradigm in a real-life field setting. Dutch regulations permit the presence of cannabis outlets ("coffeeshops"), alcohol-free establishments in which adults (18+) under certain conditions can buy and consume cannabis, creating a unique setting for the investigation of cannabis use (Niesink et al., 2015). The present study included three groups: regular cannabis users under acute influence, sober regular cannabis users, and sober controls with limited lifetime cannabis exposure. Memory performance of these groups was compared in order to assess immediate and residual effects of cannabis use, relative to controls. Based on previous findings (e.g., Riba et al., 2015), we predicted false memory performance to differ between all three groups. Specifically, acutely intoxicated users were expected to exhibit highest rates of false recognition compared to the other two groups, but given potential residual effects, sober users were also expected to show impairment. It was anticipated that the control group would exhibit low rates of false recognition.

Method

Participants

An a priori power analysis was conducted using G*Power (Faul et al., 2007), with an expected medium effect size (Cohen's d = .5), a power level of 80% and an alpha of .05, resulting in a required total sample size of N = 159. The present sample (N = 159) included 53 cannabis users under acute influence of cannabis (46 males, 6 females), 53 sober but regular cannabis users (45 males, 8 females), and 53 controls (20 males, 33 females). After reviewing the data, three participants of the sober group were excluded from the analyses due to exceeding the age limit (n = 1) or indicating that they had in fact consumed cannabis (n = 2), resulting in n = 50 for this group. Common inclusion criteria for all groups were: Age between 18-30 years old, being comfortable with taking the study in English, and no alcohol consumption on the day of the experiment. Specific inclusion criteria for the cannabis intoxication group were: acute intoxication (having smoked cannabis no longer than 60 min prior to memory testing), orientation in space and time (naming the day and place, and solving a simple math problem), and regular use of cannabis (at least 1 / month). Specific inclusion criteria for the cannabis sober group were: no use of cannabis on the day of the memory test, and regular use of cannabis. The inclusion criteria for the control group were no use of cannabis in the past 24 h and a lifetime cannabis use of ≤ 10 occasions. A detailed summary of the demographics is given in Table 1.

Table 1

Subject characteristics for all groups

Demographic Variables	Cannabis intoxication group (*N*=53)	Cannabis sober group (*N*=50)	Control group (*N*=53)	*p*
Age in years (Mean, SD)	21.6 (2.5)	21.1 (3.1)	22.5 (2.8)	.06[1]
Sex (#)				
Male	46	43	20	<.001[2]
Female	7	7	33	
Native language (#)				.26[3]
Dutch	26	30	30	
English	4	5	0	
Other language	17	16	12	
Missing data	6	0	11	
Level of education[a] (#)				.06[3]
No degree	1	4	0	
High school	34	33	33	
Bachelor's degree	13	10	14	
Master's degree	1	1	6	
Other[b]	4	3	0	
Lifetime diagnosis of a psychiatric disorder (#)				.06[3]
Never diagnosed	52	45	47	
ADHD/ADD	0	2	1	
Mood disorder	1	3	4	
Anxiety disorder	0	0	1	
PTSD	0	1	0	
Autism	0	1	0	

Note.

[a] Level of education was measured in terms of highest level of education completed.

[b] Other refers to higher professional education (Dutch: HBO), secondary vocational education (Dutch: MBO), or not specified (missing).

[1] Based on ANOVA.

[2] Based on Pearson's chi-square test.

[3] Based on Fisher's Exact test.

The cannabis intoxication group contained regular cannabis users recruited at one of several coffeeshops in the city of Maastricht. Participants in this group rated their subjective high (feeling of intoxication) on a 100 mm visual analogue scale to be 5.9 (*SD* = 2.4) on average.

Moreover, the group reported having smoked an average of 0.7 g (*SD* = 0.7) of cannabis that day, with 0.4 g (*SD* = 0.3) being in the last hour before testing. The majority had consumed cannabis through smoking a joint, i.e., a cannabis cigarette (98%). Regarding the type of cannabis used, 47% had consumed a hybrid strain, 26% had used a sativa strain, 19% had used an indica strain, and 6% had used hashish (2% missing values; data based on classification displayed in coffeeshop). Based on the type of cannabis strain that this group indicated using, we estimated the average level of THC content in percentage, using several online cannabis strain databases (such as www.wikileaf.com/strains). The estimated average THC percentage was 19.1% (*SD* = 8.4, 19 missing values).

The cannabis sober group included sober coffeeshop attendees, who were also regular users but who reported not having used any cannabis that day. The majority reported having used cannabis the last time on the day before (72.5%). The summary of cannabis use history for both the cannabis intoxication and the cannabis sober group is provided in Table 2. Furthermore, the control group consisted of non-users recruited at cafes in Maastricht or in the main buildings of the Faculty of Psychology and Neuroscience of Maastricht University (e.g., in the cafeteria or common area outside the library).

Table 2

History and patterns of cannabis use for both groups of cannabis users, mean (SD)

	Cannabis intoxication group (*N*=53)	Cannabis sober group (*N*=50)	*p*
Age of first use	15.5 (2.0)	15.3(1.9)	.67[1]
Age of regular use	17.9 (2.0)	17.5 (2.2)	.28[1]
Frequency/week	6.3 (1.2)	5.4 (2.0)	<.01[1]
Frequency/month	26.8 (5.7)	22.9 (9.0)	<.01[1]
Grams used/week	5.9 (3.3)	7.3 (9.0)	.29[1]
Grams used/month	25.5 (14.8)	30.6 (38.9)	.39[1]
Average amount of cannabis per joint (grams)	.3 (.1)	.3 (.1)	.77[1]
Percentage cannabis per joint	53.5 (19.8)	50.9 (18.6)	.51[1]
Percentage self-rated light vs. heavy user	30 / 70	28 / 72	.81[2]

Note.

[1] Based on independent samples t-test.

[2] Based on Pearson's chi-square test.

Across groups, fourteen participants (9.0%) indicated to have been diagnosed with a psychiatric disorder and a total of five participants indicated being under acute influence of medication at the moment of testing [Ritalin (1), Antidepressants (2), Antipsychotics (1), Antihistamines (1)]. These participants were retained in the sample in order to keep the sample diverse and representative of the population of individuals who use cannabis. However, their potential for confounding was evaluated by conducting the analyses both in- and excluding these cases (see section on statistical analysis).

Ethical approval for this study was obtained from the Ethical Review Committee Psychology and Neuroscience (ERCPN) from Maastricht University. All data and materials can be found on the Open Science Framework: https://osf.io/h3gsz/.

Materials

Deese/Roediger-McDermott (DRM) Paradigm

True and false memories were measured with the DRM paradigm, which has been shown to robustly elicit spontaneous false memories in previous research (Gallo, 2010). The task consists of two phases: a study phase, in which participants study the stimuli, and a testing phase, in which a recognition memory is administered. In each phase, the word lists were administered to the participant as auditory stimuli. A separate recording was made for each phase. Stimuli were spoken and recorded by a male native Canadian English speaker at a rate of 1 word every ~2 s for the study phase, and a rate of 1 word every ~6 s for the testing phase. The stimuli were administered to participants via over-ear headphones (Sony, Model MDR-ZX110). The instructions were repeated before each phase.

In the study phase, 10 DRM word lists were presented, each containing 10 words (lists: bread, cold, doctor, fruit, man, girl, sleep, soft, sweet, thief; adopted from Stadler et al., 1999). Normative data have shown that these lists vary in both their backward associative strength (BAS, index of the associative strength between the list items and the critical item) and their inter-item associative strength, with mean BAS ranging from .39 (sleep) to .06 (man), and false recognition of the critical lure ranging from 84% (cold) to 45% (fruit; see Roediger, Watson, et al., 2001; Stadler et al., 1999). The recognition phase included the auditory presentation of 60 words, consisting of 30 previously presented words (word 1, 3, and 5 from each list), 10 new words semantically related to the lists from the study phase (critical lures), and 20 new unrelated words (unrelated items, adopted from other, non-presented DRM lists). The participants were instructed to make a *yes* (studied) or *no* (unstudied) judgment for the 60 words on a score sheet containing 60 yes/no columns. The item number was repeated before each word to prevent errors in completing the score sheet. In between the phases, the demographic and cannabis use questionnaire and a filler task (coloring a mandala) were administered (total time 10 min). The stimuli from both phases including their BAS are displayed in Appendix A and B.

Outcome measures included hit rate (the proportion of studied words correctly recognized at test), false alarm rate for critical lures (the proportion of critical lures, i.e., new, strongly related words, that are incorrectly recognized at test, a measure of false memory), false alarm rate for unrelated items (proportion of incorrect recognition of new, unrelated words), and net accuracy

(total hits divided by all yes responses, an indication of overall ability to discriminate between studied and unstudied items).

Demographic and Cannabis Use Questionnaire

For all groups, the questionnaire contained five self-report screening questions to assess if the respective group inclusion criteria were met, and five items on sociodemographic variables (sex, native language, highest completed level of education, lifetime diagnosis of a psychiatric disorder, current use of medication). The questionnaire administered to both groups of cannabis users contained additional items on their patterns of cannabis use (age of first use, age of regular use, tendency to use cannabis/hash/both, usual method of consumption, frequency of use per week/month, grams used per week/month, grams per joint, percentage cannabis/tobacco per joint, and a binary rating whether they consider themselves a heavy versus light user). For the experimental group, the questionnaire included further items regarding their acute cannabis use (grams used today and within last hour, cannabis strain used, method of consumption). These subjects also rated their subjective high on visual analogue scales (100 mm, ranging from “totally not under the influence of cannabis” to “very much under the influence of cannabis”).

Procedure

Data were collected between May 2017 and October 2018 in several centrally located coffeeshops in Maastricht. Testing took place during daytime only (between 12-6 PM). The control group was recruited from local cafes and local university buildings. Owners or employees of these establishments were approached for their consent to recruit and test participants there. Potential participants were approached inside the establishment and made aware of the study by the experimenter. Specifically, potential participants for the cannabis intoxication group were approached in a coffeeshop after they had consumed a cannabis product. For the cannabis sober group, participants were recruited in a coffeeshop by approaching them directly after they had bought a cannabis product and sat down at a table. For the control group, anyone sitting in the café or Maastricht University common areas who appeared to be between the ages of 18 and 30 was approached. Before the experiment, potential participants were verbally screened for the inclusion criteria. Concerning the cannabis intoxication group, three additional screening questions were asked to ensure that these participants were oriented in time and space (naming the day, place, and solving a simple math problem). In line with good practice recommendations in intoxication research (Aldridge & Charles, 2008), this was done in order to screen out severely intoxicated individuals, given concerns regarding their capacity to give informed consent. Eligible participants were informed that it was a study on memory in cannabis users and signed the informed consent form.

The DRM assessments were then conducted in the area where the participant was seated. Participants were handed over-ear headphones, and it was made sure they were comfortable with the volume and knew how to adjust it. Participants listened to the study phase recording (~5 min). Next, the demographics and cannabis use questionnaire and the filler task were administered (timed to take 10 min in total). Participants then listened to the testing phase recording, entering their recognition responses on the score sheet (~7 min). Upon completion, the participants were debriefed and rewarded for their participation with either candy or a monetary remuneration (voucher worth €5-10).

Statistical Analysis

First, equivalence of all groups was tested by performing comparative analyses on key demographic variables. Group differences were tested for the variables age (analysis of variance), sex (Pearson's Chi-Square), native language, level of education, and diagnosis of a psychiatric disorder (Fisher's Exact Test for latter three). Moreover, intoxicated and sober cannabis users were compared with regard to variables of cannabis use history, using independent samples t-tests for continuous and Pearson's Chi-Square for categorical variables. Variables found to statistically significantly differ between groups were entered as covariates in General Linear Model analyses. As part of the exploratory analyses, findings of the covariate analyses were compared with the findings from the first-level analyses.

A first-level analysis of variance (ANOVA) was conducted on all four DRM outcome measures with group as a between-subjects factor (3 levels). When a significant overall group difference was detected, pairwise comparisons were conducted using the Bonferroni post-hoc test. A difference was considered significant for p-values < 0.05. Cohen's d was calculated as an effect size estimate. These analyses were repeated, this time excluding those participants who had reported a lifetime diagnosis of a psychiatric disorder or use of medication ($n = 16$). Removal of these participants did not change the outcome, therefore these analyses are not reported. Finally, secondary analyses were conducted to explore factors that may have contributed to the outcome, such as cannabis use history (e.g., frequency, onset of regular use, user type). Here, independent samples t-tests were conducted to compare differences in cannabis use between light vs. heavy cannabis users, and to examine group differences on the DRM outcome measures.

The assumptions underlying all analyses were checked. For independent samples t-tests, this was done by examining Levene's Test for Equality of Variances. If this test was significant, then the more robust Welch's t-test was conducted in place of the regular independent samples t-test, with corrected degrees of freedom reported to two decimal places. For ANOVA, assumptions were checked by visual inspections of Q-Q plots for Normality, and by examining Levene's test for Equality of Variances. No gross violations of assumptions were detected for ANOVA.

Results

Group Characteristics

The sociodemographic characteristics of the sample are displayed in Table 1. Analyses of these characteristics revealed that the three groups did not statistically significantly differ in age, level of education, native language, and diagnosis of a psychiatric disorder. However, groups differed statistically significantly with regard to sex distribution. This variable was entered as a covariate in a multivariate General Linear Model Analysis with all four DRM parameters as dependent variables (DVs) and group as a fixed factor. Sex was found to be statistically significantly associated with one of the DRM parameters (false alarms for critical lures), thus this factor was further investigated in an exploratory analysis (see below). Cannabis use characteristics (see Table 2) generally did not differ between cannabis using groups. Weekly and monthly frequency use differed significantly between the groups, but were very minor.

Hit Rates

All mean scores for the DRM analyses can be inspected in Figure 1. A one-way analysis of variance (ANOVA) was conducted on the proportion of hits. The hit rates did not statistically differ between the three groups [F (2, 153) = 1.75, p = 0.18, partial eta squared = .02].

False Alarm Rates

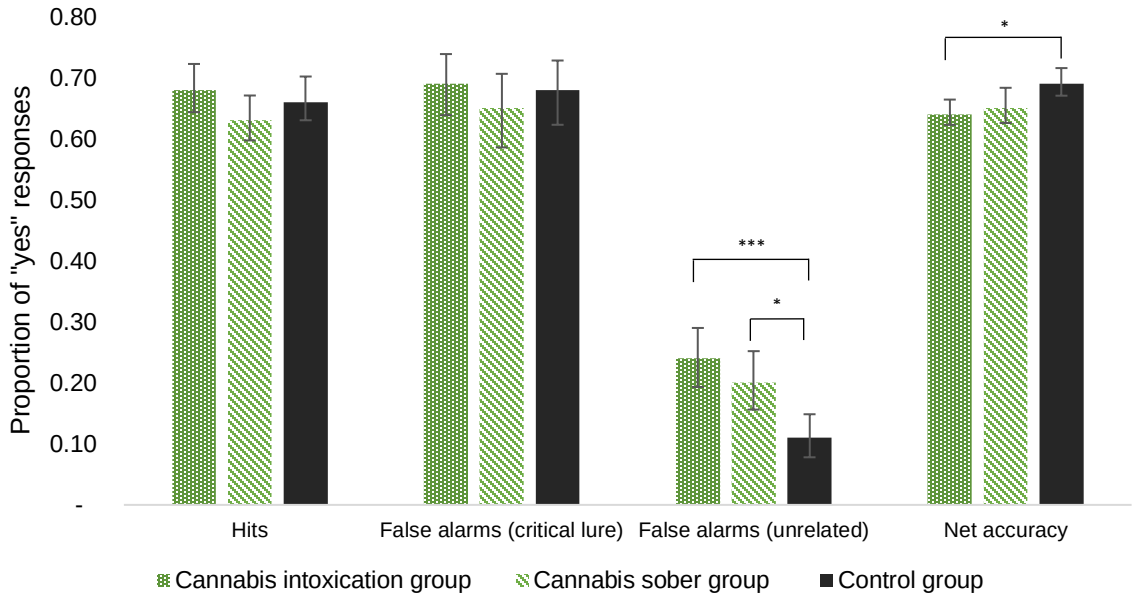
A one-way ANOVA was also conducted on the proportion of false alarms (incorrect recognition of new words). When focusing on critical lures, cannabis use did not exert any notable effect on the formation of false memories for critical lures [F (2, 153) = 0.64, p = 0.53, partial eta squared = .01]. However, when looking at false alarms in response to unrelated items, a statistically significant difference was detected between groups, and was associated with a medium-large effects size [F (2, 154) = 8.99, p = 0.0002, partial eta squared = .11]. The Bonferroni post-hoc analyses, showed that both intoxicated and sober cannabis users had higher acceptance rates of new unrelated items, compared to the control group (cannabis intoxication: p = .0002, Cohen's d = .83, cannabis sober: p = .018, Cohen's d = .59). However, the two cannabis groups did not differ from one another (p = .56, Cohen's d = .23).

Net Accuracy

We conducted a one-way ANOVA on net accuracy and detected a statistically significant difference between the three groups, with a medium effect size [F (2,153) = 4.79, p = .01, partial eta squared = .06]. Bonferroni post-hoc analyses showed that the cannabis intoxication group was less accurate compared to the control group (p = .01, Cohen's d = .63), but no difference was found for the cannabis sober group compared to the control (p = .076, Cohen's d = .44) or the cannabis intoxication group (p = .99, Cohen's d = .11).

Figure 1

DRM memory performance parameters in cannabis and control groups



Note. Rates in proportions with 95% confidence intervals as error bars, *p < .05, ***p < .001

Exploratory Analyses

Since no statistically significant differences were detected between the experimental and coffeeshop control group in terms of false memory propensity for critical lures, exploratory analyses were conducted to examine factors that might have contributed to this outcome. The two groups of cannabis users, both intoxicated and sober, were collapsed into groups of light (n = 30) and heavy (n = 73) cannabis users, according to their response to the question whether they

consider themselves to be a light or heavy user. To ensure that this division was warranted, these groups' consumption patterns were compared: light users indicated consuming cannabis on average 5.0 times and consuming on average 3.4 g per week compared to heavy users who reported using cannabis 6.2 times and an average quantity of 7.9 g per week [t (36.12) = -2.65, p = .012, Cohen's d = .73, and t (100.27) = -4.48, p < .001, Cohen's d = .70, respectively].

DRM true and false memory performance was then compared between light and heavy users using independent samples t-tests. A statistically significant difference was detected between the two groups only for the measure of net accuracy [t (101) = -2.51, p = .01, Cohen's d = .97]. An inspection of means revealed that light users demonstrated lower accuracy (M = .62, SD = .09, 95% CI = .58, .65) compared to the heavy users (M = .66, SD = .08, 95% CI = .64, .68). No statistically significant differences were detected with regard to the other DRM measures.

Moreover, as reported above, a multivariate GLM Analysis with all four DRM parameters as DVs, Group as a fixed factor, and Sex as a covariate was conducted. It was inspected whether having Sex as a covariate in the model would change any of the between-groups effects. With Sex as a covariate in the model, no statistically significant difference of group on net accuracy was detected anymore (p = .18). All other effects remained unchanged.

Discussion

The present field study was designed to assess whether cannabis use increases the susceptibility to false memory formation. To allow differentiation of acute and residual effects of cannabis, we compared true and false recognition memory performance in intoxicated and sober regular consumers of cannabis with non-user controls on the DRM paradigm. Contrary to expectations, cannabis users did not demonstrate an increase in false memory rates for critical lures, relative to controls. However, both intoxicated and sober cannabis users showed elevated false alarm rates in response to new, unrelated items. Moreover, no group differences were detected with regard to true memory performance (hit rates), but the control group demonstrated higher net accuracy in memory performance, compared to intoxicated cannabis users.

We found no evidence that cannabis use increases recognition of critical lures. At first instance, this finding seems to conflict with the findings by Riba et al. (2015) who reported elevated susceptibility to false memories in abstinent cannabis consumers. However, a closer inspection of the differences in methodology between the two studies may provide an explanation. In the study by Riba et al., a modified version of the DRM paradigm was used, exposing participants to 20 word lists each containing 4 associated words, which were preceded by an announcement of the list name (e.g., farm animals: horse, hen, sheep, goat; see supplementary materials of Riba et al., 2015). The recognition test then included lure items, which were words categorically related to the presented items (e.g., cow, pig), in addition to old, presented words and new, unrelated items. In contrast, the classic version of the DRM paradigm was employed in our study, where participants were presented with lists of 10 words that all primed identical critical lures, and the lists consisting of the first associates of the critical lure based on association word norms (Stadler et al., 1999). As such, the study by Riba et al. (2015) therefore did not include standard critical lures under the definition of the classical DRM paradigm, but words that were related to previously learned words but were not previously primed in the study phase.

DRM lists and so-called category lists such as the ones used by Riba et al. thus differ in that DRM lists typically contain multiple different associative relations (synonyms, antonyms, concept relations, etc.) whereas category lists are restricted to only one level of association, that is taxonomy (Knott et al., 2012). Moreover, DRM lists are typically higher in backwards associative strength (BAS), so associative connections from study words to the critical lures. Research has

shown that higher BAS leads to higher rates of false memories (Knott et al., 2012; Roediger, Watson, et al., 2001). Although impossible to compare directly as numbers for BAS are missing in Riba et al.'s study, it can be argued that the two measures of false memory differ in associative strength, as the lures used in Riba et al.'s study can be considered as less strongly associatively related to the initially presented lists, compared to the critical lures used in our study. The premise that high BAS tends to elicit high rates of false memories is also mirrored in the fact that in our study, false memory rates were rather high in all groups (65-69%), whereas they were relatively low in the Riba et al. study (20-30%).

On the other hand, a medium to large effect was found of cannabis use on false recognition of non-presented, associatively unrelated items, with cannabis users showing elevated false alarm rates. This effect fits well with previous findings reported in the literature of studies using non-DRM word list tasks, where acute cannabis intoxication was found to induce elevated intrusions and false alarms of new, unrelated stimuli (e.g., Hart et al., 2010). True recognition performance in our study was unimpaired by cannabis use, which mirrors other studies such as Riba et al. (2015). As mentioned in the introduction, recognition memory has only inconsistently been found to be impaired by cannabis use, a finding that has been reported both in acute and long-term studies (Broyd et al., 2016; Solowij & Battisti, 2008). However, it was found that net accuracy was highest in the control group, and although pairwise comparisons only detected a statistically significant difference between controls and intoxicated cannabis users, this indicates that cannabis impairs overall recognition accuracy.

Two theoretical frameworks can be used to explain the formation of false memories as elicited by the DRM paradigm: Associative-Activation Theory (AAT; Howe et al., 2009) and Fuzzy-Trace Theory (FTT; Brainerd et al., 2008). According to AAT, processing one word activates a corresponding node (i.e., concept), and spreads activation to surrounding, interconnected nodes within one's semantic network (i.e., knowledge base). False memories can be produced if spreading activation has automatically activated neighboring but non-presented information, leading to false memories. According to FTT, events are encoded into two types of memory traces: verbatim and gist. The verbatim trace contains item-specific details of an event, while the gist trace captures the underlying meaning of the stimulus. Because verbatim traces fade

quickly over time, people rely on gist traces when retrieving memories thereby enhancing false memory formation (Brainerd & Reyna, 2016).

Given that critical lure recognition did not differ in the cannabis use groups relative to controls, it does not appear that cannabis use enhanced activation for the related lure words in memory or produced an over-reliance on gist memory traces. However, given the observed increase in unrelated word recognition and the decrease in net accuracy for the cannabis use groups it may be the case that cannabis impairs processing of the word lists during encoding (i.e., insufficient processing prevents either extensive activation or strong verbatim and gist trace formation). The finding that light cannabis users had worse net accuracy than the heavy users may also support this suggestion as light users are arguably less tolerant to the effects of THC than the heavy users (Ramaekers et al., 2009), so any cannabis effects would be more pronounced in the light use group; i.e., decreased processing in the light use group.

According to AAT, false memories or false alarms depend on the strength of association. DRM lists with high BAS may result in stronger spreading activation, leading both controls and cannabis users alike to be certain that they remember the critical lure. They might receive a feeling of familiarity when being exposed to the critical lure. On the other hand, if there is no association as in the present study, or a lesser degree of association as in Riba et al.'s study, the level of uncertainty is greater, and thus individuals who are acutely intoxicated or have residual levels may exhibit a tendency towards more liberal responding. Multiple explanations can be put forward for this liberal responding. According to Ranganathan and D'Souza (2006), cannabinoids may induce increased intrusions due to increased mental activity, leading to irrelevant associations. In line with this idea, a recent animal study with cannabinoid receptor type 1 (CB1) knockout mice showed that hippocampal CB1 receptor activation increases the formation of incidental associations (Busquets-Garcia et al., 2018). Alternatively, cannabis use has been associated with increased impulsivity in decision-making (e.g., Metrik et al., 2012; Ramaekers et al., 2009). When making decisions under conditions of uncertainty, this may play out as a lowered decision threshold resulting in greater liberal acceptance of new information.

The current study has several strengths and novelties. Previous studies have been useful in illuminating the role of cannabis in false memory production but have several drawbacks: Specifically, in Riba et al. (2015) the participants were abstinent for at least four weeks making it

difficult to determine acute intoxication effects, whereas in Ballard et al. (2012) participants received a specific dose that may not account for individual differences in tolerance levels. While the Vredeveldt et al. (2018) study advanced on this design by testing participants who chose their own cannabis dose, false memory was not measured directly using a method known to successfully lead to reliable levels of false memories. These drawbacks have been addressed in the current design. In a between-subjects design, we compared groups of acutely intoxicated individuals who use cannabis regularly, sober individuals who use regularly, and individuals without a history of cannabis use. This allowed the distinction between acute and residual effects of cannabis use. Moreover, the study was conducted in a naturalistic setting, maximizing ecological validity, as in a coffeeshop people are more likely to consume a dose specific to their tolerance levels.

However, the study is not without limitations. There was an unequal distribution of sex across groups, with the two cannabis groups consisting largely of male participants, while the control group had a higher proportion of female participants. Although this mirrors findings of cannabis use being more prevalent in males (e.g., Cuttler et al., 2016), it might pose a confounding factor, especially since when sex was included as a covariate in the analyses, no statistically significant group difference was detected for net accuracy anymore. It should be noted though that previous research gives no reason to expect sex effects in DRM performance (Bauste & Ferraro, 2004; Seamon et al., 2002). A study by Dewhurst et al. (2012) found a sex difference but only with regard to negative stimuli while there was no difference for neutral lists. Nevertheless, future studies may need to account for sex differences by recruiting a more balanced sample.

Furthermore, as encoding and retrieval occurred in the same session (approximately 10 minutes apart), it is not clear whether cannabis impacts the encoding or retrieval of experiences. The previously described studies by Ballard et al. (2012) and Doss et al. (2018) separately examined effects of THC on encoding and recognition testing two days apart, meaning encoding occurred during intoxication and retrieval whilst sober, and vice versa. Doss et al. found that THC at retrieval increased false memory effects whereas Ballard et al., if anything, found reduced false memory effects of THC during encoding. Future studies could investigate the issue of different memory stages and cannabis further by separating the encoding and testing phases with a longer time interval and varying the timing of intoxication. Future studies should also include an additional word category consisting of related but not critical lures, similar as in the study by Riba

et al. (2015), to see whether the results converge. Measures of recall rather than just recognition memory, and metacognitive measures such as assessments of confidence would allow for a more comprehensive understanding of the effects of cannabis on multiple memory processes.

Finally, this study has important implications for legal, forensic as well as clinical settings. If cannabis users, intoxicated or sober, have a greater tendency for liberal responding when uncertain, this may have consequences in such settings. When presented with new, irrelevant information, they might be more likely to accept this new information as true or familiar, resulting in erroneous reporting. Even though DRM false memory seems far removed from autobiographical memory for a prolonged event such as a crime, the paradigm preserves an essential property of everyday false memories, namely that they arise from meaning relations (Brainerd, 2013). Spontaneous false memories such as those in the DRM can arise in and have been relevant to legal cases (Brackmann et al., 2016; Howe et al., 2017; Otgaar, Howe, et al., 2019b), underlining the importance of the current study.

Funding and Disclosure

The authors declare no conflict of interest with respect to this research. This research was supported by the NWO Research Talent grant (nr. 406.16.529), awarded to LK, HO, and JR in 2016.

Acknowledgements

We are grateful to Magdalena Bilska, Selin Mavituna, Leonie Ambraß, Ana Ricart, Franziska Göttgens, Alan Green, Dennis Brown, Beau Timmons, Didi Delsing, and Rachel Heutz for collecting data. Further, we would like to thank the coffeeshop owners for allowing us to collect data inside their coffee shops.

Appendix A

Study phase DRM lists

List / Critical Lure	Word	BAS	List / Critical Lure	Word	BAS
Bread	Butter	0.364	Girl	Dolls	0.199
	Food	0.000		Female	0.098
	Eat	0.000		Young	0.000
	Sandwich	0.067		Dress	0.063
	Flour	0.142		Pretty	0.149
	Dough	0.31		Hair	0.000
	Crust	0.243		Beautiful	0.049
	Slice	0.048		Cute	0.035
	Loaf	0.552		Daughter	0.042
	Toast	0.364		Sister	0.041
	Mean	0.209		Mean	0.068
Cold	Hot	0.676	Sleep	Bed	0.638
	Snow	0.199		Rest	0.475
	Winter	0.277		Awake	0.618
	Ice	0.364		Tired	0.493
	Wet	0.108		Dream	0.247
	Weather	0.032		Blanket	0.024
	Freeze	0.461		Snore	0.439
	Air	0.000		Nap	0.73
	Arctic	0.642		Peace	0.000
	Frost	0.37		Yawn	0.235
	Mean	0.313		Mean	0.390
Doctor	Nurse	0.574	Soft	Light	0.000
	Sick	0.031		Pillow	0.236
	Medicine	0.152		Plush	0.178
	Hospital	0.027		Cotton	0.166
	Ill	0.000		Fur	0.061
	Patient	0.365		Touch	0.061
	Office	0.014		Fluffy	0.266
	Surgeon	0.479		Feather	0.045
	Clinic	0.3		Furry	0.061
	Cure	0.028		Downey	0.221
	Mean	0.197		Mean	0.130
Fruit	Apple	0.154	Sweet	Candy	0.336

	Orange	0.194		Sugar	0.433
	Kiwi	0.709		Taste	0.071
	Citrus	0.426		Tooth	0.000
	Ripe	0.151		Honey	0.451
	Pear	0.347		Chocolate	0.101
	Banana	0.215		Heart	0.000
	Berry	0.298		Cake	0.027
	Cherry	0.168		Tart	0.223
	Salad	0.000		Pie	0.000
	Mean	0.266		Mean	0.164
Man	Husband	0.018	Thief	Steal	0.089
	Uncle	0.07		Robber	0.361
	Male	0.131		Burglar	0.257
	Father	0.048		Money	0.000
	Strong	0.02		Bad	0.000
	Friend	0.000		Rob	0.074
	Beard	0.055		Jail	0.013
	Person	0.122		Gun	0.000
	Muscle	0.048		Crime	0.028
	Suit	0.074		Criminal	0.051
	Mean	0.059		Mean	0.087

Note.

All BAS values are drawn from Roediger et al. (2001).

Appendix B

Recognition phase DRM list

1)	Strong[a]	21)	Bad[a]	41)	Tiger[b]
2)	Butter[a]	22)	Garbage[b]	42)	Dream[a]
3)	Table[b]	23)	Circus[b]	43)	Plush[a]
4)	Crown[b]	24)	Shoe[b]	44)	Taste[a]
5)	Bread[c]	25)	Apple[a]	45)	Honey[a]
6)	Eat[a]	26)	Medicine[a]	46)	Sweet[c]
7)	Nose[b]	27)	Fur[a]	47)	Steal[a]
8)	Flour[a]	28)	Fruit[c]	48)	Train[b]
9)	Hot[a]	29)	Waste[b]	49)	Shirt[b]
10)	Candy[a]	30)	Captain[b]	50)	Sleep[c]
11)	Doctor[c]	31)	Ill[a]	51)	Dolls[a]
12)	Flexible[b]	32)	Ink[b]	52)	Water[b]
13)	Winter[a]	33)	Ripe[a]	53)	Hand[b]
14)	Young[a]	34)	Wine[b]	54)	Pollution[b]
15)	Stars[b]	35)	Cold[c]	55)	Nurse[a]
16)	Girl[c]	36)	Husband[a]	56)	Light[a]
17)	Man[c]	37)	Pretty[a]	57)	Smoke[b]
18)	Wet[a]	38)	Bed[a]	58)	Burglar[a]
19)	Awake[a]	39)	Eye[b]	59)	Kiwi[a]
20)	Soft[c]	40)	Male[a]	60)	Thief[c]

Note.

Stimuli were presented in the listed order.

[a] Previously presented (old) word

[b] New, unrelated word

[c] Critical lure

Chapter 4

Cannabis Increases Susceptibility to False Memory

This chapter is an extended version of the following publication:

Kloft, L., Otgaar, H., Blokland, A., Monds, L. A., Toennes, S. W., Loftus, E. F., & Ramaekers, J. G. (2020). Cannabis increases susceptibility to false memory. *Proceedings of the National Academy of Sciences*, 201920162. doi:10.1073/pnas.1920162117

Abstract

With the growing global acceptance of cannabis and its widespread use by eyewitnesses and suspects in legal cases, understanding the popular drug's ramifications for memory is a pressing need. In a double-blind, randomized, placebo-controlled trial we examined the acute and delayed effects of THC intoxication on susceptibility to false memory in 64 healthy volunteers. Memory was tested immediately (encoding and retrieval under drug influence) and one week later (retrieval sober). We used three different methods (associative word lists and two misinformation tasks using virtual reality). Across all methods, we found evidence for enhanced false memory effects in intoxicated participants. Specifically, intoxicated participants showed higher false recognition in the associative word-list task both at immediate and delayed test than controls. This yes-bias became increasingly strong with decreasing levels of association between studied and test items. In a misinformation task, intoxicated participants were more susceptible to false memory creation using a virtual reality eyewitness scenario and virtual reality perpetrator scenario. False memory effects were mostly restricted to the acute intoxication phase. Cannabis seems to increase false memory proneness with decreasing strength of association between an event and a test item, as assessed by different false memory paradigms. Our findings have implications for how and when the police should interview suspects and eyewitnesses.

Introduction

Cannabis is the most widely used illicit substance across the world, and its main psychoactive ingredient Δ9-tetrahydrocannabinol (THC) has been associated with memory impairments (e.g., Broyd et al., 2016). As a potential factor impacting memory, cannabis intoxication is an issue of particular interest from a legal perspective. That is, testimonies by eyewitnesses or suspects are oftentimes the only piece of evidence that triers of fact can use for legal decision making, and thus gathering reliable testimony is crucial. However, memory performance is imperfect resulting sometimes in false memories (i.e., memories of non-experienced events/details; Loftus, 2016; Otgaar, Howe, et al., 2016) and such false memories can have disastrous consequences in legal cases (e.g., wrongful convictions, false accusations). This phenomenon of false memory, combined with the fact that cannabis intoxicated eyewitnesses and suspects are common (Evans et al., 2009), stresses the need to examine whether cannabis might facilitate false memory production. Empirical work in this area is rather limited (see Flowe et al., 2020 for a recent review). In the current experiment, we conducted a randomized placebo-controlled study to test the impact of cannabis on false memory formation using three prominent false memory paradigms.

Core to many false memory paradigms is the presentation of words or events to which one has been exposed before (‘old’) or not (‘new’). Old-new recognition decisions can be affected by response bias, a general tendency to respond to items in a systematic but potentially false direction (e.g., yes-bias). Some people adopt a stricter decision criterion, requiring a higher level of memory strength to call an item old, while others may respond more liberally (Wright et al., 2008). We investigated whether individuals who are under the influence of cannabis express a different bias, and if so, would it be influenced by levels of association between old and new events. Single doses of cannabis have been found to cause deficits in decision making and working memory (Adam et al., 2020; Ramaekers, Kauert, et al., 2006; Ranganathan & D'Souza, 2006) that have been associated to increased CB1 receptor activation in the hippocampus (Bloomfield et al., 2019; Mizrahi et al., 2017). It is not clear however whether cannabis also affects the tendency of how individuals respond to events that may or may not have happened. It has been suggested that hippocampal CB1 receptor activation might underlie the formation of incidental associations (Busquets-Garcia et al., 2018), which would predict an increase in false memories.

The false memory literature broadly distinguishes between two types: *Spontaneous* false memories arise due to internal cognitive processes, whereas *suggestion-based* false memories occur because of external suggestion (Brainerd, 2013; Mazzoni, 2002). A highly reliable and common method to evoke spontaneous false memories is the Deese/Roediger-McDermott (DRM) paradigm (Deese, 1959; Gallo, 2010; Roediger & McDermott, 1995), in which people falsely remember words not actually presented in an associatively related list of words. Research on cannabis and DRM false memory formation is sparse, but in a recent field study we compared intoxicated vs. non-intoxicated cannabis users vs. a non-using control group (Kloft et al., 2019). No statistical difference between groups was found for the acceptance of *critical lures* (associated but non-presented theme words). However, false alarms to non-presented irrelevant stimuli (unrelated to theme) were increased in both sober and intoxicated cannabis users. These findings might be interpreted as reminiscent of a cannabis-induced response bias ('yes-saying' bias) that might vary depending on the strength of association between studied and test items (see also Ballard et al., 2012; Doss, Weafer, Gallo, et al., 2018a for related findings).

Suggestion-based false memories are frequently studied using the misinformation paradigm. Here, participants first view or are involved in an event (e.g., mock crime), then are exposed to misinformation (e.g., suggestive questions, misleading narrative containing false details), and finally receive a memory test. Exposure to post-event misinformation often results in people incorporating the suggested details into their memory reports, a phenomenon that is also known as the "misinformation effect" (for a review see Loftus, 2005). To our knowledge, no study thus far has implemented this method to study the effects of cannabis on suggestion-based false memory.

The current experiment aimed to assess the impact of cannabis intoxication on both spontaneous (DRM) and suggestion-based (misinformation) false memory production in healthy, occasional cannabis users. The DRM method allows to specifically test recognition rates at different levels of association between old and new items. Thus, the level of association is highest for old (i.e., studied) words. Compared to this, the association for new words is lower, but highest for critical lures, less for related lures, and lowest for unrelated words. In general, the misinformation method is not constructed using similar associative mechanisms as in the DRM method, but does contain questions about presented or non-presented details that also differ in their level of association. That is, truly presented details were present at encoding, and thus were highly

linked with the experience, while suggested details were linked through the suggestion of being present in the scenario. Non-suggested, non-presented details were weakly linked to the experience. Since CB1 activation facilitates formation of incidental associations (Busquets-Garcia et al., 2018), we tested how cannabis affected the response bias for items with different associative strengths.

Another novel element of the current experiment was that we used virtual reality as a way to test the misinformation effect in subjects acting as eyewitnesses and perpetrators. Studies have traditionally employed methods such as case vignettes or videos (Vredeveldt et al., 2018), but also staged events (Yuille et al., 1998) to expose participants to a mock crime event, presenting a trade-off of either maximizing internal or external validity. The scenarios in this study were administered in virtual reality (VR), a fully immersive technology that can overcome this tradeoff by combining high experimental control and reusability with high degrees of realism, ecological validity, and feelings of *presence* (van Gelder et al., 2014). Misinformation was introduced through a combination of suggestive questions in a later interview and a virtual co-witness. The interview contained questions about truly presented details (*presented*), leading questions about non-presented details (*suggested*), and neutral questions about non-presented details (*non-suggested*).

The study was conducted according to a double-blind, mixed model, placebo-controlled design. Suggestion-induced false memory in VR scenarios was tested in a between-subjects design, whereas spontaneous false memory using the DRM paradigm was tested in a within-subjects design. In order to differentiate between acute and long-term drug effects, spontaneous and suggestion-based false memory were assessed at two time points: shortly after encoding (*immediate*) and one week later (*delayed*). Both assessments are of practical relevance. Intoxication during encoding and retrieval phases often occurs in eyewitness situations, which may affect immediate memory of the witnessed event. However, people are not always interviewed immediately following a crime, so it is also imperative to include a retrieval condition in which participants are sober. Given the previously described findings of cannabis-induced memory impairment (Broyd et al., 2016; Doss, Weafer, Gallo, et al., 2018a; Kloft et al., 2019), cannabis intoxication was generally expected to result in higher false memory rates, compared to a placebo condition.

Results

Means and standard errors (*SE*) for all DRM and misinformation parameters can be viewed in Table 1. Demographic information, intoxication parameters, and additional analyses are displayed in the Supplementary Information (SI Appendix).

Table 1

Means from DRM and Misinformation parameters (rates in proportions): M (SE)

	Cannabis condition		Placebo condition	
	Immediate	*Delayed*	*Immediate*	*Delayed*
DRM	*n* = 63	*n* = 63	*n* = 64	*n* = 63
True recognition (old)	.68 (.02)	.46 (.02)	.68 (.02)	.51 (.02)
False alarms (critical)	.62 (.02)	.59 (.03)	.56 (.03)	.64 (.02)
False alarms (related)	.42 (.03)	.44 (.03)	.27 (.03)	.44 (.03)
False alarms (unrelated)	.40 (.03)	.39 (.03)	.16 (.02)	.31 (.03)
Net accuracy	.68 (.08)	.54 (.05)	.75 (.13)	.57 (.08)
Misinformation Eyewitness	*n* = 32	*n* = 31	*n* = 32	*n* = 31
Presented	.78 (.02)	.71 (.02)	.78 (.02)	.74 (.02)
Suggested	.19 (.04)	.19 (.03)	.08 (.02)	.17 (.03)
Non-suggested	.06 (.02)	.17 (.03)	.01 (.01)	.10 (.02)
Misinformation Perpetrator	*n* = 31	*n* = 31	*n* = 32	*n* = 31
Presented	.68 (.03)	.62 (.03)	.65 (.03)	.67 (.03)
Suggested	.31 (.05)	.28 (.04)	.23 (.03)	.27 (.03)
Non-suggested	.08 (.02)	.07 (.02)	.01 (.01)	.03 (.01)

DRM

Fig. 1 depicts the mean DRM true and false memory rates for the two drug conditions at immediate (1a) and delayed test (1b). As can be seen in Fig. 1a, cannabis-intoxicated individuals had higher false memory rates compared to the placebo condition at immediate test. This effect depended on the level of association between studied and tested words. Statistically, this was reflected in an interaction effect between Drug and Level of association [F (2.67, 167.52) = 14.83, $p < .001$, $\omega^2 = .08$]. Cannabis increased false memories of related lures [F (1, 62) = 21.50, $p < .001$,

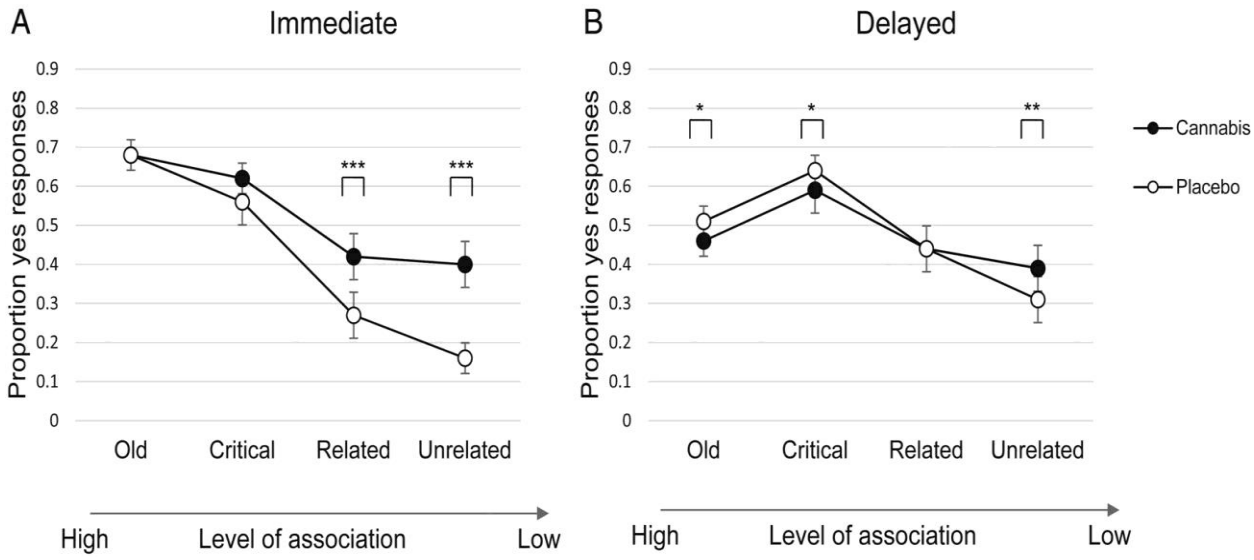
Cohen's d = .58] and unrelated words [F (1, 62) = 62.53, p < .001, Cohen's d = 1.0], where levels of association were low. However, cannabis did not affect the response to old words (true memory) and critical lures, where levels of association were high.

The delayed test also revealed a significant interaction between Drug and Level of association [F (2.59, 155.46) = 7.60, p < .001, ω^2 = .02]. Cannabis increased false memories for unrelated words [F (1, 60) = 8.85, p = .004, Cohen's d = .38;], but decreased false memories of critical lures [F (1, 60) = 4.37, p = .041, Cohen's d = .27] and true memory [F (1, 60) = 6.20, p = .016, Cohen's d = .32].

Overall, cannabis-intoxicated participants had lower memory accuracy (net accuracy = ratio of true memory to total memory), both in the immediate [t (62) = 3.67, p < .001, Cohen's d = .46] and the delayed test [t (60) = 2.49, p = .015, Cohen's d = .32], as compared to placebo.

Figure 1

DRM mean scores in proportions from immediate test (a) and delayed test (b) by drug condition



Note. *p < 0.05, **p < 0.01, ***p < 0.001, pairwise comparisons. Error bars represent 95% CIs.

Misinformation Paradigm

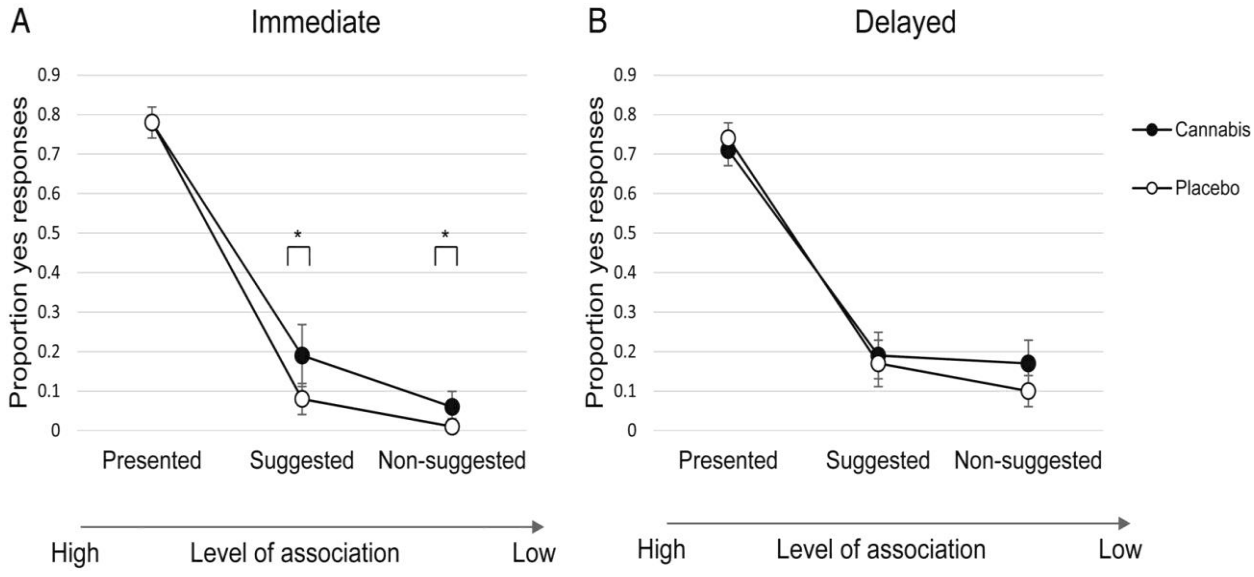
Eyewitness Scenario

Fig. 2 shows the cannabis and placebo groups' true and false memory rates for the eyewitness VR scenario at immediate (2a) and delayed test (2b). As can be seen in the figure, the cannabis group had higher false memory rates when still intoxicated (2a), but this effect disappeared after one week when sober again (2b). True memory was not affected by cannabis at immediate test [presented details; F (1, 62) = 2.76^{-30}, p = 1.0]. However, cannabis-intoxicated participants showed higher false memories of suggested and non-suggested details than the placebo group [F (1, 62) = 6.19, p = .016, Cohen's d = .62, and F (1, 62) = 4.59, p = .036, Cohen's d = .54, respectively]. This was reflected by a Group by Level of association interaction [F (1.62, 100.19) = 3.43, p = .046, ω^2 = .02].

Regarding the analyses of the delayed condition, no statistically significant interaction was detected anymore.

Figure 2

Eyewitness mean scores in proportions from immediate test (a) and delayed test (b) by drug condition



Note. *p < 0.05, **p < 0.01, ***p < 0.001, pairwise comparisons. Error bars represent 95% CIs.

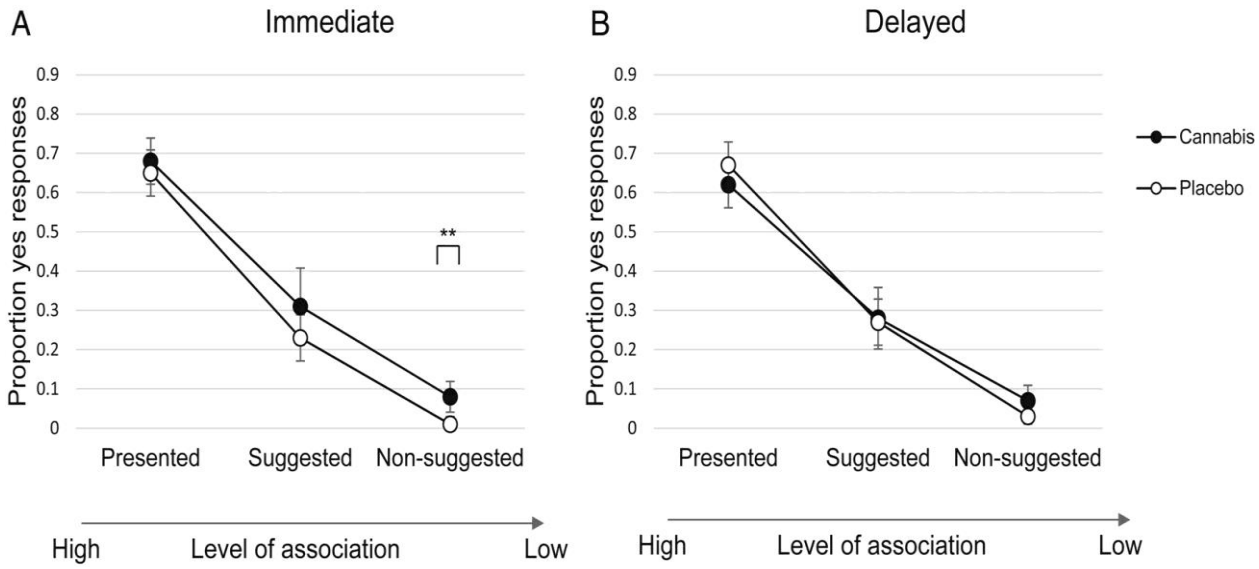
Perpetrator Scenario

Fig. 3 depicts the two groups' true and false memory rates for the perpetrator VR scenario in the immediate (3a) and delayed conditions (3b). In Fig. 3a it is visible that the cannabis group had higher false memory rates while under the influence, compared to placebo. At 1-week follow-up no group differences were detectable anymore (3b). Analysis of the immediate condition revealed a main effect of Group [F (1, 61) = 5.79, p = .019, ω^2 = .07], with cannabis-intoxicated participants showing the highest false memory rates of non-suggested details [F (1, 61) = 11.56, p = .001, Cohen's d = .86]. No statistically significant differences between cannabis and placebo were detected for true memory [F (1, 61) = .40, p = .53] or false memory for suggested details [F (1, 61) = 2.23, p = .14].

At delayed test, no statistically significant interaction effect or Group main effect emerged.

Figure 3

Perpetrator mean scores in proportions from immediate test (a) and delayed test (b) by drug condition



Note. *p < 0.05, **p < 0.01, ***p < 0.001, pairwise comparisons. Error bars represent 95% CIs.

Discussion

We exampled the effects of cannabis on the susceptibility to form spontaneous and suggestion-based false memories, and generally found more false memories in intoxicated participants. These elevated false memory rates were observed in all paradigms and were most pronounced in the immediate condition, when memory tests took place while people were still acutely intoxicated. This fits well with research suggesting that cannabis robustly increases false memory at the retrieval stage (i.e., the memory test; Doss, Weafer, Gallo, et al., 2018a). However, some effects in the DRM persisted after one week when people were sober again, indicating some THC-induced encoding (i.e., intake of information) impairments as well.

The findings obtained from the DRM paradigm extend and replicate previous findings in several ways. Acute cannabis use did not significantly affect immediate true recognition performance, or false recognition of critical lures, which was similarly shown in the coffeeshop field study (Kloft et al., 2019). However, cannabis elevated immediate false memory rates for related and unrelated stimuli (medium and large effect sizes, respectively). Moreover, memory performance during cannabis and placebo was similar when presented with old words and critical lures, but false recognition rates were much higher during cannabis intoxication when confronted with words that were poorly associated to the old words, suggesting that cannabis induced a response bias towards less associated new items. Remarkably, this latter effect was still present at follow-up one week later when participants were sober again. At follow-up we also found that the cannabis condition had lower true memories and lower false memories of critical lures, compared to placebo (although not robustly, see SI). This could be reflective of THC-induced encoding impairments, where impaired processing during the study phase could result in decreased memory for studied words, thereby also reducing memory for similar, easily confusable items. This is consistent with other research in this field where THC at encoding reduced DRM false memory formation (Ballard et al., 2012), suggesting that at encoding cannabis might reduce memory for the relatedness of presented words. This seems also in line with the current finding that the decrease in false memory frequency for unrelated words as compared to related words was most pronounced in the placebo condition. Overall, these results fit well with previous studies that disentangled the effects of cannabis on different memory stages (Ballard et al., 2012; Doss, Weafer, Gallo, et al., 2018a), and an emerging picture seems to be that elevated false memories are the norm when THC affects retrieval.

Cannabis also amplified susceptibility to suggestion-based false memories in the misinformation paradigm. In the eyewitness scenario, intoxicated participants showed the highest false memory rates in response to leading questions about suggested details but also neutral questions about non-presented details. In the perpetrator scenario, an overall higher tendency to respond 'yes' to all questions among intoxicated participants was detected. This effect was primarily driven by false memories of non-suggested, non-presented details, a response pattern that might increase the risk of false reporting and might be more indicative of a general response bias. These differences between groups were restricted to the immediate condition and disappeared at follow-up one week later, indicating that THC-induced impairments might be most detrimental to retrieval. However, inspecting the mean scores it becomes clear that the cannabis group did not necessarily improve over time, but rather the placebo group worsened at follow-up, thus performing more similar to the cannabis group after one week has passed. This is in line with research showing that memory decays over time and that people are more prone to be influenced by misinformation with increasing length between event and post-event misinformation because they are less likely to detect discrepancies (discrepancy-detection principle; Loftus, 2005; Loftus et al., 1978). Due to the placebo group deteriorating with time, no statistical differences in memory performance were detected at follow-up.

On a broader level, we detected that cannabis intoxicated people seemed to show a tendency towards more liberal responding under conditions of uncertainty. Why might this be so? An increase in irrelevant associations might stem from increased incidental learning due to activation of hippocampal CB1 receptors (Busquets-Garcia et al., 2018). High densities of cannabinoid receptors in the hippocampus and cortex have previously been suggested as playing a role in the cognitive effects of cannabis (Solowij, 2006). These effects include a loosening of associations, fragmentation of thought, and heightened distractibility. Such reductions in focus and increments in mental activity could well account for the increase in false recognitions of irrelevant or unrelated words or events on all memory tasks. Some responses might also be explained by impaired source-monitoring, for example, by confusing information from external sources (e.g., co-witness) with internal ones (own memory; Johnson et al., 1993). Increased irrelevant associations due to cannabis might contribute to source misattributions, and therefore, memory errors.

The current study has several practical implications. The most important message from this study is that cannabis exerted a general impact on memory by increasing various types of recollective errors. Although there is debate on whether different types of false memories are related to each other (Ost et al., 2013; Otgaar, Howe, et al., 2016), the current study shows that intoxicated individuals might be at high risk to form all kinds of memory errors which can be perilous in investigative interviewing settings. In addition, intoxicated individuals were more vulnerable to suggestive questions while still under acute influence, but this effect disappeared at 1-week follow-up. In terms of interviewing witnesses, victims, or suspects after the incidence of a crime, this means that interviewing while the individual is still intoxicated should be minimized due to elevated risk of false reporting. Questioning should ideally take place as soon as the person has sobered up to prevent memory decay due to time. However, a person under the influence of cannabis during an event might still show a yes-bias towards some new information later. Thus, cannabis intoxicated individuals might have to be treated as a vulnerable group, similar to child or elderly witnesses/suspects.

Future replication is needed to support this study's findings, and could include measures of free recall and metacognition on top of recognition memory. For example, it is important to examine how confident cannabis-intoxicated individuals are when making memory errors. Future studies might also explore whether memory errors introduced during an intoxicated interview would persist and appear in later interviews, adding to the potential costs of interviewing people while they are still intoxicated.

To recap, this study has provided some of the very first evidence that using cannabis elevates the risk of creating different types of false memories. Cannabis intoxicated witnesses and suspects pose a vulnerable group and might profitably be identified as such, and while drug-testing is a routine procedure with suspects, this is not the case for witnesses or victims (Crossland et al., 2018). Although cannabis is oftentimes connected with positive effects (e.g., pain reduction), it might also lead to hazy memories which eventually opens the door for a negative effect: increases in false memories.

Materials and Methods

The study was approved by the standing Medical Ethics Committee of Maastricht University (METC azM/UM) and the South East Sydney Local Health District (SESLHD) Human Research Ethics Committee, and was conducted according to the current revision of the Declaration of Helsinki (amended in 2013, Fortaleza) and the International Conference on Harmonization guidelines for Good Clinical Practice. All subjects were fully informed of study procedures, adverse reactions to drug treatments, legal rights and responsibilities, expected benefits of a general scientific nature, and their right for voluntary termination without penalty or censure. All subjects gave written informed consent and received financial compensation (€150/AUS$200) for their participation. A permit for obtaining, storing and administering medicinal cannabis was obtained from the Dutch drug enforcement administration (Sydney: New South Wales Ministry of Health). The study was registered at the Netherlands National Trial Register (Nederlandse Trial Register, NL6494).

The study was set up as an international multi-center clinical drug trial between two sites: Maastricht University and Sydney University. A total of 64 healthy, occasional cannabis users (32 female, 32 male, mean age and *SD*: 22.7, 2.6) completed the present study, i.e., underwent a medical screening, a training, and both treatment conditions including follow-up (for demographic and drug history information see Table S1). On separate test days, each subject inhaled the vapor of a single dose of cannabis (300 µg THC/kg bodyweight) or a placebo. A single dose of vaporized THC has a rapid onset and reaches peak concentration in blood plasma within 10 minutes. The psychoactive effects of cannabis are experienced immediately after smoking, with peak levels of intoxication occurring after 15-30 minutes. Cognitive impairment is most prominent during 2 hours after smoking but may be detectable up to 4-6 hours after smoking (Grotenhermen, 2003; Ramaekers, Kauert, et al., 2006).

Table S1

Subject demographics and drug history

Native language (#)	
English	10
Dutch	13
German	18
Other language	23
Level of education[a] (#)	
High school	30
Bachelor's degree	30
Master's degree	3
Other	1
Drug history [*M* (*SD*)]	
Age of first use	17.8 (2.5)
Years since using cannabis	4.6 (2.2)
Frequency/month	3.1 (1.9)

Note.

[a] Level of education was measured in terms of highest level of education completed.

Fifteen DRM associative word lists were presented on each test day, followed by a recognition test. Misinformation paradigm materials were presented in form of a virtual reality scenario (eyewitness vs. perpetrator), followed by a forced-choice memory interview. The eyewitness scenario showed a fight at a train station (5 min total duration) whereas the perpetrator scenario involved theft of a handbag at a bar (2 min duration, see SI Appendix for more detail). Each participant was exposed once to each scenario on separate test days, counterbalanced with treatment condition (see Fig. S1 for a detailed schematic representation of randomization sequences). Follow-up memory tests were conducted 7 (± 1) days following each test day. All materials and data can be found on the Open Science Framework (https://osf.io/k5v8c/). Detailed explanations of the materials used, procedure, study design, and administration can be found in the supplementary information (SI Appendix).

Figure S1

Schematic representation of counterbalanced randomization sequences A-D with the variables treatment (drug vs. placebo) and mock crime scenario (eyewitness vs. perpetrator)

<table>
<tr><th>Participants (N=64)</th><th colspan="2">Week 1</th><th colspan="2">Week 2: Testday 1</th><th colspan="2">Week 3: Testday 2</th><th>Week 4</th></tr>
<tr><td>Sequence A (n=16)</td><td rowspan="4">Medical exam</td><td rowspan="4">Training Day</td><td>Drug + Eyewitness</td><td rowspan="4">Immediate memory tests</td><td rowspan="4">Follow-up memory tests (Testday 1)</td><td>Placebo + Perpetrator</td><td rowspan="4">Immediate memory tests</td><td rowspan="4">Follow-up memory tests (Testday 2)</td></tr>
<tr><td>Sequence B (n=16)</td><td>Drug + Perpetrator</td><td>Placebo + Eyewitness</td></tr>
<tr><td>Sequence C (n=16)</td><td>Placebo + Eyewitness</td><td>Drug + Perpetrator</td></tr>
<tr><td>Sequence D (n=16)</td><td>Placebo + Perpetrator</td><td>Drug + Eyewitness</td></tr>
</table>

Funding and Disclosure

The authors declare no conflict of interest with respect to this research. This research was supported by the Nederlandse Organisatie voor Wetenschappelijk Onderzoek (NWO) Research Talent grant (nr. 406.16.529), awarded to LK, HO, and JR in 2016.

Acknowledgements

We thank Richard Benning from Maastricht University for creating the virtual reality environments used in this research. Moreover, we are grateful to our colleagues Consuelo Rivas, Sarah Hutchinson, Nicholas Lintzeris, Therese Chan, Man Cho Leung, Kelvin Cao, Vicky Hayes, and Apo Demirkol at the Langton Center, Sydney NSW Australia, and Elodie Chiarovano and Hamish MacDougall from University of Sydney. Further, we are grateful to students Marius Cordt, Julia Gros, Kayley van Uden, Rosalie Mourmans, Floor van der Steur, Didi Delsing, Rachel Heutz, Eva van Rosmalen, Elsa Roudot, Beatrice da Rios, and Naemi Welter for collecting data.

Author Contributions

HO, AB, JR, and LK designed research; LK collected data; LK, ST, HO, AB, and JR analyzed data; and LK, EL, LM, HO, AB, and JR wrote the paper.

Supplementary Information

Participants

Sample size was determined by use of a power calculation based on results of the misinformation method obtained in a previous experiment. In a field study on the effects of alcohol on memory and susceptibility to suggestive cues (van Oorsouw et al., 2015), sober and intoxicated participants (n = 67) were asked to commit a mock crime. Intoxicated participants displayed an increased tendency to go along with misleading questions compared to sober participants with a medium to large effect size (η^2 = .12, which equals Cohen's f = .37). An a priori statistical power analysis by means of G*Power 3.1 (Faul et al., 2007) showed that to detect comparable effects using a slightly more conservative estimate (Cohen's f = 0.30), a sample size of 64 participants would be required, using a repeated measures between-subjects ANOVA with a power of 0.80, and a significance level alpha of 0.05.

The majority of participants completed testing at the lab site in Maastricht (n = 56). Participants were recruited via online as well as offline advertisements posted around Maastricht University and Sydney University. Subjects were screened using a medical history and drug use questionnaire, and underwent a general medical examination including routine laboratory tests through a medical supervisor. Inclusion criteria were: occasional cannabis use (minimum 1/month and maximum 2/week on average during the past 12 months); aged between 18 and 40 years; free from psychotropic medication; good physical health as determined by medical examination and laboratory analysis; absence of any major medical, endocrine and neurological condition; body mass index (weight/height^2) between 18 and 28 kg/m^2; good knowledge and understanding of the English language (≥5 years of English language education), and written informed consent). Exclusion criteria were: history of drug abuse (other than cannabis) or addiction (determined by the medical questionnaire, drug questionnaire and medical examination); pregnancy or lactation (determined by pregnancy test on test day); hypertension (diastolic >90 mmHg; systolic >140 mmHg); history of psychiatric disorders; liver dysfunction; (serious) side effects due to previous cannabis consumption and history of cardiac dysfunctions (arrhythmia, ischemic heart disease, etc.).

Design, Doses and Administration

The study was conducted according to a double-blind, placebo-controlled, 2 (Group: Treatment vs. Control) by 2 (Time: Time 1 vs. Time 2) mixed design with Group as a between subjects factor and Time as a within-subjects factor. All participants were randomly assigned to one out of 4 possible randomization sequences, counterbalancing the order of the treatment and VR scenario (see Fig. S1). Treatment consisted of Bedrobinol, which is medicinal cannabis containing 13.5% THC and <1% cannabidiol (CBD). Placebo consisted of Knaster Hemp, which is a non-psychoactive herbal plant mixture containing 0.0% THC. Bedrobinol was forwarded by the Office for Medicinal Cannabis (Ministerie van Volksgezondheid, n.d.) at the site in Maastricht, and by the company Novachem at the Sydney site.

On separate test days, each subject inhaled the vapor of a single dose of Bedrobinol (300 µg THC/kg bodyweight) or a placebo (150 mg Knaster Hemp). This dose of cannabis has been used in previous studies and can be seen as an average dose (Theunissen et al., 2015). Knaster Hemp has been used as placebo in previous studies (Ramaekers et al., 2016). Administration took place by using the Volcano vaporizer (volume 8l). To prepare the vaporizer, its temperature was set at position nine (225 °C). Ten minutes before administration, the vaporizer was switched on to heat up. By placing the valve balloon on the filling chamber (containing either Bedrobinol or Knaster Hemp), hot air was blended with the THC or Knaster Hemp. For administration, participants were instructed to inhale deeply and subsequently hold their breath for 10 s before exhaling. This continued until the balloon was emptied. An investigator was present in the room while administration took place. Treatment preparation was done by a different researcher from the one performing the administration and testing.

Measures and Materials

Deese/Roediger-McDermott (DRM) Paradigm

The DRM was used to induce spontaneous false memories. Two parallel versions of the DRM were used (day 1: version A, day 2: version B), which were counterbalanced with treatment order. For each version, the study phase consisted of 15 DRM word lists containing ten words each (total 150 stimuli; first ten words of the respective lists by Roediger et al., Stadler et al., 1999). Normative data have shown that these lists vary in both their backward associative strength (BAS, index of the associative strength between the list items and the critical item) and their inter-item associative strength (see Roediger, Watson, et al., 2001; Stadler et al., 1999). An overview of the lists by version and their BAS is displayed in Table S2. The two versions did not statistically significantly differ in BAS [t (28) = .41, p = .68]. Lists were presented visually via PowerPoint, starting with an announcement of the list number (e.g., List 1), followed by the respective study words being shown one-by-one in the center of the screen (duration 2 s per word). All stimuli were separated by a 2 s interstimulus interval, during which the plus symbol was shown in the center of the screen. The total duration of the study phase was 640 s. Participants were instructed to pay attention and try to remember the words as their memory for these words would be tested later in the session.

Table S2

DRM lists with backward associative strength (BAS) parameters

Version A		Version B	
List = Critical Lure	Mean BAS	List = Critical Lure	Mean BAS
Anger	0.181	High	0.109
Black	0.094	Lion	0.125
Bread	0.179	Man	0.131
Car	0.348	Mountain	0.157
Chair	0.284	Music	0.210
City	0.180	Needle	0.205
Cold	0.315	Pen	0.176
Cup	0.154	River	0.145
Doctor	0.234	Shirt	0.242
Foot	0.184	Sleep	0.452
Fruit	0.288	Smell	0.294
Girl	0.129	Soft	0.191
King	0.240	Sweet	0.223
Rough	0.165	Trash	0.118
Smoke	0.197	Window	0.221
Mean	*0.212*	*Mean*	*0.200*
SD	*0.072*	*SD*	*0.087*

Note.

All mean BAS values have been calculated based on Roediger et al. (2001).

For each DRM version, there were two testing phases: one administered immediately (approximately ten minutes after end of study phase), and one administered 7 (± 1) days later. These will be referred to as the immediate and the delayed tests, respectively. Thus, two test versions were created per DRM version, resulting in total in four test instances per participant. The immediate version consisted of 75 words: 45 previously presented words (words 1, 3, and 5 from each list), 10 new words critically related to the studied lists (*critical lures*), 10 new words related to the studied lists (*related lures*, partly taken from words 11-15 from the original DRM lists, and partly from https://wordassociations.net/en), and 10 new unrelated words (*unrelated words*, adopted from other, non-presented DRM lists). The delayed version consisted of 100 words: 55

presented words (10 of these had been already presented at immediate test), 15 critical lures (10 from immediate test), 15 related lures (5 from immediate test), and 15 unrelated words (5 from immediate test). Before testing commenced, participants were instructed to indicate whether they recognized the words from the previous list presentation (yes or no). The words appeared on the computer screen one at a time in random order. The study and immediate testing phases were separated by a subjective high measurement and two 5 min filler tasks (attention tasks: Psychovigilance Test and Deary-Liewald reaction time task; Deary et al., 2011; Loh et al., 2004).

Outcome measures included *true memory rates* (the proportion of studied words correctly recognized at test), false alarm rates for *critical lures* (the proportion of critical lures, i.e., new, strongly related words, that are incorrectly recognized at test, a measure of false memory), false alarm rates for *related lures* (proportion of incorrect recognition of new, related words) false alarm rates for *unrelated words* (proportion of incorrect recognition of new, unrelated words), and net accuracy (ratio of true memory to all memory, an indication of overall ability to discriminate between studied and unstudied items).

Misinformation Paradigm

In order to investigate suggestion-based false memory formation, an adjusted version of the misinformation paradigm was used (Loftus, 2005; Otgaar, Howe, et al., 2016). On separate test days, participants were involved in two distinct crime scenarios, simulated in a fully immersive virtual environment. The virtual reality headset *HTC* Vive was used. The device uses “room scale” tracking technology in order to turn the environment into a 3D space in which the user can move freely. Motion-tracked controllers were used so that the participant could interact with the environment. VR has been previously applied successfully in eyewitness memory studies conducted by our lab (Romeo et al., 2019). An image section of both VR scenarios is displayed in Fig. S2, and respective videos can be viewed on the Open Science Framework (https://osf.io/k5v8c/).

Figure S2

Screenshots from eyewitness (left) and perpetrator (right) virtual reality scenarios

Interviews to assess true and false memory were conducted about 30 min post the VR simulation (i.e., *immediately*) and once during the follow-up session (7 ± 1 days later, i.e., *delayed*). Before the interview, subjects were instructed to answer with yes or no, to be as truthful as possible, and to guess if they did not know the answer. Interviews consisted of non-leading questions about truly presented details (e.g., "Were the seats on the train blue?"), leading questions about suggested details (e.g., "It was a black purse, right?"), and non-leading questions about non-presented details (e.g., "Was there a cat in the bar?"). Details of the latter category varied in their event plausibility (i.e., included questions about plausible details, such as person selling snacks on train, but also implausible details, such as clown on the platform). For the eyewitness scenario, the immediate interview consisted of 25 questions (15 presented, 5 suggested, 5 non-suggested), and the delayed of 29 questions (15 presented, 9 suggested, 5 non-suggested; 20 new and 9 old items). For the perpetrator scenario, the immediate interview contained 25 questions (15 presented, 5 suggested, 5 non-suggested), and the delayed of 27 questions (15 presented, 7 suggested, 5 non-suggested; 20 new and 7 old items[5]). The order of the questions remained the same for all participants. A Qualtrics file on a tablet was used to record the answers.

Eyewitness scenario. In the eyewitness scenario participants were passive witness to the physical attack on a policeman and a security guard by one man (the attacker). In this scenario the crime took place on a platform at a train station and participants witnessed the scenario from inside

[5] For analysis, 2 questions about presented details from the perpetrator scenario were excluded due to VR-related difficulties

the train, among other virtual passengers. Prior to the simulation participants were instructed to imagine that they were on a train traveling with a friend who was sitting opposite to the participant in the train, to remain seated during the simulation, and that at one point a crime would take place, which they should observe. Two min after the crime occurred, the friend (co-witness) engaged in a monologue directed towards the participant and recalled some aspects of the attack. She provided correct information (e.g., the attacker kicked the security guard) as well as misinformation (e.g., there was a police dog on the platform). The simulation ended after she provided all information.

Perpetrator scenario. The perpetrator VR-scenario was designed in a way that participants were in a bar setting where they were able to walk and explore the bar. Furthermore, some avatars would engage in a monologue when participants approached them. Prior to the simulation participants received instructions about the scenario. They were instructed to imagine themselves in the role of a student who had lost their job and was in urgent need of money to pay their rent, thus deciding to obtain some money from someone in their local bar. They were encouraged to explore the bar and instructed to grab the strap of the purse when the people who were playing a game started cheering. The trigger stimulus was presented after 2 min. A motion-tracked controller was used to simulate the purse that was visible for the participants in the VR simulation. A leather handle was mounted onto the controller in order to create the haptic feel of a purse strap. The scenario was manually ended when participants grabbed the controller.

Physiological Measures

Blood samples (5 ml) were taken at THC peak concentration and after completion of the testing procedure (~5 and ~120 min post-administration). All blood samples were centrifuged and the serum was frozen at -20°C and transported to an external lab for pharmacokinetic assessments of cannabinoids (analyses described in Toennes et al., 2015).

Measures of heart rate were taken shortly before (2 min baseline) and during the VR simulations, using the Garmin watch Forerunner® 15 heart rate monitoring belt (recorded every 20 s).

Subjective High

In line with other work from our lab (see e.g., Ramaekers et al., 2009), participants were asked to rate how affected they were by cannabis at the present moment by placing a vertical dash

on two visual analogue scales (100 mm), stating their subjective feeling of cannabis influence (*subjective high*, ranging from "totally not under the influence of cannabis" to "very much under the influence of cannabis") and in comparison to previous experiences with cannabis (*subjective experience*, "much less under the influence" to "much stronger than usual"). Subjects rated this ~20 min, ~80 min and ~110 min after administration.

Procedure

A full timetable of procedures can be viewed in Table S3. Participants who passed all screening procedures were invited for a training session in order to get acquainted with the virtual reality (VR) program, the vaporizer used for administration of the cannabis/placebo, and other tests used during test days. Testing consisted of two similar test days, which were scheduled 7 (± 1) days apart, and one follow-up meeting 7 (± 1) days after the second test day. All meetings took place in a laboratory at the study site, with the exception of 6 final follow-up meetings that were conducted via phone/email due to the participant's unforeseen unavailability. Participants were requested to abstain from drug use 7 days and from alcohol use 24 h prior to testing, to have a light breakfast/lunch before, to not consume any caffeine-containing products throughout the day, and to arrive well-rested. Drug and alcohol screens were conducted before the start of every testing day (incl. the follow-up session). An additional urine pregnancy test was performed for women. All breath alcohol concentration readings showed 0.00 (missing data $n = 7$). All pregnancy tests showed a negative result. In case of a positive drug test before the start of the first testing day, participants were rescheduled for a later date. In case of a positive drug test before the start of the second testing day or final follow-up session, a blood sample was taken but the test day was carried out nonetheless. The sample was analyzed for active THC metabolites, and data from participants with THC levels >2.0 ng/ml was later excluded from further analysis ($n = 1$).

Following the cannabis/placebo administration and the first blood sample, all memory and other cognitive procedures were conducted at fixed intervals during ~120 min post-administration. Upon completion of all tests, a final blood sample was taken. The participant was obliged to remain at the lab until minimum 3 h after drug administration. The researcher would determine, with help of a discharge form, whether it was deemed safe for the participant to go home. After study completion, participants received a short debriefing explaining the goals of the study.

Table S3

Overview of testing procedures

	Procedure	Time after treatment (minutes)
Testday 1		
	Drug and alcohol screens	0
	Baseline questionnaires	0
	Administration cannabis/placebo	0
	Blood sample 1	5
	DRM A study phase	10
	Subjective high 1	20
	Cognitive tasks	22
	DRM A immediate test	32
	Virtual Reality scenario	37
	Cognitive tasks/Questionnaires	50
	Misinformation interview	75
	Subjective high 2	80
	Cognitive tasks	82
	Subjective high 3	110
	Blood sample 2	115
Testday 2		
	Drug and alcohol screens	0
	Baseline questionnaires	0
	Follow-up testday 1:	0
	DRM A delayed test	0
	Misinformation delayed interview	0
	Administration cannabis/placebo	0
	Remaining procedures of testday 2 are equal to testday 1	
Follow-up		
	Drug and alcohol screens	-
	Baseline questionnaires	-
	Follow-up testday 2:	-
	DRM B delayed test	-
	Misinformation delayed interview	-
	Debriefing	-

Note.

Schedule is hypothetical and deviation could occur.

Statistical Approach

To test drug effects on DRM memory recognition performance in the immediate condition, a 2 (Drug: cannabis vs. placebo) x 4 (Level of association: old words, critical lures, related lures, unrelated words) repeated measures analysis of variance (ANOVA) was conducted. The same was repeated for delayed DRM performance. To compare the groups' eyewitness memory performance at immediate and delayed test respectively, we conducted two separate 2 (Group: cannabis vs. placebo) x 3 (Question type: true, suggestive, irrelevant) repeated measures ANOVA. Equivalent analyses were conducted for perpetrator memory. When a statistically significant interaction effect was detected, simple main effects were assessed. If a statistically significant main effect was detected, post-hoc comparisons were conducted using the Bonferroni correction. T-tests were used for pairwise comparisons. Visual inspection of mean scores was also used to aid interpretation. A difference was considered statistically significant for p-values < 0.05. Cohen's *d* (pairwise comparisons) and ω^2 (ANOVA) were calculated as effect size estimates. All values are reported including two decimals, except for p-values where three decimals are reported. The assumptions underlying all analyses were checked. For ANOVA, assumptions were checked by visual inspections of boxplots for normality. No gross violations of assumptions were detected for ANOVA. When sphericity was violated, a Greenhouse–Geisser correction was applied to the degrees of freedom.

To exclude any potential differences caused by the study site, all main analyses to investigate effects of cannabis in the two false memory paradigms were repeated, excluding the participants recruited in Sydney ($n = 8$, *Site* section, SI). Only results where a change in effects was found are reported. Subjective high results were analysed using repeated measures ANOVA. All analyses were conducted using JASP, version 0.11.1 (JASP Team, 2020).

Additional Analyses

Site

All effects detected in the DRM immediate analyses remained unaffected when including only the Maastricht participants ($n = 56$). Similarly, the interaction between Drug and Level of association was statistically significant in this reduced sample; however, statistical significance was not maintained for some effects according to the simple main effects analysis ($n = 54$).

Whereas statistically significant effects had been detected before true memory and false memory of critical lures, the p-values for these now exceeded the alpha level of .05 (p = .075 and p = .12, respectively). These effects thus appear not very robust.

With regard to the immediate analyses of the eyewitness misinformation task, the interaction remained statistically significant, but the simple main effect for questions about non-suggested details lost significance (p = .11; n = 28). For the immediate analyses of the perpetrator scenario, the main effect of Group did not attain statistical significance (p = .06). All other effects reported remained unchanged.

Subjective high and THC serum concentration

Mean values for subjective high and subjective experience for both placebo and cannabis conditions as a function of time are shown in Fig. S3. Repeated measures ANOVA revealed a statistically significant difference in subjective high [F (1, 62) = 529.50, p < .001, ω^2 = .81] and subjective experience [F (1, 61) = 374.55, p < .001, ω^2 = .77] between both conditions. A summary of mean (*SD*) and range of THC, THC-OH and THC- COOH concentrations in serum as a function of time after smoking is given in Table S4.

Figure S3

Visual analogue scale ratings (0-10 cm) of subjective high (a) and subjective experience (b) as a function of time. Error bars represent 95% CIs.

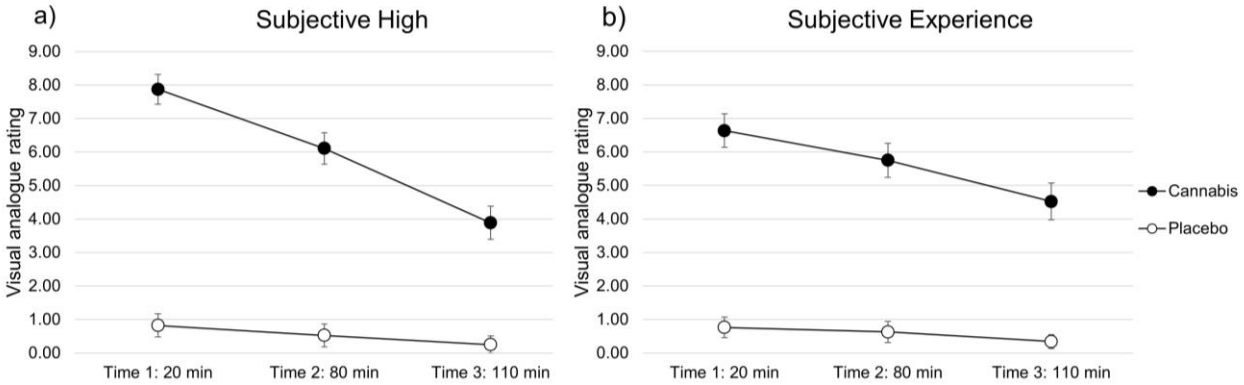


Table S4

Serum concentration values

	Mean	SD	Range
Sample 1[1]			
THC	77.31	64.37	0.90 - 325.70
THC-OH	4.37	3.15	0.50 - 15.90
THC-COOH	10.02	7.58	0.00 - 39.30
Sample 2[2]			
THC	4.19	2.16	0.70 - 10.90
THC-OH	1.66	0.75	0.60 - 4.20
THC-COOH	11.21	7.30	1.70 - 44.80

Note.

[1]Sample taken immediately after administration. Missing data $n = 3$

[2] Sample taken after last testing procedure. Missing data $n = 10$

Repeated vs. Novel Recognition Test Items

Primary analyses pertaining to the delayed condition as reported in the main manuscript were conducted on all recognition test items. Since the DRM and misinformation delayed tests contained a combination of once-presented (novel items) and items that were repeatedly tested (once during the immediate test and then again at delayed test), we report here analyses that distinguish these to better isolate pure effects of THC on encoding.

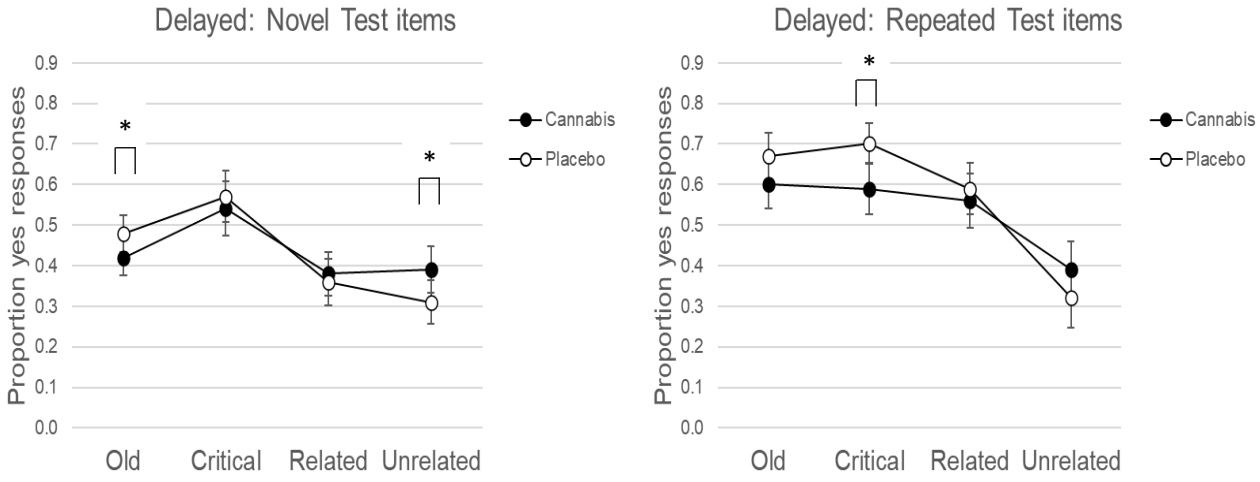
DRM. A 2x2x4 repeated measures ANOVA was conducted using the factors Novelty (Novel vs. Repeated), Drug (THC vs. placebo), and Level of association (Old vs. Critical vs. Related vs. Unrelated). Separate means plots for novel and repeated items are depicted in Figure S4, and separate mean scores and SEs are displayed in Table S5. Novel items were: n=45 old/presented items, n=5 critical lures, n=10 related lures, and n=10 unrelated lures. Repeated items were n=10 old, n=10 critical, n=5 related, and n=5 unrelated items. The three-way interaction was not statistically significant, but significant effects were detected for the Novelty x Level of Association [F (2.72, 157.79) = 21.11, p <.001, ω^2 =.05] and the Drug x Level of Association interactions [F (2.55, 157.79) = 7.63, p <.001, ω^2 = .025], as well as a large main effect of Novelty [F (1, 60) = 140.86, p < .001, ω^2 = .13]. Recognition rates for repeated items were generally higher, compared to the items that were only tested once [t (60) = 11.87, p_{Bonf} < .001, Cohen's d = 1.52].

Inspecting simple main effects of Drug as moderated by the factors Level of association and Novelty, we detected the following statistically significant differences: the placebo condition outperformed the cannabis condition on true recognition when it came to novel test items [F (1, 60) = 5.85, p = .019, Cohen's d = .31], but this difference did not quite reach statistical significance when looking at the repeated test items. [F (1, 60) = 3.63, p = .062, Cohen's d = .24]. Regarding false recognition of critical lures, the placebo condition was more susceptible to false alarms for critical lures that had also been presented at the immediate test [F (1, 60) = 9.10, p = .004, Cohen's d = .39], but there was no significant difference for novel critical lures [F (1, 60) = .60, p = .443, Cohen's d = .10]. As reported in the main chapter, false recognition of related lures did not differ between conditions regardless of whether they were novel or repeated (p's > .5). Finally, cannabis induced higher false recognition of unrelated lures particularly with regard to novel lures [F (1, 60) = 8.74, p = .004, Cohen's d = .38]; this effect was on the border of statistical significance for repeated lures [F (1, 60) = 3.97, p = .051, Cohen's d = .26].

In summary this pattern indicates on the one hand a global THC-induced encoding impairment: when participants studied the word lists while sober, they were better at correctly recognizing studied words one week later, compared to when having studied them during intoxication. This advantage of placebo over cannabis however also played out in terms of increased false recognition of (repeated) critical lures, which are similar to studied words in content and therefore easily confusable. THC in that regard appeared to reduce the testing effect, since repeated critical lures were more often falsely recognized in the placebo condition. Finally, false alarms to unrelated and previously untested lures were elevated, indicating that a THC-induced response or yes-saying bias was detected not only during acute intoxication but also when sober again.

Figure S4

DRM mean scores in proportions from delayed test for novel items (a) and repeated items (b) by drug condition



Note. *$p < 0.05$, **$p < 0.01$, pairwise comparisons. Error bars represent 95% CIs.

Misinformation paradigms. For the misinformation tasks, analyzing the recognition test data split into novel and repeated items was not feasible due to the small numbers of repeated items (some n <5, all numbers displayed in Table S5). Thus, we repeated the repeated measures ANOVA for the eyewitness and perpetrator delayed conditions reported in the main manuscript, this time only taking into account the novel items. Running the two RM ANOVA only using these untested items, we detected no statistically significant interaction of Drug with Level of association, or Drug main effect in the perpetrator condition. However, a statistically significant interaction was detected in the eyewitness condition [F (2, 120) = 4.16, p = .018, ω^2 = .01], which was driven by the placebo group demonstrating elevated suggestion-based false memories for the eyewitness scenario at follow-up [F (1, 60) = 4.29, p = .043, Cohen's d = .17]. Whether cannabis during an event protects from later misinformation could be explored in further research; however this is not a robust finding given that the proportions in this case were based on only four items.

Table S5

Means and SEs from DRM and Misinformation parameters (rates in proportions) split by Novelty (novel vs. repeated)

	Novel test items					Repeated test items				
		Cannabis		Placebo			Cannabis		Placebo	
	n test items[a]	*M*	*SE*	*M*	*SE*	*n* test items[a]	*M*	*SE*	*M*	*SE*
DRM										
True recognition (old)	45	0.42	0.02	.48	0.02	10	0.60	0.03	0.67	0.03
False alarms (critical)	5	0.54	0.03	0.57	0.03	10	0.59	0.03	0.70	0.03
False alarms (related)	10	0.38	0.03	0.36	0.03	5	0.56	0.03	0.59	0.03
False alarms (unrelated)	10	0.39	0.03	0.31	0.03	5	0.39	0.04	0.32	0.04
Misinformation Eyewitness										
Presented	10	0.61	0.03	0.63	0.03	5	0.92	0.03	0.96	0.02
Suggested	4	0.1	0.03	0.19	0.03	5	0.27	0.04	0.16	0.03
Non-suggested	5	0.17	0.03	0.1	0.02		NA			
Misinformation Perpetrator										
Presented	9	0.58	0.04	0.63	0.04	4	0.73	0.05	0.77	0.04
Suggested	5	0.28	0.04	0.28	0.03	2	0.29	0.07	0.24	0.06
Non-suggested	5	0.07	0.02	0.03	0.01		NA			

Note.

[a] Number of recognition test items based on which the rates were calculated

Chapter 5

Remembering Molly: immediate and delayed false memory formation after acute MDMA exposure

Submitted as:

Kloft, L., Otgaar, H., Blokland, A., Toennes, S. W., & Ramaekers, J. G. (submitted). Remembering Molly: immediate and delayed false memory formation after acute MDMA exposure. Under review at *European Neuropsychopharmacology*.

Abstract

The entactogen 3,4-Methylenedioxymethamphetamine (MDMA) is increasingly being recognized for its therapeutic potential but is also widespread in nightlife settings where it may co-occur with crime. Since previous research detected impaired verbal memory during acute MDMA intoxication, understanding the drug's ramifications in an applied legal context becomes crucial. We conducted a double-blind, placebo-controlled trial to examine acute and delayed effects of MDMA (75 mg) on false memory in 60 healthy volunteers, using three well-established false memory methods: a basic, associative word list (Deese/Roediger-McDermott (DRM)) paradigm and two applied misinformation tasks using a virtual reality crime. Memory was tested immediately (encoding and retrieval under drug influence) and 1 week later (retrieval when sober). Small MDMA-induced impairments of true memory in the word list task were detected at both time points. On the immediate test, MDMA increased related but non-critical lures, whereas after a delay MDMA reduced critical lures, as these were similar to old words in content and were to some extent presented on the prior test. Episodic memory assessed in the misinformation tasks was not consistently affected. Findings indicate no heightened vulnerability to external suggestion in response to MDMA intoxication at the observed dose. Recommendations for future applied legal psychological research include adding measures of recall on top of recognition, using study designs that separate the different memory phases, and potentially testing higher doses. Further research on false memories and suggestibility using imagination procedures can also be relevant for the clinical context.

Introduction

3,4-Methylenedioxymethamphetamine (MDMA) also known under its street name "Molly" is the major psychoactive compound in ecstasy pills, a popular nightlife drug, and among the most commonly used illicit substances worldwide (EMCDDA, 2012; UNODC, 2019; Winstock et al., 2017). MDMA is a phenethylamine and a potent indirect monoaminergic agonist, producing stimulant amphetamine-like properties. In addition, it facilitates release and reuptake inhibition of serotonin (5-HT), thus combining entactogenic effects such as increased euphoria and sociability with weak psychedelic effects (5-HT_{2a} agonist; Nichols, 1986; Vollenweider et al., 1998). (Nichols, 1986; Vollenweider et al., 1998). Currently, MDMA is under empirical scrutiny in clinical trials as an addition to psychotherapy to treat post-traumatic stress disorder (PTSD, Mithoefer et al., 2019). In line with its unique pharmacological profile, MDMA has been observed to affect cognition in diverse ways. While some cognitive domains are left intact or even improved (e.g., attention, psychomotor performance, Dumont & Verkes, 2006; Lamers et al., 2003; Ramaekers, Kuypers, et al., 2006; Vollenweider et al., 1998), others tend to be prone to impairment. Specifically, acute MDMA intoxication has been found to impair *true* memory functioning by, for example, decreasing verbal recall (Kuypers & Ramaekers, 2005).

Evidence that MDMA affects memory functioning comes from two lines of experimentation. In retrospective studies, comparisons of current or abstinent MDMA users with polydrug-users or drug-naïve subjects have revealed neurocognitive deficits particularly in prospective (Platt et al., 2019), verbal and working memory (e.g., lower recall in MDMA users, Kalechstein et al., 2007; Nulsen et al., 2010; Rogers et al., 2009). However, two recent well-controlled studies concluded that effect sizes of memory deficits tended to be small, and that light ecstasy use was not associated with clinically deficient verbal memory performance (Kuypers et al., 2016; Rogers et al., 2009). Similarly, placebo-controlled studies have shown that a single dose of MDMA (75 mg) reduced verbal memory during acute intoxication, but this impairment was transient and could not be detected 24 h later (de Sousa Fernandes Perna et al., 2014; Kuypers et al., 2013; Kuypers & Ramaekers, 2005; Kuypers et al., 2016; van Wel et al., 2011). Recently, Doss and colleagues (Doss, Weafer, Gallo, et al., 2018b) found that MDMA (1 mg/kg) administered before encoding or retrieval did not impair overall memory accuracy in an emotional episodic memory task. At encoding, however, MDMA attenuated the recollection of positive and negative pictures (*remember*) but left familiarity (*know*) judgements intact. They also reported a trend for

MDMA to increase false alarm rates at retrieval, predominantly for positive stimuli. Therefore, MDMA seems to affect memory in consistent but subtle ways.

In terms of pharmacological similarity, a finding of relevance here is that Ballard and colleagues (2012) found that the non-specific stimulant dextroamphetamine increased false memories in a word list task when administered prior to encoding, with memory tested 48 h later under sober conditions (compared to cannabis). However, stimulant properties might be less of a determinant of MDMA's effects on memory, since these have been found to be specifically mediated by its 5-HT_{2A} agonism (van Wel et al., 2012), i.e., blockage of 5-HT_{2A} prevents MDMA's usually observed impairment of verbal memory recall. Thus, MDMA might more closely resemble serotonergic psychedelics when it comes to memory. The only contemporary episodic memory study that has been conducted with psychedelics (Barrett et al., 2018) examined effects of psilocybin (psychoactive ingredient of 'magic mushrooms/truffles') and found that the drug decreased verbal recall (administered prior to encoding with memory tested shortly after). The study did not report how psilocybin affected false recall or recognition.

Solid and reliable memory functioning is of high relevance to the legal field, particularly in court cases where legal decision-making is largely based on testimonies from witnesses, victims, and/or offenders. However, witnesses and suspects are frequently intoxicated, and particularly so in cases of violent crime (Evans et al., 2009; Kloft et al., 2021; Francesca T Palmer et al., 2013). Violence and substance use commonly co-occur in nightlife settings. For example, a Norwegian study showed that illicit drug use was more prevalent among people who reported being involved in physical violence during nightlife, 29% of whom reported being MDMA/ecstasy users (N = 103; Nordfjaern, 2017). Therefore, it is likely that a substantial number of people who are involved in or witness a crime in this setting are intoxicated with MDMA.

Intoxication during a crime, during police interviewing, or both might render an individual particularly susceptible to spontaneous false memories (i.e., memories of nonexperienced events/details) or false memories due to external suggestion (Loftus, 2016; Mazzoni, 2002; Otgaar, Howe, et al., 2016). In a recent study from our lab (Kloft et al., 2020), 64 healthy participants received vaporized cannabis or placebo and completed three false memory tasks during the acute intoxication phase (*immediate* condition) and at a sober 1-week follow-up (*delayed* condition). Tasks included the Deese/Roediger–McDermott (DRM) word list paradigm, in which people spontaneously falsely remember words not presented in an associatively related list of words

(Deese, 1959; Gallo, 2010; Roediger & McDermott, 1995), and two versions of the misinformation paradigm, in which exposure to misleading information following an event often leads people to report suggested details in their final memory statements (Loftus, 2005). Cannabis elevated susceptibility to false memory across all tasks: in the DRM, intoxicated participants had higher false recognition rates of words that had low or no association to studied lists than a placebo condition, and in the misinformation tasks, they exhibited higher false memory rates for both suggestive as well as neutral questions about virtual reality eyewitness and perpetrator scenarios. False memory effects were most pronounced during acute intoxication, with only subtle impairments detected at a sober 1-week follow-up. To date, no research has investigated how MDMA impacts false memory production. Given the applied relevance of examining potential false memory effects of MDMA, we conducted a randomized, placebo-controlled study examining MDMA's effects on false memory formation using three well-established false memory tasks.

A similar design as used in Kloft and colleagues' study (Kloft et al., 2020) to assess the effects of MDMA on false memory formation was employed. Participants received 75 mg MDMA and placebo on separate testing days 7 (±1) days apart, and were subjected to the DRM (within-subjects) and one virtual reality (VR) scenario plus misinformation task per test-day (counterbalanced between-subjects). Memory tests were administered when drug effects were maximal (between 60-120 min post administration, immediate condition), and at a 1-week sober follow-up meeting. Given that previous studies indicated MDMA-induced impairments of true memory (memory of truly presented stimuli; e.g., Kuypers & Ramaekers, 2005) but potentially also false memory (Doss, Weafer, Gallo, et al., 2018b), we generally expected MDMA to impair memory performance, reflected in higher false memory and lower true memory rates, compared to placebo.

Experimental Procedures

A detailed description of the materials used, procedure, study design, and administration is provided in the Supplementary Information (SI), and is briefly summarized here. All materials and data can be found on the Open Science Framework (https://osf.io/8tjkr/).

The present study employed a randomized, placebo-controlled, double-blind mixed design as used previously (Kloft et al., 2020). Sixty-one healthy participants with previous MDMA experience (lifetime use 3-60 occasions) were included in the study (28 female, 33 male, mean age and *SD*: 23.0, 3.3, age range: 18-32) of which 60 completed all procedures, i.e., underwent a pre-screening, a medical screening (assessment of medical history, physical examination including blood- and urine analyses and electrocardiogram), a VR and cognitive task training, and both treatment conditions including follow-up (for demographic and drug history information, see Table 1). Participants with prior drug experience were recruited in order to comply with local ethical regulations. Subjects were asked to abstain from drug use 7 days before and from alcohol use 24 h before each test day, and were drug-screened and breathalyzed before each testing occasion. Participants received a single dose of MDMA (75 mg) and placebo on separate test days. This dose has previously been shown to impair verbal memory performance (Kuypers & Ramaekers, 2005), and is also relevant from a clinical point of view (Mithoefer et al., 2018). Psychoactive effects of MDMA appear between 30-60 min after ingestion lasting for 2-4 h, and plasma levels peak at 90-120 min (Dumont & Verkes, 2006). A venous blood sample was collected 90 min post-ingestion in order to assess concentrations of MDMA and its metabolite 3,4-methylenedioxyamphetamine (MDA). Subjects rated their subjective level of intoxication on 100mm visual analogue scales.

Table 1

Subject demographics and drug history

Native language	
English	26%
Dutch	23%
German	25%
Other language	26%
Level of education[a]	
High school	52%
Bachelor's degree	38%
Master's degree	10%
Years of English education [*M* (*SD*)]	11.0 (4.1)
MDMA history [*M* (*SD*)]	
Age of first use	19.6 (1.9)
Years since using MDMA	3.5 (2.2)
Times used	12.4 (11.4)
Frequency/past year	3.9 (2.4)
Regular dose (mg, *n* = 39)	230 (222.0)
Regular dose (pills, *n* = 16)	Range: 0.5-2
Lifetime drug use (at least once)	
Alcohol	97%
Cannabis	90%
Amphetamines	28%
Cocaine	48%
LSD	26%
Truffles/psychedelic mushrooms	61%

Note.

[a] Level of education was measured in terms of highest level of education completed.

The study was approved by the Medical Ethics Committee of Maastricht University and was conducted according to the Declaration of Helsinki (amended in 2013, Fortaleza) and in accordance with the Medical Research Involving Human Subjects Act (WMO). All participants were fully informed of all procedures, possible adverse reactions, legal rights and responsibilities, expected benefits, and their right for voluntary termination without consequences. All subjects gave written informed consent and received financial compensation (€150) for their participation.

A permit for obtaining, storing and administering MDMA was obtained from the Dutch drug enforcement administration. The study was registered at the Netherlands National Trial Register (Nederlandse Trial Register, NL7423).

False Memory Measures

The same false memory tasks as in Kloft et al. (2020) were used in this study. The DRM task was employed to assess spontaneous false memory. Fifteen lists each containing ten associatively related words (e.g., *bed, dream, wake, rest, tired* etc.) were presented on each test day (study phase), followed by two unrelated attention tasks (total ~10 minutes), and a subsequent recognition test (testing phase, immediate). The recognition test contained old, previously studied words, and new, non-studied words of differing levels of association to the studied lists: *critical lures* (i.e., *sleep*) were highly associated to the studied words, *related lures* were less associated (e.g., nap), whereas *unrelated lures* were completely unassociated (e.g., table). *Old* words had been previously presented, thus had the highest association.

For each DRM version (two parallel versions, counterbalanced with treatment order), there were two testing phases: one administered immediately (approximately ten minutes after end of study phase), and one administered 7 (± 1) days later. These will be referred to as the immediate and the delayed tests, respectively. Thus, two test versions were created per DRM version, resulting in total in four test instances per participant. The immediate version consisted of 75 words: 45 previously presented words (words 1, 3, and 5 from each list), 10 new words critically related to the studied lists (*critical lures*), 10 new words related to the studied lists (*related lures*, partly taken from words 11-15 from the original DRM lists, and partly from https://wordassociations.net/en), and 10 new unrelated words (*unrelated words*, adopted from other, non-presented DRM lists). The delayed version consisted of 100 words: 55 presented words (10 of these had been already presented at immediate test), 15 critical lures (10 from immediate test), 15 related lures (5 from immediate test), and 15 unrelated words (5 from immediate test). Before testing commenced, participants were instructed to indicate whether they recognized the words from the previous list presentation (yes or no). The words appeared on the computer screen one at a time in random order. The study and immediate testing phases were separated by a subjective high measurement and two 5 min filler tasks (attention tasks: Psychovigilance Test and Deary-Liewald reaction time task; Deary et al., 2011; Loh et al., 2004).

Two versions of the misinformation paradigm were used to measure suggestion-based false memory. Participants were exposed to one mock crime scenario per test day (eyewitness vs. perpetrator), counterbalanced with treatment condition, and presented in a fully immersive interactive virtual reality (VR) environment, using the virtual reality headset *HTC* Vive. VR technology allows for high degrees of experimental control combined with high ecological validity (Kloft et al., 2021; van Gelder et al., 2014). In the eyewitness scenario (5 min total duration), participants were virtually seated on a train witnessing a fight between a man, a police officer and a security guard outside on the platform of a train station. Misinformation was introduced through a virtual co-witness recounting true and false details related to the scenario, but also through suggestive questions in the later memory test. In the perpetrator scenario (2 min duration) the participant could move around in a crowded bar and was instructed to steal a purse (grabbing a physical controller). Misinformation was introduced through leading questions at the memory test. The memory test assessed recognition memory in a forced-choice interview, administered 30 min after encoding either scenario (*immediate*), and once during the follow-up session (7 ± 1 days later, i.e., delayed), and consisted of questions about truly presented details in the scenario (*presented*), leading questions about non-presented details (*suggested*), and control questions about non-presented details (*non-suggested*). As explained in Kloft et al. (2020) the (non)presented details varied in their strength of association to the VR scenario, with presented details strongly linked, suggested details moderately linked, and non-suggested details weakly linked to the experienced scenario[6].

Before the interview, subjects were instructed to answer with yes or no, to be as truthful as possible, and to guess if they did not know the answer. Interviews consisted of non-leading questions about truly presented details (e.g., “Were the seats on the train blue?”), leading questions about suggested details (e.g., “It was a black purse, right?”), and non-leading questions about non-presented details (e.g., “Was there a cat in the bar?”). Details of the latter category varied in their event plausibility (i.e., included questions about plausible details, such as person selling snacks on train, but also implausible details, such as clown on the platform). For the eyewitness scenario, the immediate interview consisted of 25 questions (15 presented, 5 suggested, 5 non-suggested), and the delayed of 29 questions (15 presented, 9 suggested, 5 non-suggested; 20 new and 9 old items).

[6] See https://osf.io/8tjkr/ for videos of the scenarios and interview transcripts

For the perpetrator scenario, the immediate interview contained 25 questions (15 presented, 5 suggested, 5 non-suggested), and the delayed of 27 questions (15 presented, 7 suggested, 5 non-suggested; 20 new and 7 old items[7]). The order of the questions remained the same for all participants. A Qualtrics file on a tablet was used to record the answers.

Importantly, all follow-up memory tests for all tasks consisted of a combination of old (i.e., from immediate condition) and new test items.

Statistical Analysis

Primary Analyses

True memory (proportion of correctly recognized stimuli, or hit rate) and false memory rates (false alarm rate, proportion of incorrectly recognized stimuli, cumulative and for each level of association) were calculated for the misinformation tasks and DRM, where hit rates = *p*("old"|target) and false alarm rate = *p*("old"| critical, related, unrelated, or all types of lure). In addition, signal detection parameters were calculated to assess sensitivity as $d' = Z(\text{hit rate}) - Z(\text{false alarm rate})$ with higher values signaling greater discrimination ability, and response bias as $c = -1/2\ [(Z(\text{hit rate}) + Z(\text{false alarm rate})]$, where positive values indicate conservative and negative values indicate liberal response tendencies (Macmillan & Creelman, 2004). Signal detection parameters were calculated based on all lure types. A correction was applied to true memory rates of 1 and false memory rates of 0 ($1 - 1/2n$ and $1/2n$, respectively) (Wixted & Lee, 2013).

To test MDMA effects on DRM recognition performance at immediate and delayed test respectively, two separate 2 (Drug: MDMA vs. placebo) x 4 (Level of association: old words, critical lures, related lures, unrelated words) repeated measures ANOVAs were conducted (within-subjects comparison). To compare between groups' eyewitness memory performance at immediate and delayed test respectively, two separate 2 (Group: MDMA vs. placebo) x 3 (Level of association: presented, suggested, non-suggested) repeated measures ANOVAs were conducted When a statistically significant interaction effect (i.e., between Drug/Group and Level of

[7] For analysis, 2 questions about presented details from the perpetrator scenario were excluded due to VR-related difficulties

association) or main effect of Drug/Group was detected, simple main effects were assessed to compare MDMA and placebo at each level of association. Two-tailed t-tests were used for pairwise comparisons of the signal detection parameters. Visual inspection of mean scores was also used to aid interpretation. A difference was considered statistically significant for p-values < 0.05. Cohen's *d* (pairwise comparisons) and ω^2 (ANOVA) were calculated as effect size estimates. For ANOVA, assumptions were checked by visual inspections of boxplots for normality. No gross violations of assumptions were detected for ANOVA. When sphericity was violated, a Greenhouse–Geisser correction was applied to the degrees of freedom. Analyses were conducted using JASP, version 0.12.2 (JASP Team, 2020).

In addition, equivalence tests were carried out to further explore null findings and to determine equivalence of false memory performance during MDMA and placebo. Equivalence testing can be used to statistically reject the presence of effects large enough to be considered meaningful (Lakens, 2017; Lakens et al., 2018). When a hypothesis test is non-significant, this method can be used to improve inferences about the presence or absence of an effect.

Additional Analyses

Analyses to explore whether external factors (i.e., VR telepresence, the subjective feeling of being immersed) confounded encoding during the VR experience were conducted and are reported in the Supplementary Information. Similarly, analyses discriminating between novel and repeated recognition test items were conducted in order to further distinguish MDMA effects on encoding and are reported in the SI.

Results

Means and standard errors for all memory parameters are displayed in Table 2. Demographic information, intoxication parameters, and additional analyses can be viewed in the Supplementary Information.

Table 2

Means from DRM and Misinformation parameters (rates in proportions): M (SE)

	MDMA condition		Placebo condition	
	Immediate	*Delayed*	*Immediate*	*Delayed*
DRM	*n* = 58	*n* = 57	*n* = 58	*n* = 60
True recognition (old)	.66 (.02)	.47 (.02)	.72 (.02)	.51 (.02)
False alarms (critical)	.53 (.03)	.54 (.03)	.51 (.03)	.61 (.02)
False alarms (related)	.27 (.02)	.41 (.03)	.20 (.02)	.40 (.02)
False alarms (unrelated)	.18 (.02)	.28 (.03)	.17 (.02)	.25 (.03)
Sensitivity *d'*	.98 (.09)	.17 (.05)	1.23 (.09)	.25 (.05)
Response bias *c*	.03 (.05)	.18 (.06)	-.01 (.04)	.11 (.05)
Misinformation Eyewitness	*n* = 30	*n* = 29	*n* = 31	*n* = 30
Presented	.75 (.02)	.72 (.02)	.77 (.02)	.75 (.02)
Suggested	.03 (.01)	.07 (.02)	.07 (.02)	.16 (.02)
Non-suggested	.01 (.01)	.06 (.02)	.03 (.02)	.11 (.03)
Sensitivity *d'*	2.30 (.08)	2.10 (.09)	2.28 (.11)	1.86 (.09)
Response bias *c*	.42 (.04)	.42 (.05)	.34 (.04)	.22 (.05)
Misinformation Perpetrator	*n* = 30	*n* = 29	*n* = 30	*n* = 30
Presented	.62 (.02)	.68 (.03)	.61 (.03)	.61 (.03)
Suggested	.25 (.03)	.27 (.04)	.24 (.03)	.23 (.02)
Non-suggested	.01 (.01)	.03 (.01)	.03 (.02)	.01 (.01)
Sensitivity *d'*	1.46 (.09)	1.53 (.12)	1.47 (.12)	1.47 (.09)
Response bias *c*	.41 (.04)	.25 (.06)	.41 (.06)	.40 (.07)

MDMA Concentration Levels and Subjective Intoxication

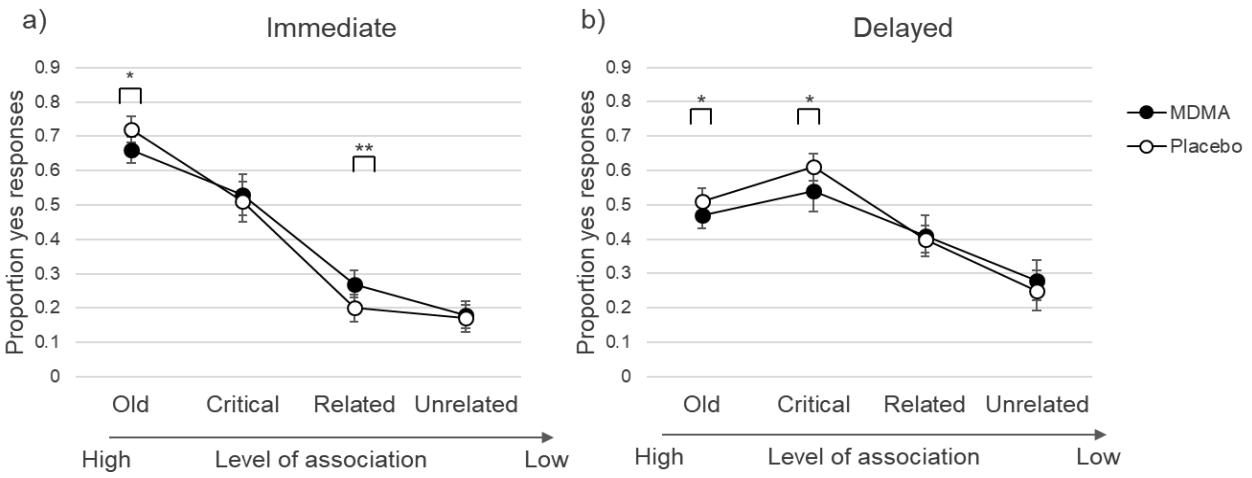
MDMA concentrations in serum ranged from 51.2-287.9 ng/ml (M = 147.9, SD = 46.0) and MDA levels ranged from 0.0-137.3 ng/ml (M = 12.1, SD = 23.5). Administration of MDMA was associated with increased ratings of intoxication on all visual analogue scales (all p's < .001, effect size ω^2 = .56-.58, see SI for details).

DRM Paradigm

Figure 1 depicts the mean DRM true and false memory rates for the two drug conditions at immediate (1a) and delayed test (1b). Figure 1a shows that, as would be expected, memory rates were overall highest for old (studied) words, and gradually decreasing for new (non-studied) words with decreasing levels of associations. Differences in immediate DRM performance between MDMA and placebo seemed to exist for some word categories but not others. This was reflected in a statistically significant Drug x Level of association interaction [F (2.62, 143.99) = 3.98, p = .013, ω^2 = .02]. MDMA decreased true memory [F (1, 55) = 4.05, p = .049, Cohen's d = .27] and increased false memory of related lures [F (1, 55) = 9.70, p = .003, Cohen's d = .42]. However, MDMA did not affect false memory for critical or unrelated lures. Better memory performance during placebo as opposed to the MDMA condition was also reflected in higher discrimination ability d' [t (55) = -2.30, p = .025, Cohen's d = -.31], but response bias c was unaffected.

Figure 1

DRM mean scores in proportions from immediate test (a) and delayed test (b) by drug condition



Note. *p < 0.05, **p < 0.01, pairwise comparisons. Error bars represent 95% CIs. Note that yes responses to old words signify correct recognition, whereas yes responses to critical, related, and unrelated lures signify false recognition.

At the delayed test (Figure 1b), the level of association effect was still visible for all three false memory rates in that there was an apparent gradual decrease in recognition from higher to lower associated lures, but this time true memory rates were overall lower than false memories for

critical lures[8]. The delayed test also revealed a statistically significant Drug x Level of association interaction [F (2.61, 145.88) = 3.86, p = .015, ω^2 = .01]. MDMA decreased true memory [F (1, 56) = 5.17, p = .027, Cohen's d = .30] and false memory for critical lures [F (1, 56) = 5.11, p = .028, Cohen's d = .30]. False memory rates of related and unrelated lures were not affected by the drug, and neither were any of the signal detection parameters at the delayed test.

Misinformation Paradigm

Eyewitness Scenario

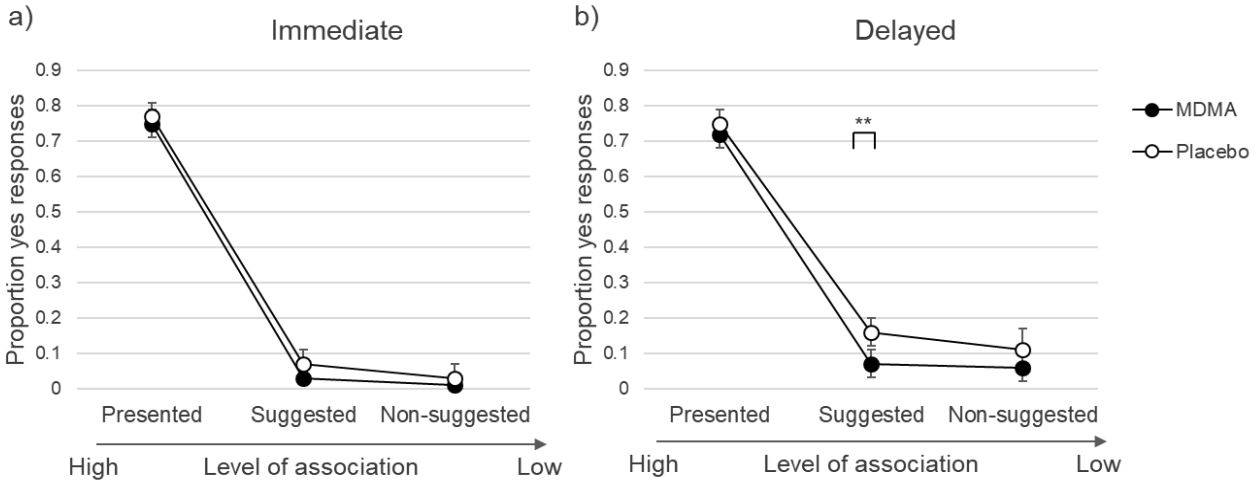
Figure 2 shows the MDMA and placebo groups' true and false memory rates for the eyewitness VR scenario at the immediate (2a) and delayed test (2b). As Figure 2a shows, overall, true memory rates at the immediate test were high while suggestion-based and non-suggestion-based false memory rates were rather low. Moreover, judging from the figure the MDMA and placebo group seemed to have performed rather similarly. In line with this, no statistically significant Group x Level of association effect or main effect of Group were detected. Neither sensitivity nor response bias were found to statistically differ between groups.

However, at the delayed test some statistical differences between MDMA and placebo groups were detected. A statistically significant main effect of Group [F (1, 57) = 7.88, p = .007, ω^2 = .06] indicated that the placebo group had overall higher recognition rates. This effect was driven by the placebo group showing elevated suggestion-based false memories [F (1, 57) = 8.68, p = .005, Cohen's d = .77]. Analysis of the signal detection parameters showed that response bias but not sensitivity differed statistically significantly between groups [t (57) = -2.70, p = .009, Cohen's d = .70, t (57) = -1.90, p = .063, respectively] with the MDMA group showing more conservative responding compared to the placebo group at follow-up (see Table 1).

[8] This could stem from a potential confounding effect of true memory being measured primarily with words that were not present during the immediate test, whereas false memory for critical lures was measured with ten critical lures from the immediate test and 5 new ones.

Figure 2

Eyewitness mean scores in proportions from immediate test (a) and delayed test (b) by drug condition



Note. **p < 0.01, pairwise comparisons. Error bars represent 95% CIs. Note that yes responses to presented items signify correct recognition, whereas yes responses to suggested and non-suggested items signify false recognition.

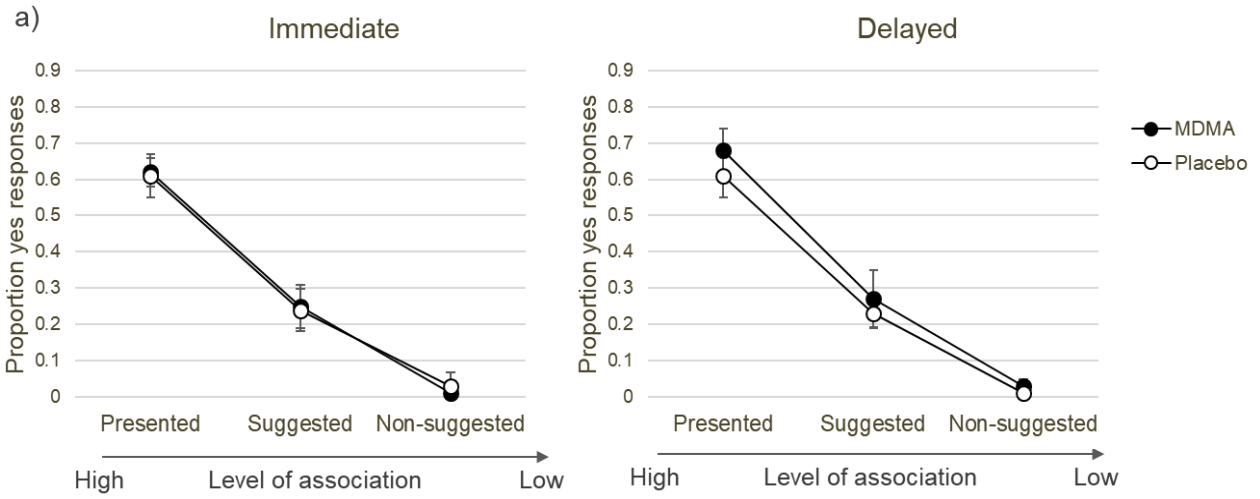
Perpetrator Scenario

Figure 3 depicts the two groups' true and false memory rates for the perpetrator VR scenario in the immediate (3a) and delayed conditions (3b). A clear level of association effect in the expected direction is visible in both figures. At the immediate test, again no visible differences in memory performance emerged (Fig. 3a), and statistically no interaction or main effect of Group was detected, meaning that MDMA-intoxicated individuals showed similar memory performance as their sober counterparts at immediate test. Analysis of the signal detection parameters did not show significant differences between groups.

At the delayed test (Fig. 3b), no statistically significant interaction effect or Group main effect emerged (however note that $p = .052$ for Group main effect). No statistically significant group differences were detected on the signal detection parameters.

Figure 3

Perpetrator mean scores in proportions from immediate test (a) and delayed test (b) by drug condition



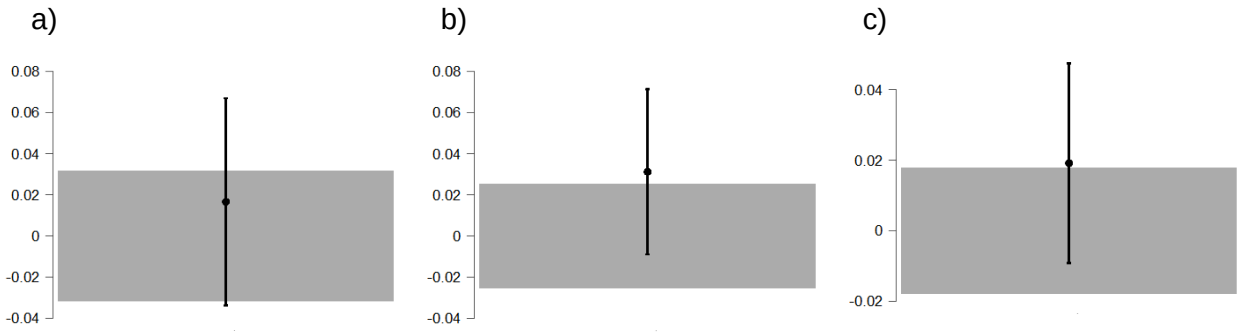
Note. Error bars represent 95% CIs. Note that yes responses to presented items signify correct recognition, whereas yes responses to suggested and non-suggested items signify false recognition

Equivalence Testing

Given the null findings in some of the misinformation analyses, equivalence tests were conducted for those conditions where no statistically significant effects were detected (i.e., eyewitness immediate, perpetrator immediate and delayed). We specified the smallest effect size of interest (SESOI) as the smallest effect we detected in our DRM analyses, i.e., a Cohen's *d* of .27. In the procedure, the first one-sided test is used to test the estimate against values at least as extreme as the lower equivalence bound (Δ_L) and the second one-sided test tests the estimate against values at least as extreme as the upper equivalence bound (Δ_U) (Lakens, 2017; Lakens et al., 2018). Both tests need to be statistically significant in order to draw a conclusion of statistical equivalence, so it suffices to report the one-sided test with the smaller test statistic and thus the larger p-value. In all tests, at least one p-value was > 0.05. This means that we cannot conclude equivalence, and we cannot reject a true effect of at least d = .027. Results are therefore inconclusive. All equivalence bounds plots are depicted in Figures 4-6.

Figure 4

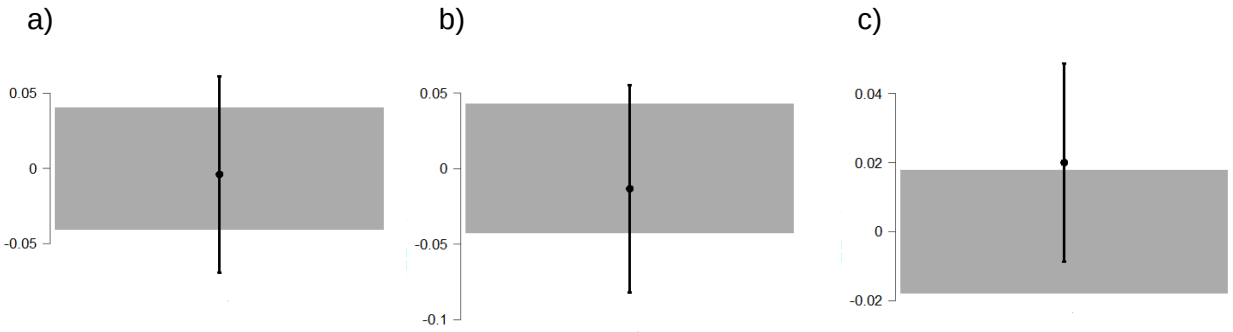
Equivalence bounds plot for eyewitness immediate condition, a) True memory (presented), b) False Memory (suggested), c) False memory (non-suggested)



Note. In the plots, the thick dot represents the difference between means, the vertical lines indicate the 90% confidence intervals from the two one-sided tests procedure, and the grey area indicates the equivalence bounds (in raw scores).

Figure 5

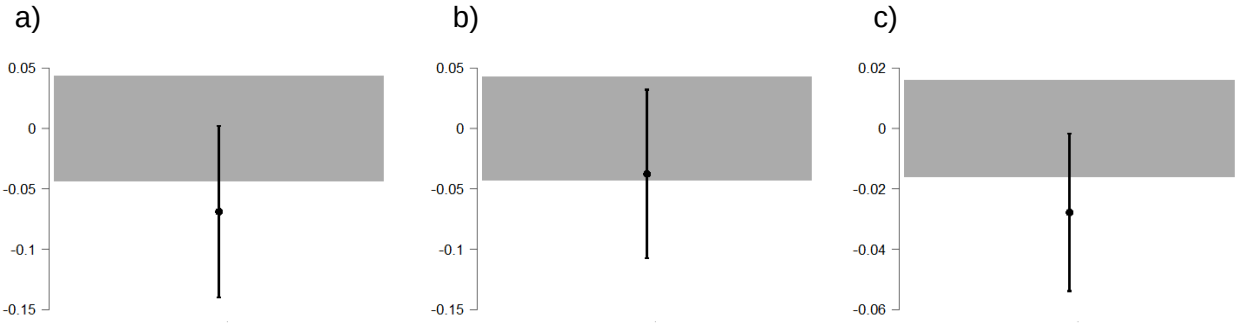
Equivalence bounds plot for perpetrator immediate condition, a) True memory (presented), b) False Memory (suggested), c) False memory (non-suggested)



Note. In the plots, the thick dot represents the difference between means, the vertical lines indicate the 90% confidence intervals from the two one-sided tests procedure, and the grey area indicates the equivalence bounds (in raw scores).

Figure 6

Equivalence bounds plot for perpetrator delayed condition, a) True memory (presented), b) False Memory (suggested), c) False memory (non-suggested)



Note. In the plots, the thick dot represents the difference between means, the vertical lines indicate the 90% confidence intervals from the two one-sided tests procedure, and the grey area indicates the equivalence bounds (in raw scores).

Additional Analyses

In short (see SI for details), the subjective sense of presence in the VR simulation was elevated in MDMA-intoxicated subjects, but was not a statistically significant covariate. Isolating effects of MDMA at encoding by differentiating between novel and repeated test items indicated that in the DRM paradigm, the most robust effects were for true memory, but did not affect findings in the misinformation paradigms.

Discussion

This is the first study examining effects of the entactogen MDMA on the susceptibility to form false memories, using a basic (DRM) and two applied (misinformation) paradigms. Small memory impairments in response to MDMA were detected in the DRM at both time points, particularly pertaining to true recognition. However, MDMA did not consistently affect recognition performance in the two misinformation tasks, and we did not find any evidence that MDMA increased the tendency to go along with suggestive questions.

In the DRM paradigm, true recognition was impaired during acute MDMA intoxication but also one week later when sober. Although verbal recognition memory was not affected in previous research (Kuypers & Ramaekers, 2005), this generally conforms with findings of impaired verbal memory. Moreover, the fact that impairments were detected at both time points fits with the findings by Doss et al. (2018b) that MDMA impairs both the encoding and the retrieval stage. MDMA also elevated DRM false memories of related lures during acute intoxication, which is in line with the trend of MDMA-induced increase in false alarms during retrieval as reported by Doss and colleagues. In our study however this seemed to be an isolated finding, and no other false memory measure was increased by MDMA. In terms of signal detection parameters, intoxicated participants were less able to correctly discriminate between presented and nonpresented words (i.e., sensitivity) compared to their unintoxicated state, but their response bias was not affected by MDMA intoxication at any point.

At the delayed test, false memory for critical, thus highly associated lures was reduced following MDMA. This finding as well as the detected true memory impairments might result from encoding deficits of the studied word lists, preventing adequate processing of their underlying meaning or overarching associated theme. False memory theories such as Fuzzy-Trace-Theory (Brainerd & Reyna, 2019) and Associative-Activation Theory (Otgaar, Howe, et al., 2019a) postulate that gist processing and associative activation, respectively, support false memory. Drugs that impair encoding and true memory performance might reduce these mechanisms, resulting in reduced associative or gist-based false memory (Ballard et al., 2012; Kloft et al., 2021). The current findings provide some support for this explanation. Furthermore, the finding that associative false memory is differentially affected depending on whether a drug is present mostly at encoding versus retrieval is reminiscent of research on THC (main psychoactive cannabis compound; Ballard et al., 2012; Doss, Weafer, Gallo, et al., 2018a; Kloft et al., 2021; Kloft et al., 2019; Kloft et al., 2020).

Although the current study design does not permit full disentanglement of these memory stages, we see tendencies that MDMA, similarly to THC, increases DRM false memory at retrieval but reduces it when encoding effects are isolated.

Contrary to expectation, no acute MDMA effects on memory were detected in the two misinformation tasks. That is, when answering leading and non-leading questions about presented and non-presented details of a mock eyewitness and perpetrator crime experienced in virtual reality, intoxicated participants performed similarly to sober individuals. At the delayed test, participants who had experienced the crime under MDMA influence even showed reduced false memories in response to suggestive questions, exhibiting a more conservative responding pattern compared to the placebo group, but these effects were found only in the eyewitness condition. This leads us to conclude that any effects of MDMA on episodic recognition memory using the misinformation paradigm, at least in the procedure that we used, were weak to perhaps nonexistent. In any case, our results suggest that MDMA does not seem to heighten suggestibility or response bias. However, equivalence analyses could not entirely reject the presence of a small effect.

In sum, MDMA-intoxicated people recognized fewer correct stimuli both when questioned immediately and a week later, but these were small-to-moderate effects and were not found in the misinformation paradigms, where true memory was not affected. False memory rates increased after MDMA at immediate retrieval on one DRM measure, but decreased on some measures at 1-week follow-up. Importantly, MDMA did not induce a more liberal response bias (as e.g. with cannabis, Kloft et al., 2020); rather, the response bias did not change overall, or was more conservative at one occasion. Possibly, the DRM paradigm was more sensitive in detecting memory effects due to the higher statistical power that is inherent to a within-subjects comparison, as opposed to the between-groups analyses of the misinformation tasks. Also, recognition memory tends to be less consistently affected by drugs, compared to measures of recall (Flowe et al., 2020; Söderlund et al., 2005).

The memory impairments detected in this study seem to mirror the generally small effect sizes in the MDMA memory literature and may in part reflect its psychostimulant effects. For example, participants viewed the VR scenarios 60 min post-administration, a point where the onset of MDMA's stimulant effects such as rising blood pressure levels and pulse rate was likely (de la Torre et al., 2000). This might have potentially helped the encoding (e.g., sharpening attention) of

this fully immersive complex autobiographical event, which is arguably more attention-grabbing compared to a rather monotonous word list task, and might have protected against misinformation.

The present study reconfirms that MDMA impairs true memory, which is potentially problematic in the applied legal context where intoxicated individuals might remember fewer details. However, small effect sizes and inconsistent results preclude making strong claims about practical relevance, and whether lower true memory performance is also evident in more applied settings first has to be examined in more depth. Therefore, future studies should assess whether MDMA affects recall (instead of recognition) of a forensically relevant event, using study designs that separate different memory phases, and potentially testing higher doses. Intoxicated participants reported being less under influence, on average, compared to their usual experiences with the drug (Fig. S3) and regular self-reported doses were around 230 mg (Table S1); however, observed MDMA blood concentrations were very much comparable to those observed in recreational users (Morefield et al., 2011), confirming that the given dose was forensically and clinically relevant. Additionally, future research could test memory when stimulant versus entactogenic effects are dominant, similar to alcohol research where cognition is differentially affected during the ascending versus descending limbs of the blood alcohol concentration curve (Schweizer et al., 2006; Söderlund et al., 2005).

With respect to future research applications, it is further important to evaluate false memories in the context of MDMA-assisted cognitive therapy to treat PTSD. Such therapies strongly rely on trust and openness between counselors and patients when evaluating, destabilizing, and reprocessing traumatic events, and memory reconsolidation has been suggested a key mechanism to symptom improvement (Feduccia & Mithoefer, 2018). If MDMA were to cause false memories in patients due to suggestive pressure of a counselor, this might potentially result in false diagnoses and other adverse consequences. Our data from the misinformation tasks suggest that vulnerability to suggestive pressure and misinformation might not be increased during or after MDMA intoxication in recognition tasks. Further research could explore this more thoroughly, using imagination inflation or primary suggestibility measures (Carhart-Harris et al., 2015; Otgaar, Scoboria, et al., 2016) to assess whether MDMA's entactogenic effects translate into people misremembering things they merely imagined.

To summarize, MDMA seems to have a complex memory profile, with much more subtle memory impairments compared to, for example, cannabis (Kloft et al., 2020). An associative word

list task indicated small but robust effects on true memory, and differential effects on associative false memory that varied with immediate (intoxicated) and delayed (sober) retrieval. True and false recognition in two applied false memory tasks was not consistently affected. Studies that consider the complexity of how drug effects interact with memory phases are needed to elucidate the boundary conditions of MDMA-induced memory distortion.

Funding and Disclosure

This research was supported by the Nederlandse Organisatie voor Wetenschappelijk Onderzoek (NWO) Research Talent grant (nr. 406.16.529), awarded to LK, HO, and JR in 2016. NWO had no further role in study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication. The authors declare no conflict of interest with respect to this research.

Acknowledgements

We thank Dr. Cees van Leeuwen and Dr. Rob van Gassel for medical supervision and Richard Benning from Maastricht University for creating the virtual reality environments used in this research. Moreover, we are grateful to students Julia Gros, Kayley van Uden, Rosalie Mourmans, Floor van der Steur, Didi Delsing, Rachel Heutz, Eva van Rosmalen, Elsa Roudot, Beatrice da Rios, Naemi Welter, and Leonie Maatz for collecting data.

Author Contributions

HO, AB, JR, and LK designed the research; LK collected data; LK, ST, HO, AB, and JR analyzed data; and LK, HO, AB, and JR wrote the paper.

Supplementary Information

Please note that some of the methods described here have been described in the supplementary information of Chapter 4.

Participants

Sample size was determined through a power calculation based on results of the misinformation paradigm from a previous experiment. In a study on the effects of alcohol on memory and susceptibility to suggestive cues (van Oorsouw et al., 2015), sober and intoxicated participants (n = 67) committed a mock crime in a field setting. Intoxicated participants showed an increased tendency to go along with misleading questions compared to sober participants with a medium to large effect size (η^2 = .12, which equals Cohen's f = .37). An a priori statistical power analysis with G*Power 3.1 (Faul et al., 2007) indicated that to detect comparable effects using a slightly more conservative estimate (Cohen's f = 0.30), a sample size of 64 participants would be required, using a repeated measures between-subjects ANOVA with a power of 0.80, and a significance level alpha of 0.05. We decided to stop data collection at N=60 for a very practical reason: continuing recruitment to reach 64 would have necessitated re-ordering of additional treatments for a very small number of subjects. Our final sample size of 60 was deemed sufficient in power (2 groups of n = 30 rather than 32 for the planned between-groups comparisons).

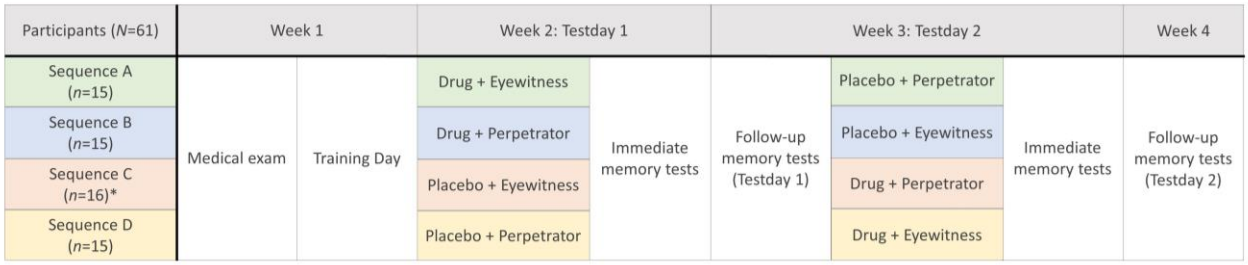
Participants were recruited via online and offline advertisements posted around Maastricht University. Subjects were screened using a medical history and drug use questionnaire, and underwent a medical examination through a medical supervisor. Inclusion criteria were: age 18-40 years; self-reported experience with MDMA/ecstasy (3-200x lifetime use and minimum 1x/past year) with no serious side effects; free from psychotropic medication; good physical health; BMI 18-28 kg/m2; ⩾5 years of English language education, and written informed consent. Exclusion criteria were: history of drug abuse (besides MDMA) or addiction; cannabis use (>2 times/week); use of a psychedelic drug during the past 4 weeks; pregnancy/lactation; hypertension; presence or history of psychiatric or neurological disorder; liver dysfunction; cardiovascular abnormalities, and prior participation in Kloft et al. (2020).

Design, Doses and Administration

We used a double-blind, placebo-controlled, 2 (Group: Treatment vs. Control) by 2 (Time: Time 1 vs. Time 2) mixed design with Group as a between subjects factor and Time as a within-subjects factor. Groups were matched for age, sex, and education level. All participants were randomly assigned to one out of 4 possible randomization sequences, counterbalancing the order of the treatment and VR scenario (see Fig. S1). Treatment consisted of 75 mg 3,4-methylenedioxymethamphetamine (MDMA) powder, mixed with 200 ml Bitter Lemon soft drink in an opaque 400 ml cup with a lid. MDMA was prepared by a different researcher from the one performing the administration and testing, out of sight from the participant and experimenter. Placebo consisted of only Bitter Lemon served in the same cup. For administration, subjects were handed the cup, which they drank under supervision. To avoid any potential residue of the drug, the cup was then refilled with 100 ml Bitter Lemon and the process repeated. Participants received once MDMA and once placebo on separate test days.

Figure S1

Schematic representation of counterbalanced randomization sequences A-D with the variables treatment (drug vs. placebo) and mock crime scenario (eyewitness vs. perpetrator).



Note. * this includes the subject who was excluded after testday 2 due to a drug administration error.

Procedure

A full timetable of procedures can be viewed in Table S1. Eligible participants attended a training session for baseline assessment and to become acquainted with the virtual reality (VR) setup and other cognitive tests. Testing consisted of two similar test days, which were scheduled 7 (± 1) days apart, and one follow-up meeting 7 (± 1) days after test day 2 (either all morning or all afternoon timeslots). All meetings took place in a laboratory at the study site, with the exception of 3 final follow-up meetings that were conducted via phone/email due to the participant's unforeseen unavailability. Participants were requested to abstain from drug use 7 days and from alcohol use 24 h prior to testing, not to eat breakfast/lunch before test sessions 1 and 2, to not consume any caffeine-containing products throughout the day, and to arrive well-rested. Drug and alcohol screens were conducted before the start of every test day (incl. the follow-up session). An additional urine pregnancy test was performed for women. All breath alcohol concentration readings showed 0.00. All pregnancy tests showed a negative result. In case of a positive drug test before the start of the first test day, participants were rescheduled for a later date (n = 3, all THC). In case of a positive drug test before the start of the second test day or final follow-up session, a blood sample was taken but the test day was continued and the samples analyzed for active drug metabolites (see data exclusion section below for further information).

Table S1

Overview of testing procedures

	Procedure	Time after treatment (minutes)
Training		-
	Virtual reality introduction	
	DAT training	
	DES	
	GCS	
	PVT training	
	DLRT training	
	PCT training	
	MET training	
Testday 1		
	Drug and alcohol screens	0
	Baseline questionnaires[a]	0
	Breakfast/lunch	0
	Administration MDMA/placebo	0
	Waiting period	5
	Virtual Reality scenario	60
	Subjective high 1	72
	Telepresence	
	Attentional focus	
	Cognitive task (divided attention)	78
	Blood sample	90
	Misinformation interview	95
	Subjective high 2	100
	DRM A study phase	102
	Cognitive tasks[b]	112
	DRM A immediate test	122
	Cognitive tasks/Questionnaires[c]	130
	Subjective high 3	164
	Participant discharged	240
Testday 2		
	Drug and alcohol screens	0
	Baseline questionnaires[a]	0
	Breakfast/lunch	0
	Follow-up testday 1:	0
	DRM A delayed test	0
	Misinformation delayed interview	0
	Administration MDMA/placebo	0
	Remaining procedures of testday 2 are equivalent to testday 1	

Follow-up		
	Drug and alcohol screens	-
	Baseline questionnaires	-
	Follow-up testday 2:	-
	DRM B delayed test	-
	Misinformation delayed interview	-
	Debriefing	-

Note.

Deviations could occur.

[a] Groningen Sleep scale (self-reported sleep quality and quantity)
[b] PVT, DLRT
[c] PCT, MET, CADSS, EDI, FFMQ

Prior to MDMA/placebo administration, participants received a standardized breakfast/lunch (2 slides of pumpernickel bread, 1 portion jam, 1 portion cream cheese, 1 butter, 1 piece of fruit, 1 juice, 1 tea without caffeine). Participants were also provided with sweet snacks (e.g., raisins, lollies) and electrolytic drinks throughout the testday, and with gum in case that they reported bruxism. Participants were seated in a furnished room with access to magazines and an ensuite bathroom and were allowed to use their phones or computers for leisure or work. Testing commenced 60 min post-administration, and all biological sampling, memory tests, and other cognitive procedures were conducted at fixed intervals during ~240 min post-administration. Participants were safely discharged minimum 4 h post-administration based on a screening form assessing any remaining intoxication effects using visual analog scales (0-100 mm). Participants were allowed to leave if they scored below 10% on all scales and had a safe method of transport. After study completion, participants received a short debriefing explaining the goals of the study.

Imaging

A sub-sample (n = 13) of the described sample underwent fMRI procedures after completion of all other study procedures (3.5 h post-administration), results of which will be reported elsewhere. This part of the study was a voluntary option for participants.

Measures and Materials

Deese/Roediger-McDermott (DRM) Paradigm

Two parallel versions of the DRM were administered (day 1: version A, day 2: version B), counterbalanced with treatment order. In each version, the study phase included the presentation of 15 DRM word lists containing ten words each (total 150 stimuli; first ten words of the respective lists by Roediger et al., Stadler et al., 1999). Lists were selected for each version to include a range of backward associative strengths (BAS, index of the associative strength between the list items and the critical item) and inter-item associative strengths (see Roediger, Watson, et al., 2001; Stadler et al., 1999). An overview of version A and B lists and their BAS is displayed in Table S2. The two versions did not statistically significantly differ in terms of BAS [t (28) = .41, p = .68]. Lists were presented visually via PowerPoint, preceded by an announcement of the list number (e.g., List 1), followed by the respective study words shown one-by-one in the center of the screen (duration 2 s per word). All stimuli were separated by a 2 s interstimulus interval, during which the plus (+) symbol was shown in the center of the screen. The total duration of the study phase was 640 s. Participants were instructed to pay attention and try to remember the words as their memory for these words would be tested later in the session.

Outcome measures included *true memory rates* (the proportion of studied words correctly recognized at test), false alarm rates for *critical lures* (the proportion of critical lures, i.e., new, strongly related words, that are incorrectly recognized at test, a measure of false memory), false alarm rates for *related lures* (proportion of incorrect recognition of new, related words), and false alarm rates for *unrelated words* (proportion of incorrect recognition of new, unrelated words).

Table S2

DRM lists with backward associative strength (BAS) parameters

Version A		Version B	
List = Critical Lure	Mean BAS	List = Critical Lure	Mean BAS
Anger	0.181	High	0.109
Black	0.094	Lion	0.125
Bread	0.179	Man	0.131
Car	0.348	Mountain	0.157
Chair	0.284	Music	0.210
City	0.180	Needle	0.205
Cold	0.315	Pen	0.176
Cup	0.154	River	0.145
Doctor	0.234	Shirt	0.242
Foot	0.184	Sleep	0.452
Fruit	0.288	Smell	0.294
Girl	0.129	Soft	0.191
King	0.240	Sweet	0.223
Rough	0.165	Trash	0.118
Smoke	0.197	Window	0.221
Mean	*0.212*	*Mean*	*0.200*
SD	*0.072*	*SD*	*0.087*

Note.

All mean BAS values have been calculated based on Roediger et al. (2001).

Misinformation Paradigm

In order to investigate suggestion-based false memory formation, two versions of the misinformation paradigm were used (Loftus, 2005; Otgaar, Howe, et al., 2016). On separate test days, participants were involved in two distinct crime scenarios, simulated in a fully immersive virtual environment. The virtual reality headset *HTC* Vive was used. The device uses "room scale" tracking technology in order to turn the environment into a 3D space in which the user can move freely. Motion-tracked controllers were used so that the participant could interact with the environment. VR has been previously applied successfully in eyewitness memory studies

conducted by our lab (Kloft et al., 2020; Romeo et al., 2019). An image section of both VR scenarios is displayed in Fig. S2, and respective videos can be viewed on the Open Science Framework (https://osf.io/8tjkr/).

Figure S2

Screenshots from eyewitness (left) and perpetrator (right) virtual reality scenarios

Eyewitness Scenario. In the eyewitness scenario participants were passive witness to the physical attack on a policeman and a security guard by one man (the attacker). In this scenario the crime took place on a platform at a train station and participants witnessed the scenario from inside the train, among other virtual passengers. Prior to the simulation participants were instructed to imagine that they were on a train traveling with a friend who was sitting opposite of the participant in the train, to remain seated during the simulation, and that at one point a crime would take place, which they should observe. Two min after the crime occurred, the friend (co-witness) engaged in a monologue directed towards the participant and recalled some aspects of the attack. She provided correct information (e.g., the attacker kicked the security guard) as well as misinformation (e.g., there was a police dog on the platform). The simulation ended after she provided all information.

Perpetrator Scenario. The perpetrator VR-scenario was designed in a way that participants were in a bar setting where they were able to walk and explore the bar. Furthermore, some avatars would engage in a monologue directed at the participant when participants approached them (e.g., bartender: “Hey there, you thirsty? I’ll get you your usual!”). Prior to the simulation participants were instructed to imagine themselves in the role of a student who had lost their job and was in desperate need of money to pay their rent, thus deciding to steal some money from someone in their local bar. They were encouraged to explore the bar and instructed to grab

the strap of the purse when the people who were playing a game started cheering. The trigger stimulus was presented after 2 min. A motion-tracked controller was used to simulate the purse that was visible for the participants in the VR simulation (placed on a table). A leather handle was mounted onto the controller in order to create the haptic feel of a purse strap. The scenario was manually ended when participants grabbed the controller.

Other Measures

Telepresence. Telepresence refers to a subjective sense of being in the place depicted by the VR rather than the physical place where the user's body is actually located, and the tendency to respond to the virtual environment as if it were real. Presence in the VR mock crime was assessed using the Telepresence scale (Klein, 2003), an 8-item self-report instrument using 7-point Likert scales (1= strongly disagree, 7= strongly agree). It has high reliability (Cronbach's $\alpha = .84$, see Klein, 2003), and an example item is "During the VR simulation, I felt I was in the world the computer created".

Attentional Focus. A scale to assess subjective internal and external focus during the virtual reality scenarios was developed by our lab, consisting of 4 items to assess external [e.g., "During the VR simulation, I paid full attention to what was happening around me (within the simulation)"] and 5 to assess internal attentional focus [e.g., "During the VR simulation, I thought about other things (unrelated to the scenario)"]. Items were partly adapted from Piyathasanan et al. (2015). Each item was scored on a visual analogue scale from 0 to 100 with the following statements at the lower and upper end, respectively: "strongly disagree" and "strongly agree", and mean scores were calculated for external and internal focus, respectively.

Physiological Measures. A single blood sample (5 ml) was taken at MDMA peak concentration at ca. 90 min post-administration. For participants who underwent fMRI testing, a second blood sample was taken after completion of the fMRI procedure (not reported here). All blood samples were centrifuged and the serum was frozen at -20°C and transported to an external lab for pharmacokinetic assessments of MDMA and its metabolite 3,4-methylenedioxyamphetamine (MDA, Toennes & Kauert, 2001).

Measures of heart rate were taken shortly before (2 min baseline) and during the VR simulations, using the Garmin watch Forerunner® 15 heart rate monitoring belt (recorded every 20 s).

Subjective High. In line with other work from our lab (see e.g., Ramaekers et al., 2009), participants were asked to rate how affected they were by MDMA at the present moment by placing a vertical dash on two visual analogue scales (100 mm), stating their subjective feeling of MDMA influence (*subjective high*, ranging from "totally not under the influence of MDMA" to "very much under the influence of MDMA") and in comparison to previous experiences with MDMA (*subjective experience*, "much less under the influence" to "much stronger than usual"). Subjects rated this ~72 min, ~100 min and ~164 min after administration.

Reports on other tasks and questionnaires employed in this research are beyond the scope of this paper but include the following: Gudjonsson compliance scale (GCS), Dissociative Experiences Scale (DES), Clinician Administered Dissociative States Scale (CADSS), Psychomotor vigilance task (PVT), Divided Attention task (DAT), Deary-Liewald reaction time task (DLRT), Multifaceted Empathy Test (MET), Picture Concept Task (PCT), Ego-dissolution inventory (EDI), Five Facet Mindfulness Questionnaire (FFMQ), and for a sub-sample of 11 participants a dictator game task.

Data Exclusion

Six people had a positive urine drug screen on testday 2 or 3. For $n = 4$ (THC), a blood sample was taken and analyzed for active THC and its metabolites (Toennes et al., 2015). Three of them appeared not to be actively intoxicated (THC levels <2.0 ng/ml) and thus were retained for analyses. The fourth sample was incorrectly shipped to a different lab before THC analysis could be carried out, thus memory analyses were carried out with and without the observation in question in the dataset. Excluding the observation did not change the results, therefore results were reported with the observation retained in the sample. In two cases no blood sample could be obtained ($n = 1$ THC, $n = 1$ cocaine) so these were excluded from analyses. Due to a treatment administration error, one participant was excluded after testday 2 but data from testday 1 were retained for analysis. One participant's DRM data were entirely excluded due to faulty administration of tasks.

Additional Analyses

Exploratory Analyses

To further explore and account for findings in the misinformation tasks, we analyzed some variables thought to play a role in processing the VR scenario (telepresence, attentional focus). Variables found to statistically significantly differ between MDMA and placebo were entered as covariates in repeated measures ANOVAs. As part of the exploratory analyses, findings of the covariate analyses were compared with the findings from the first-level analyses.

Telepresence. Across eyewitness and perpetrator conditions, MDMA intoxicated subjects reported a higher degree of telepresence [$M = 4.68$, $SD = 1.07$, $t\ (59) = 4.16$, $p < .001$, Cohen's $d = .54$], feeling more immersed in the VR compared to the placebo condition ($M = 4.23$, $SD = 1.10$). Therefore, all four repeated measures ANOVA with the misinformation variables were repeated with telepresence added as a covariate. No statistically significant interaction effects with telepresence, or main effects of telepresence were detected in any of the analyses. Moreover, adding telepresence as a covariate did not change any of the previously detected effects, with the previously reported main effect of Group still detected in the eyewitness delayed condition [$F\ (1, 56) = 6.56$, $p = .013$, $\omega^2 = .05$], and no other statistically significant effects detected (Group main effect in perpetrator delayed condition now $p = .13$).

Attentional focus. No statistically significant differences between MDMA and placebo were detected for external attentional focus during the VR scenarios [MDMA: $M = 71.22$, $SD = 14.46$, placebo: $M = 69.99$, $SD = 10.55$, $t\ (59) = .73$, $p = .469$, Cohen's $d = .09$] nor for internal attentional focus [MDMA: $M = 20.92$, $SD = 15.69$, placebo: $M = 24.68$, $SD = 16.94$, $t\ (59) = -1.33$, $p = .189$, Cohen's $d = -.17$]. Conducting these analyses for each scenario separately did not yield statistically significant differences either. Thus, attentional focus was not pursued in further covariate analyses. However, collapsing the drug conditions and comparing the two scenarios with each other, it was found that participants reported higher external focus for the eyewitness compared to the perpetrator scenario [eyewitness: $M = 72.82$, $SD = 11.61$, perpetrator: $M = 68.34$, $SD = 13.25$, $t\ (59) = 2.76$, $p = .008$, Cohen's $d = .36$]. No such difference was detected for internal focus between the two scenarios [eyewitness: $M = 22.23$, $SD = 16.18$, perpetrator: $M = 23.41$, $SD = 16.68$, $t\ (59) = -.71$, $p = .481$, Cohen's $d = -.09$]. Potentially being instructed that a crime will

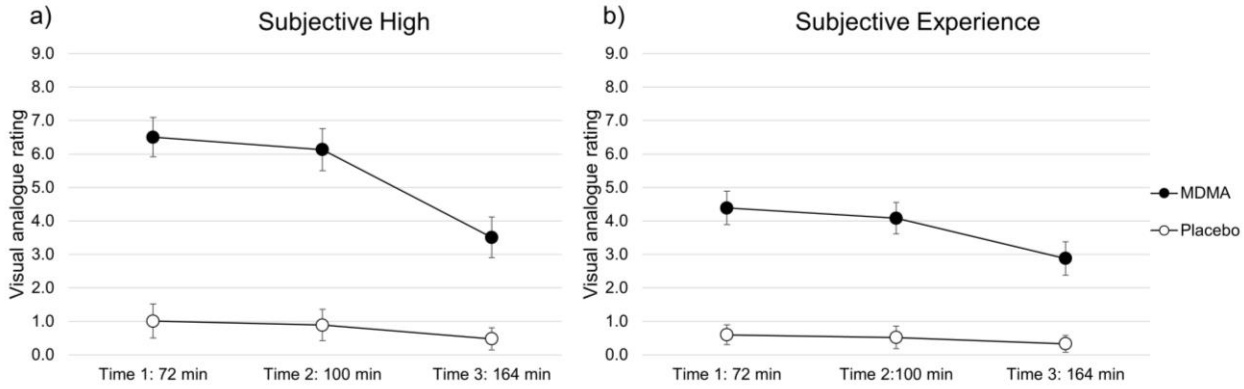
occur that the participant should observe might have resulted in higher attention to participants' surroundings within the VR, compared to when committing a virtual crime.

Subjective high and MDMA serum concentration

Mean values for subjective high and subjective experience for both placebo and MDMA conditions as a function of time are shown in Fig. S3. Subjective high results were analyzed using repeated measures ANOVA, revealing a statistically significant difference in subjective high [F (1, 56) = 147.14, $p < .001$, $\omega^2 = .58$] and subjective experience [F (1, 56) = 129.83, $p < .001$, $\omega^2 = .56$] between MDMA and placebo, indicating that overall participants felt more intoxicated in the MDMA condition than in the placebo condition (missing values for n = 4 cases). A summary of mean (*SD*) and range of MDMA and MDA concentrations in serum is given in Table S3.

Figure S3

Visual analogue scale ratings (0-10 cm) of subjective high (a) and subjective experience (b) as a function of time



Note. Error bars represent 95% CIs.

Table S3

Serum concentration values (ng/ml)

	Mean	SD	Range
Sample 1[1]			
MDMA	147.9	46.0	51.2-287.9
MDA	12.1	23.5	0.0-137.3

Note.

[1]Sample taken ca. 90 min after MDMA ingestion. Missing data $n = 3$.

Repeated vs. Novel Recognition Test Items

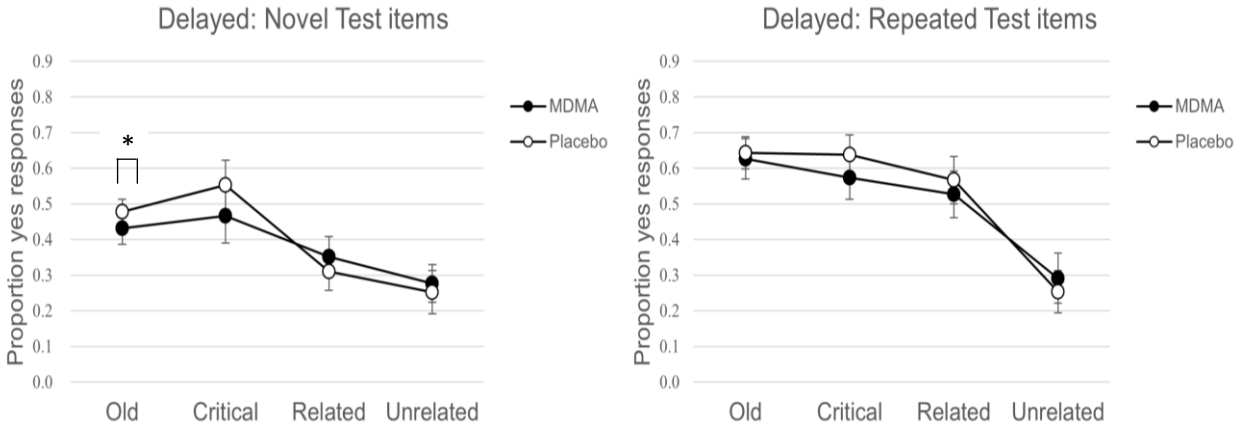
Primary analyses reported in the main manuscript were conducted on all recognition test items. Since the DRM and misinformation delayed tests contained a combination of once-presented (novel items) and items that were repeatedly tested (once during the immediate test and then again at delayed test), we report here analyses that distinguish these in order to better isolate pure effects of MDMA on encoding.

DRM. A 2x2x4 repeated measures ANOVA was conducted using the factors Novelty (Novel vs. Repeated), Drug (MDMA vs. placebo), and Level of association (Old vs. Critical vs. Related vs. Unrelated). Separate means plots for novel and repeated items are depicted in Fig. S4, and separate mean scores and SEs are displayed in Table S4. Novel items were: n=45 old/presented items, n=5 critical lures, n=10 related lures, and n=10 unrelated lures. Repeated items were n=10 old, n=10 critical, n=5 related, and n=5 unrelated items. The three-way interaction was not statistically significant, but significant effects were detected for the Novelty x Level of Association [F (2.61, 146.14) = 19.28, p<.001, ω^2 =.05] and the Drug x Level of Association interactions [F (2.62, 146.90) = 3.14, p = .033, ω^2 = .01], as well as a large main effect of Novelty [F (1, 56) = 128.91, p < .001, ω^2 = .14]. Recognition rates for repeated items were generally higher, compared to the items that were only tested once [t (56) = -11.35, p_{Bonf} < .001, Cohen's d = -1.50]. Inspecting simple main effects of Drug as moderated by the factors Level of association and Novelty, only one statistically significant difference was detected: the MDMA condition scored statistically significantly lower on true memory (memory for old words) compared to the placebo condition when these items were novel [F (1, 56) = 5.94, p = .018, Cohen's d = .32]. This indicates a small but robust effect on true memory, which was reduced through MDMA at encoding when subjects

were tested 1 week later when sober again. Critical lures seemed to be affected (p ~.10 and Cohen's *d* ~.23 in both separate analyses) but not as robustly when the old and new items were split. This might perhaps be due to the small numbers of test items (only *n* = 5 new CL and *n* = 10 old CL), leading to large standard errors. All other simple main effects were *p* >.25.

Figure S4

DRM mean scores in proportions from delayed test for novel items (a) and repeated items (b) by drug condition



Note. **p* < 0.05, ***p* < 0.01, pairwise comparisons. Error bars represent 95% CIs.

Misinformation paradigms. For the misinformation tasks, analyzing the recognition test data split into novel and repeated items was not feasible due to the small numbers of repeated items (some *n* <5, all numbers displayed in Table S4). Thus, we repeated the repeated measures ANOVA for the eyewitness and perpetrator delayed conditions reported in the main manuscript, this time only taking into account the novel items. Running the two RM ANOVA only using these items, the same pattern of findings emerged for the eyewitness delayed condition as well as the same null findings for the perpetrator delayed condition. Thus, a statistically significant main effect of Group was still detected [F (1, 57) = 8.44, p = .005, ω^2 = .06], which was driven by the placebo group demonstrating elevated suggestion-based false memories for the eyewitness scenario at follow-up [F (1, 57) = 5.25, p = .026, Cohen's d = .60]. For the perpetrator condition, no statistically significant Group main or interaction effect was detected. In conclusion, isolating the non-repeated items in the misinformation tasks still gives the same (null) findings.

Table S4

Means and SEs from DRM and Misinformation parameters (rates in proportions) split by Novelty (novel vs. repeated)

	Novel test items					Repeated test items				
		MDMA		Placebo			MDMA		Placebo	
	n test items[a]	*M*	*SE*	*M*	*SE*	*n* test items[a]	*M*	*SE*	*M*	*SE*
DRM										
True recognition (old)	45	.43	.02	.48	.02	10	.63	.03	.64	.02
False alarms (critical)	5	.47	.04	.55	.04	10	.57	.03	.64	.03
False alarms (related)	10	.35	.03	.31	.03	5	.53	.03	.57	.03
False alarms (unrelated)	10	.28	.03	.25	.03	5	.29	.04	.25	.03
Misinformation Eyewitness										
Presented	10	.63	.03	.66	.03	5	.74	.02	.73	.02
Suggested	4	.08	.02	.17	.04	5	.08	.02	.15	.03
Non-suggested	5	.06	.02	.11	.03		NA			
Misinformation Perpetrator										
Presented	9	.64	.03	.60	.04	4	.77	.04	.65	.05
Suggested	5	.29	.04	.25	.03	2	.22	.06	.20	.05
Non-suggested	5	.03	.01	.01	.01		NA			

Note.

[a] Number of recognition test items based on which the rates were calculated.

Chapter 6

False memories in the field: impact of substance intoxication and sleep restriction on false memory formation

Submitted as:

Kloft, L., Otgaar, H., Blokland, A., van Oorsouw, K., Schepers, J., Steinmeyer, S., & Ramaekers, J.G. (submitted). False memories in the field: impact of substance intoxication and sleep restriction on false memory formation. Under review at *Journal of Applied Research on Memory and Cognition.*

Abstract

We conducted a field study at a music festival to examine effects of naturally-occurring sleep deficits and substance intoxication on false memory formation and suggestibility, using two paradigms. In a misinformation-suggestibility task, sleep restriction was associated with increased levels of suggestibility and false alarms to non-suggestive questions for a virtual reality eyewitness scenario. Use of some drugs (THC, amphetamines) was also related to increased false alarms to non-suggestive questions, indicating that this category of questions might be a sensitive marker for those drugs. In an implantation paradigm, neither sleep restriction, substances, nor exposure to fake social media content increased the likelihood of falsely believing or recollecting a purportedly experienced festival event. However, some people came to falsely believe (13%, $n = 30$) or falsely remember (6%, $n = 14$) the false suggested event. Findings indicate that some established lab effects can also be observed in a less controlled environment.

Introduction

Human memory is prone to distortion. Decades of research have revealed its malleability through socio-cognitive factors, showing that false memories can arise after exposure to misinformation or external suggestion (Frenda et al., 2011; Loftus, 2005). False memories can range from people recalling benign details to even entire autobiographical events that were never experienced (e.g., Mazzoni, 2002; Otgaar, Howe, et al., 2016). Recently, research has shifted gears towards the examination of the impact of drug intoxication and sleep deprivation on false memory proneness (Frenda et al., 2014; Kloft et al., 2019; Kloft et al., 2020; Kloft, Otgaar, et al., submitted). Given that both recreational use of mind-altering substances (e.g., alcohol, cannabis) and sleep loss tend to be abundant at music festivals (e.g., Mackuľak et al., 2019; Schlicht et al., 1972), we conducted a field study to assess false memory formation in visitors of a popular music festival, using several suggestion-based false memory methods.

False memories and suggestibility as well as the factors that perpetuate them are of high interest to the legal field, where reliable testimonies from witnesses or suspects are crucial. A frequently used laboratory method to study suggestion-based false memory is the *misinformation paradigm* (Loftus, 2005; Loftus et al., 1978) which exposes individuals to an event (e.g., crime video), followed by misleading information about the encoded material, and finally a memory test to see whether participants report the misinformation (i.e., the *misinformation effect*). Closely related to this method are measures of suggestibility, such as the use of misleading questioning (e.g., posing two incorrect options in a forced-choice test; e.g., van Oorsouw et al., 2019). Another false memory method is the *implantation paradigm* (Loftus & Pickrell, 1995), which typically merges suggestive techniques (e.g., confrontation with doctored photographs or fabricated narratives) with social influence (e.g., repeated interviewing) to convince participants of the occurrence of entire false autobiographical events such as a flight in a hot air balloon (Calado et al., 2020, April 6; Otgaar et al., 2013; Wade et al., 2002). In the field experiment reported here, we used multiple methods to induce false memories both for a mock crime as well as for a suggested recent event at a festival in its visitors.

Substances and false memory

How alcohol and other substances affect false memory formation and suggestibility is of considerable interest from a legal-psychological point of view, since a large proportion of crimes are witnessed or committed by intoxicated individuals (Evans et al., 2009; Francesca T Palmer et al., 2013). The best-studied substance in this context is alcohol, for which studies using misinformation and suggestibility methods have yielded mixed findings. At low to moderate levels, alcohol did not impact the misinformation effect (Flowe et al., 2019; N. Schreiber Compo et al., 2012), but the susceptibility to suggestion was elevated at high alcohol levels (van Oorsouw et al., 2019; van Oorsouw et al., 2015), as well as with a delay between the event during intoxication and its retrieval attempt (Evans et al., 2019). Research on other substances found that cannabis-intoxicated participants displayed greater false memory formation in response to (non-) suggestive questions about virtual-reality eyewitness and perpetrator scenarios (Kloft et al., 2020). In contrast, MDMA did not increase false memory formation in the same tasks (Kloft, Otgaar, et al., submitted).

Laboratory studies on substance effects have several limitations, such as that i) ethical reasons sometimes prevent dosage levels that reflect those in the real world, e.g., alcohol laboratory studies mostly employ moderate doses around the legal driving limit [blood alcohol concentrations (BACs) of ~0.06-0.08%], whereas higher levels are frequent in drinkers (e.g., Hagemann et al., 2013); ii) usually single substances only can be studied, whereas people frequently engage in polydrug-use (e.g., Evans et al., 2009; Winstock et al., 2017); and iii) they are often limited to university students as participants (e.g., Pezdek et al., 2020). Naturalistic studies can provide a remedy in these respects, affording the possibility to capture false memory effects of more severe intoxication in a diverse crowd. For example, in field studies BACs up to .16-.20% were measured (Sauerland et al., 2018; van Oorsouw et al., 2019; van Oorsouw & Merckelbach, 2012; van Oorsouw et al., 2015). Additionally, recreational drug use is widespread at music events, with polydrug-use behaviors being particularly common (Riley et al., 2001). Polysubstance effects on false memory and suggestibility are still unexplored and not always feasible to investigate in a lab setting, so a field study at a music festival provides a viable solution.

Sleep restriction and false memory

Lack of sleep impairs cognitive functioning in a way that is similar to alcohol (Williamson & Feyer, 2000). Recent studies using the misinformation paradigm demonstrated that reduced sleep might increase the risk for forming false memories. Frenda et al. (2014) found that both total and partial sleep deprivation elevated the tendency of people to report misinformation, and people with restricted sleep were more likely to report having seen a news event of which no footage exists (see also Lo et al., 2016). Sleep-deprived individuals also were especially susceptible to interrogative suggestibility (Blagrove, 1996). Thus, sleep deprivation and restricted sleep during the encoding and retrieval of an event have been linked to increased endorsement of false memories.

The Current Study

The aim of this field study was to investigate the effects of substance intoxication and sleep restriction on false memory formation and suggestibility at a large music festival (*Lowlands*). We adopted a two-fold approach towards testing false memory susceptibility by first using a misinformation-suggestibility framework, exposing participants to a mock crime and subsequently interviewing them with a mix of suggestive and non-suggestive questions. We used Virtual Reality (VR) technology to simulate an eyewitness scenario that fully immerses and engages participants to attract a high number of visitors.

Second, we employed a version of the memory implantation method, in which we suggested to participants that they experienced an event that recently occurred at the festival. This was a novel aspect, since implantation studies have solely focused on implanting events from childhood or adolescence (for an overview see Calado et al., 2020, April 6). We used fake news items to foment such false memories as such material has been shown to increase false memory proneness (Murphy et al., 2019). Specifically, participants were presented with Instagram posts about true and false events at Lowlands, with only half the sample receiving the fake news item. Subsequently, all were interviewed about their experiences at Lowlands (e.g., gigs of the bands mentioned in the posts). It was strongly suggested by the experimenter that a specific event was experienced by both the participant and the experimenter (e.g., that both saw a band that never

played at Lowlands, the experimenter claiming that they spotted the participant in the crowd), thus inducing social pressure. Participants' (false) belief in the occurrence of the event and recollection of it were measured, both being critical components of false memories (Scoboria et al., 2004; Scoboria et al., 2017). We expected that sleep restriction, intoxication by alcohol and other substances, and fake news exposure would increase susceptibility to false memory formation.

Method

The study was conducted by researchers from the Faculty of Psychology and Neuroscience, Maastricht University over the three days of the Lowlands festival in August 2018 as part of the Lowlands Science initiative, and was approved by Lowlands Science as well as the university's standing ethics committee.

Participants

All participants attended the Lowlands music festival in the Netherlands and found this study as part of the side attraction "Lowlands Science", an initiative by the organization of the festival. N = 279 participants were recruited for and enrolled in the study. Out of those, N = 276 completed the entire study procedure (169 females, 60.7%). The age range was 16-64 (M = 29.36, SD = 9.12). The vast majority of the sample were Dutch native speakers (96.1%). Inclusion criteria were: minimum age 16 years, written informed consent, and passing three screening questions to ensure that participants were oriented in time and space (naming the day, place, and solving a simple math problem). An exclusion criterion was displaying an observably very high level of intoxication through tumbling or aggressive behavior. Participants' levels of education were as follows (highest completed): primary school (0.4%), secondary school (21.7%), vocational training (9.7%), Bachelor's/HBO degree (42.2%), Master's degree (23.1%), PhD (2.9%; all data and analyses available on OSF).

Measures

Alcohol and Substance Use

Self-report. Participants received a questionnaire in which they were asked how many alcoholic beverages they had consumed on the day of testing (beer, wine, liquor/spirits), how many hours ago since waking up they had started drinking, whether they had eaten, whether they had had alcohol the day before, whether they had had coffee or an energy drink, and some general questions about experiences with alcohol-induced blackouts. In addition, they were asked to indicate use of any other substances on the day of testing [options were: none, cannabis/hashish (natural or synthetic), cocaine, amphetamines (e.g., speed, MDMA/ecstasy), hallucinogens (e.g., ketamine, psilocybin mushrooms, LSD), opioids (e.g., heroine), sedatives (e.g., benzodiazepines

such as Valium, sleeping medication, GHB (e.g., liquid ecstasy), other. See Table 1 for these self-report data.

Objective. Breath alcohol concentrations *(n* = 276) were collected with a breathalyzer (Dräger Alcotest 6510). To assess other substance use, oral fluid samples were collected from *N* = 277 participants using the Dräger DrugCheck® 3000, a point-of-collection (POC) drug testing device based on lateral flow immunochromatographic technology and designed to detect six drug groups in oral fluid (qualitative assessment). Detected drug groups (target compound) and their cut-off values were: amphetamines (amphetamine) 70 ng/mL, methamphetamines (methamphetamine) 70 ng/mL, cocaine (cocaine) 20 ng/mL, opiates (morphine) 20 ng/mL, cannabis (Δ9-THC) 15 ng/mL, and benzodiazepines (alprazolam) 15 ng/mL. The sensitivity (≥ 80 %) and specificity (≥ 97 %) of this device was recently established (Zorec Karlovsek et al., in preparation). An additional sample for drug quantitative analysis was subsequently collected from all participants with an oral fluid collection device (Dräger DCD 5000) for a laboratory based confirmatory analysis (UPLC–MS/MS, Böttcher et al., 2019), targeting for amphetamine and amphetamine-related substances (15, cut-off 1-5 ng/mL OF), cocaine and metabolites (3, cut-off 1 ng/mL OF), opiates (7, cut-off 1 ng/mL OF), cannabinoids (THC, cut-off 1 ng/mL OF) and benzodiazepines (14, cut-off 0.1 – 1 ng/mL OF).

Sleep Restriction

Several self-report measures were used to tap into sleep restriction (see Table 1 for responses). Participants were asked if they felt tired (slider scale, 0-100, rating “tiredness” from “not at all” to “extremely”), if they slept well last night (yes/no), how many hours they slept last night (options: 1-10, >10), how many hours a night they usually sleep (options: 1-10, >10), how many days they had been at Lowlands, and whether they had had enough sleep in the past three days (yes/no).

Table 1

Self-report: substance use and sleep variables

Number of drinks today	
Beer[a]	39.7%: 0; 34.3%: 1-3; 21.0%: >3
Wine[b]	59.2%: 0; 3.2%: 1-3; 0.4%: >3
Liquor/spirits[c]	53.1%: 0; 18.4%: 1-3; 2.6%: >3
Hours since started drinking[d]	
0-2 h	24.6%
3-5 h	27.5%
>5 h	11.6%
Did not drink today	35.0%
Drank alcohol yesterday	90.6%
Had coffee/energy drink	60.3%
Has eaten	98.6%
Other substances used today	
None	85.9%
Cannabis/Hashish	7.6%
Cocaine	1.4%
Amphetamines	6.5%
Hallucinogens	0.4%
Opioids	0.0%
Sedatives	0.0%
GHB	0.0%
Other	1.8%
Sleep variables	
Tiredness	*M*: 40.4; *SD:* 21.7
Number of hours sleep last night	*M*: 5.9; *SD*: 1.7
Number of hours sleep usually	*M:* 7.5; *SD*: 0.8
Slept well last night	65.0%
Enough sleep during past 3 days	36.8%
# days at Lowlands	*M*: 2.4; *SD*: 1.0

Note.

[a] Missing 5.1%

[b] Missing 37.2%

[c] Missing 26.0%

[d] Missing values 1.4%

Misinformation Paradigm and Suggestibility

We used a virtual reality version of a misinformation paradigm as used successfully in previous research (Kloft et al., 2020). Subjects experienced an eyewitness mock crime in an immersive virtual environment, using the virtual reality headset 'HTC Vive'. The headset is designed around a standout feature called "room scale" that allows the headset to utilize technology to turn a room into a 3D space within the virtual reality environment. This allows a user to mimic the physical environment around them using motion tracked handheld controllers to interact and manipulate objects for a fully immersive environment. Subjects viewed a VR simulation of a crime taking place. In this scenario, the participant was inside a bar where they could walk around in a 3x3 m space. The space was secured by some barrier posts and researchers paid close attention that the participant did not exit this area or walk against an object. Instructions given to participants were as follows: "You will now enter a virtual reality simulation where you will be inside a bar. You can walk around in the bar but please do not walk into objects or people. You have about one minute to walk around and explore the bar. After one minute, a crime will take place. Please just observe what happens. The scenario will end automatically after the crime. Be aware that you are attached to a cable, so please do not make any fast or sudden movements." Additionally, they were informed that they would be tapped on the shoulder by the experimenter if they were to walk too close towards a wall.

After one minute, a fight involving a bar costumer and two bouncers/security guards broke out. Prior to the physical fight, the "attacker" started shouting loudly and insulting the security personnel, which was purposefully designed in order to attract the visual attention of participants, who were anticipated to automatically orient themselves towards the sound (see https://osf.io/a7tmp for a video of the VR simulation). The total duration of the simulation was 1.5 min. Following this, subjects were interviewed by an experimenter in order to assess both true and false memory and suggestibility. Misinformation was introduced directly in the interview through several leading questions. The interview consisted of intermixing suggestive questions with regular forced-choice recognition questions. Instructions to participants were as follows: 'I would like to ask you a few questions about what just happened in the VR scenario. I would like you to answer with 'yes' or 'no', if you do not know something just guess, and try to answer as truthful as you can. This only applies to the yes-no questions. There are also some other questions you need to answer.'

The interview consisted out of 31 questions, orally administered through an experimenter in each time the same order (see https://osf.io/a7tmp for full transcript). There were 15 non-leading questions about truly presented details, or *true memory questions* (e.g., "Did the security guard wear a yellow vest?", "Did you see guitars on the walls?"), 6 *suggestive false memory* questions about non-presented details (e.g., "The attacker had a black coat on, right?", "Did you see the Elvis poster on the wall?"), and 5 *non-suggestive false memory* questions about non-presented details (e.g., "Was there a pizza place next door?", "Were there Christmas decorations in the bar?"). The latter category asked about details that the participant could not have seen (e.g., nothing visible out the window of the bar so no visible pizza place) or details that were unusual or distinct given the bar setting (e.g., Christmas decorations), and were included to ensure the subject is not simply yielding to any type of questions posed by the experimenter. Additionally, *suggestibility* was measured as the tendency to yield to 5 false alternative questions (e.g., "Was the lady watching the attack holding a glass of red or white wine?", "Was the backpack on the chair blue or green?", when in fact there was no backpack and the lady was not holding a glass) as employed in previous research (van Oorsouw et al., 2019).

Implantation Paradigm

In the first step of this procedure, participants were confronted with a total of four screenshots of Instagram posts related to the festival (see Fig. 3 for study flow). At the outset, participants were instructed that they would see some screenshots of social media posts made by other visitors or organizations of the Lowlands festival, and, as a cover story, were asked how likely they would share the post in their own social media feed (scale from 0-100). They were explicitly instructed to take into account both the picture content and the caption, in order to ensure that they would pay attention to the title of the post. Half of the participants (all with even participant numbers) were presented with only true posts, which had been screenshotted directly from Instagram during the days leading up to the festival (e.g., depicting jewelry to be sold at the festival, see Fig. 1). The other half (all with odd numbers) were exposed to three true posts and one out of two fabricated posts containing fake news (A or B, according to participant number). The fake post in version A (Fig. 2a) showed a stage where the band "The Kooks" had supposedly given a surprise concert at Lowlands, naming one of the bigger stages of the festival by name. Version B showed a supposed beer tent sponsored by beer manufacturer Heineken that was giving

out free (non-alcoholic) beer[9] (Fig. 2b). In reality, there was no Heineken free beer tent, and the band "The Kooks" did not play at the festival. The fabricated posts were similar in design to the posts depicting true events, and displayed comments to add to the illusion of a real post. All posts were presented one by one in randomized order, accompanied by a likelihood-to-share rating scale. Subsequent to each post, a multiple-choice question depicting three options was posed, asking about the caption (title) of the previously viewed post. This served as a manipulation check to ensure that participants paid attention to the captions.

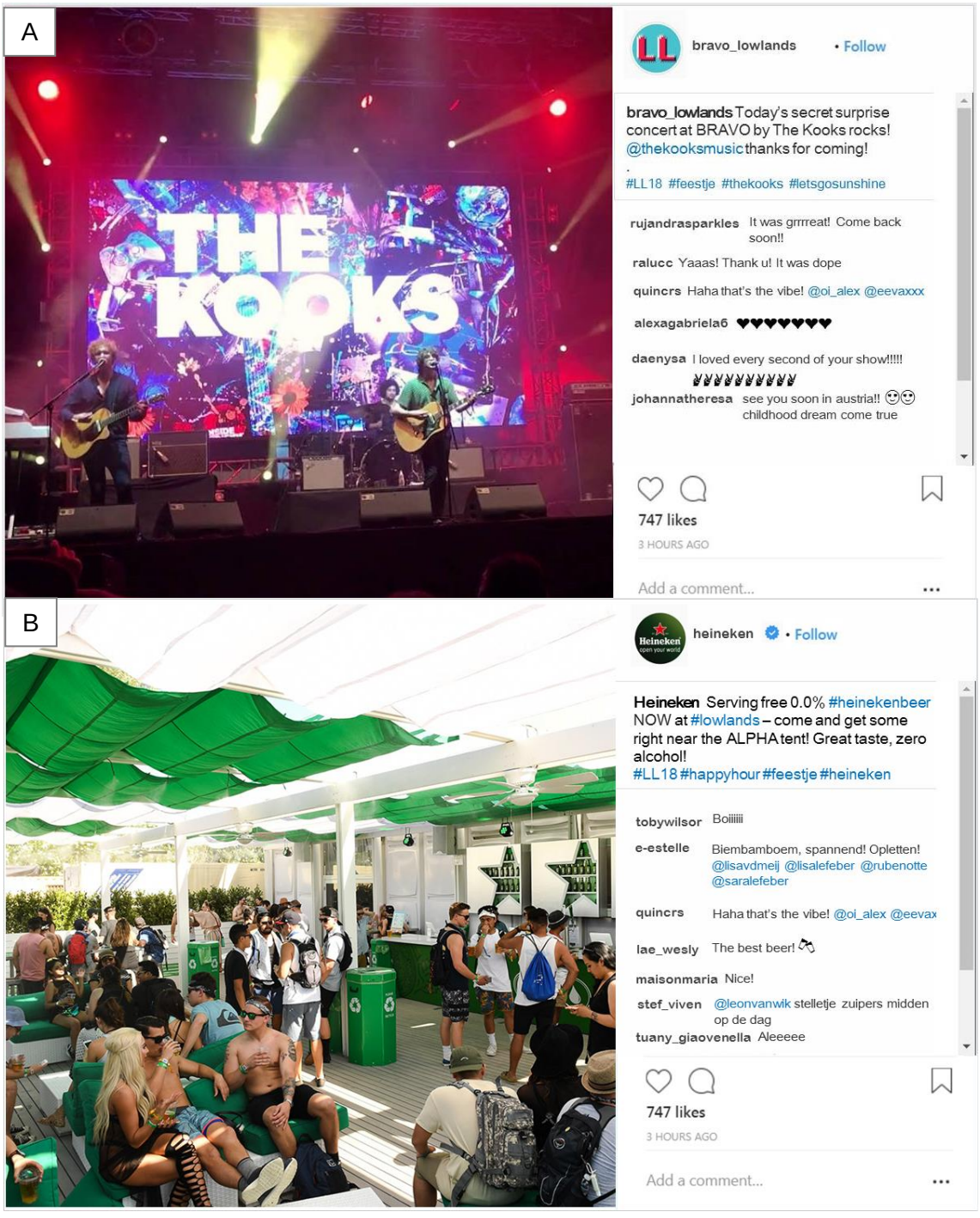
Figure 1

Example of a true post from implantation paradigm

[9] The post had previously been approved by a Heineken Nederland B.V. brand management team member

Figure 2

Fake posts from implantation paradigm, version A and B



In a later phase of the research, participants underwent an interview in which they were asked about their experiences at the festival. This interview contained the implantation manipulation, which all participants received, but there were parallel versions (A or B). In version

A participants received the suggestion that they had been to the surprise concert by the Kooks, and in version B it was suggested that they had been to the Heineken free beer tent. At the outset, participants were told that since the study was focused on memory, it was also of interest how well they would remember things at the festival. They were asked about a total of five events in randomized order. Four were distractor events that visitors might have come across at the festival (e.g., "Did you go to the silent disco?"). The fifth event was the fake event, entailing the implantation manipulation. Here, the experimenter initially asked whether the participant went to the fake event (A: "Did you go to the "The Kooks" surprise concert?", B: "Did you go to the Heineken free beer tent?"). Subsequently, the experimenter pretended being highly certain that the participant had in fact been at the suggested event, verbally claiming that he/she spotted the participant in the crowd, (e.g., "Hey, that's why you seem familiar, I think I saw you there! I'm sure I spotted you in the crowd."). Thus, the manipulation involved some acting on behalf of the experimenter to convince participants, which did not follow a standardized script. For each event, participants were asked to separately rate their *belief* that the event happened, and their *recollection* of it each on an 8-point Likert scale adopted from Scoboria et al. (2004). For example, to assess belief they were asked "How likely is it that you did in fact go to the Heineken free beer tent?" on a scale from 1 ("definitely did not happen") to 8 ("definitely did happen"), and to assess recollection "Do you actually remember going to the Heineken free beer tent?" on a scale from 1 ("no memory of event at all") to 8 ("clear and complete memory of event"). It was explained to participants that when experiencing events, it is possible to believe that an event happened but to not have a vivid memory of it, and vice versa. In addition, for the fake news item, it was logged whether the participant accepted the misinformation (yes/no/maybe but unsure), and whether they came up with additional details (yes/no).

Procedure

The study flow is depicted in Fig. 3. The study was set up in a 4x6 m lab space within a large container containing multiple labs, as part of the Lowlands Science side attraction. The study was advertised by the festival as a "Virtual reality crime study". As a cover story, the study was described as focusing on the virtual reality eyewitness scenario, with the aim of investigating effects of alcohol and lack of sleep on memory for a witnessed criminal event. Additionally, before the exposure to true and fake news, participants were informed that they would view social media

posts that were recently posted by other festival visitors. These measures were taken to prevent suspicion.

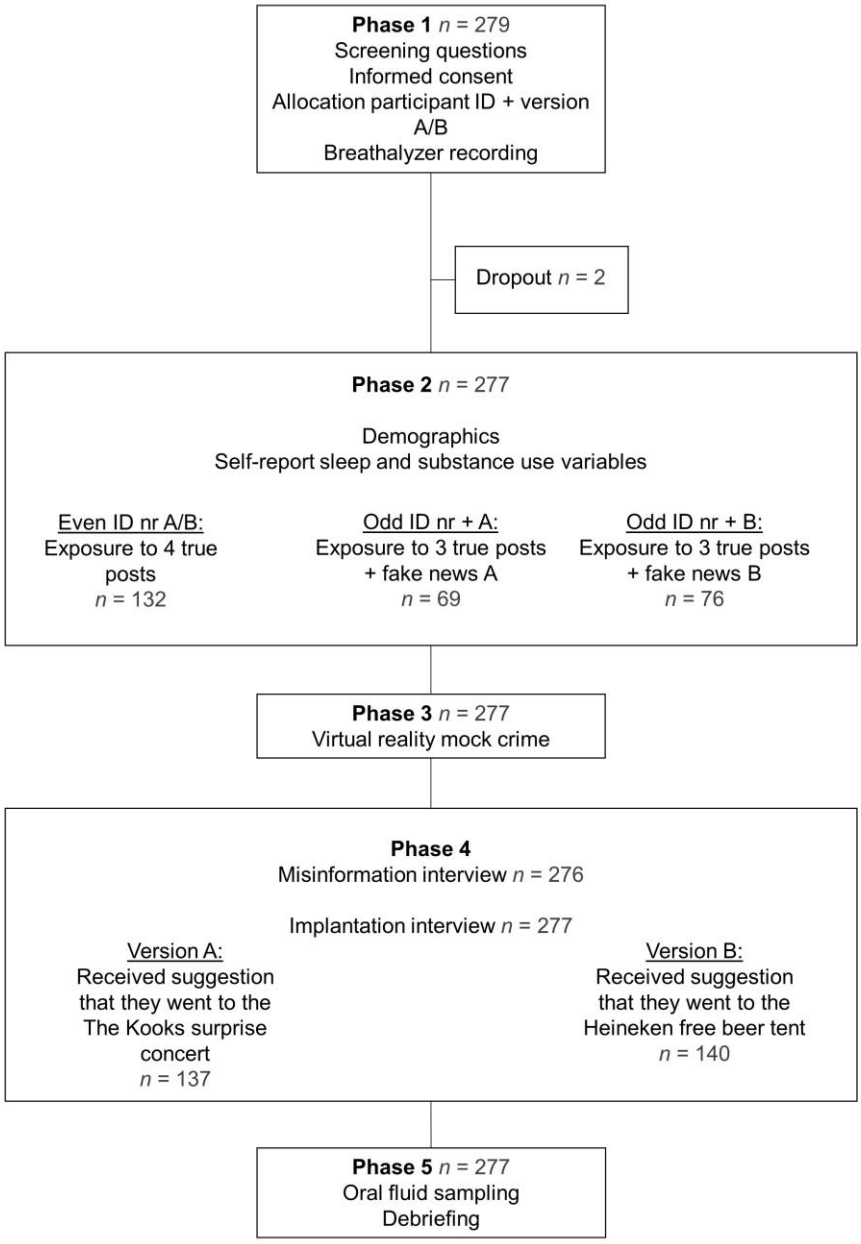
Given the small lab space, the space was divided into five research stations corresponding to five research phases, each carried out by 1-2 experimenters, respectively. In phase 1, when an interested participant approached the lab, they were provided with oral and written information about the study, given the opportunity to ask questions, and asked to sign informed consent. Three screening questions were asked (orientation to space and time, simple math equation) to determine capability of giving informed consent (none failed). Subsequently, a sticker was attached to the participant's shirt, displaying their participant number and randomization (A or B, randomly allocated). The sticker also contained the main researcher's contact information and a statement that they may contact the team if they wished to withdraw their consent at a later point, or to request further information about the study. Participants were then given a sip of water to rinse their mouth before they were breathalyzed. This completed phase 1.

In phase 2, participants were sat at a table on one of four laptops and were handed soundproof over-ear headphones to prevent them from overhearing interviews conducted by other experimenters. To allocate which participant received the fake news, we used separate survey versions using the web-based survey tool "Qualtrics". All participants were asked to answer demographic questions and to provide information about their sleep as well as alcohol and drug use. Next, they were shown 5 Instagram posts: half of the participants received true posts only, and half received 4 true posts and 1 fake post. Only the participants with odd participant numbers received the version containing fake news (all three versions visible on https://osf.io/a7tmp).

In phase 3, participants underwent the virtual reality simulation in a 3x3 m area separated by barrier poles in the back of the lab. This eyewitness scenario depicts a bar, which the participant can explore, until after 1 min a fight breaks out between some guests. The scenario ends automatically after the perpetrator has run away (total length of 1.5 min).

Figure 3

Study flow diagram



In phase 4, participants were interviewed by an experimenter about their experiences at Lowlands (implantation paradigm), and about the virtual reality scenario (misinformation paradigm), using a YUNTAB 10,1-inch PC k17 Android tablet. Participants were also asked to identify the VR perpetrator from a lineup (analyses will be reported elsewhere).

Phase 5 entailed providing participants with two collectors to obtain oral fluid samples, one for the onsite screening (Dräger DrugCheck 3000), and one for the confirmation analysis (Dräger DCD 5000). The major benefits to testing of oral fluid is an easy and hygienic sample collection that can occur in the presence of another person without invasion of the donor's privacy. Additionally, it is characterized by reduced risk of sample adulteration, dilution, and substitution. Oral fluids normally contain the parent drug substance rather than drug metabolites, which makes oral fluid an attractive matrix for use in detection of recent drug use and in interpretation of possible drug-induced behavioral effects.

This concluded the study and participants received a debriefing statement as well as the opportunity to ask questions. In accordance with Lowlands Science policy participants were not reimbursed for their time since only experiments deemed attractive and interesting for participants were accepted in the first place. The entire study was conducted in the English language. Participants also had the opportunity to learn their BrAC level once the study was completed, which for some was a motivation to complete the study.

Statistical Approach

Misinformation and Suggestibility

Primary Analyses. We calculated the following dependent variables (DVs): hits (proportion correctly recognized true details), critical false alarms (proportion falsely recognized suggested details), control false alarms (proportion falsely recognized non-suggested details), suggestibility (sum of items yielded to, 0-5). In addition, signal detection parameters were calculated to assess sensitivity as $d' = Z(\text{hits}) - Z(\text{false alarms})$ with higher values signaling greater discrimination ability, and response bias as $c = -1/2\ [(Z(\text{hits}) + Z(\text{false alarms})]$, where positive values indicate conservative and negative values liberal response tendencies (Macmillan & Creelman, 2004).

Stepwise multiple regression analyses were conducted to assess the ability of sleep restriction and substance intoxication to predict memory performance on the six DVs. In line with Frenda et al. (2014), the number of *hours of sleep* last night was utilized as our measure of sleep restriction (continuous predictor, lower levels representing more sleep restriction). Substance intoxication was operationalized as the *number of active substances* that a participant had recently used, as indicated using the breathalyzer and oral fluid tests. In a large number of cases, alcohol and/or other substances were detected (see results below); however, many of the detected concentrations were rather low. Therefore, to identify participants that had recently used a substance and thus could be assumed to be under acute influence, we applied established cut-off thresholds in oral fluid signaling recent use (e.g., as applied in roadside drug testing) of Tetrahydrocannabinol (THC, 30 ng/l), cocaine (20 ng/ml), amphetamines (50 ng/ml), and MDMA (50 ng/ml). For alcohol, we set the cut-off at breath alcohol levels of 0.07%. Therefore, the variable *number of active substances* represented intoxication above these cut-off values, with higher scores indicating intoxication with more substances. Six cases were excluded from the primary analyses due to use of the following: Ritalin (n = 1), Diphenhydramine (n = 1), Tramadol (n = 1), Oxazepam (n = 1), Methadone (n = 1), Lidocaine (n = 1).

Exploratory analyses. In the primary analyses, we considered multiple active substances lumped together. However, a fair point of criticism of that approach is that not all substances have equal effects on true and false memory (for a review see Kloft et al., 2021). Therefore, in exploratory analyses we aimed to gain a more nuanced picture, zooming in on each substance's effects. We used the above-mentioned impairment cut-off thresholds to identify *active* substance use groups for THC (n = 10), amphetamines (n = 11), MDMA (n = 40), cocaine (n = 9), and alcohol (n = 23)[10]. However, it has to be noted that these groups were not mutually exclusive, as e.g., some individuals were positive in saliva for multiple substances, both above and below the cut-off threshold. We also used the dichotomization adopted by Frenda et al. (2014) to identify sleep-restricted individuals (5 h or less of sleep last night) and non-sleep-restricted individuals (6 h or more), and coded a control group, consisting of individuals who had no sleep restriction and had

[10] 26 concentrations of ketamine were detected, ranging from 0.2-23.6 ng/ml. Recent use of ketamine is signaled by oral fluid concentrations far exceeding 1000 ng/ml (Tsui et al., 2012), therefore it is fair to assume that all concentrations in our sample were negligible and were not taken into account in further analyses

not used any alcohol or other substances (neither below or above the cut-off), resulting in $n = 64$. Identifying these groups led to a sub-sample of $n = 140$. In a series of six hierarchical stepwise multiple linear regression analyses within this sub-sample, we tested the effects of substance intoxication with THC, amphetamine, MDMA, cocaine, and alcohol use as binary predictors on the six DVs while controlling for sleep restriction (*hours of sleep* as a covariate; model 1 = covariate only, model 2 = all predictors).

Implantation Paradigm

To obtain an overall picture of the success of our implantation we first examined the percentages of participants that indicated elevated (>1) belief, elevated recollection, and both elevated belief and recollection in response to manipulation A (The Kooks surprise concert), B (Heineken free beer tent), and both collapsed together. To test the effects of fake news exposure, substance intoxication, and sleep restriction and their interaction on false belief and false recollection, we conducted General Linear Model (GLM) analyses using a hierarchical approach. Using the categorical predictors fake news exposure (yes/no), sleep restriction (yes/no), and substance intoxication (number of active substances: 0-3), analyses were conducted with initially all interaction terms included in the model. If the highest-order term did not meet statistical significance, the analyses were repeated with that term removed. This procedure was repeated, further simplifying the model by removing the highest-order term with the largest p-value, until no more terms could be removed. Each predictor was also tested in isolation of the others. Participants who had received fake news but did not pass the manipulation check for the fake news item were excluded from the GLM analyses.

Results

Alcohol and Substance Use

Objective

Breathalyzer results showed a reading of 0.00% for 162 participants, whereas 114 participants had a reading >0.00% (n = 1 missing). Of the ones who tested positive for alcohol, breath alcohol concentrations ranged from 0.08-1.49% (M = .48, SD = 0.29).

According to the oral fluid tests, 114 participants were positive for any substance, and in total 170 times was a substance detected. This included the following substances/substance classes: amphetamines (in 26.7% of the whole sample, concentrations above the limit of detection (LOD) of this substance were detected), cocaine (10.8%), THC (11.9%), ketamine (9.0%), opioids/opiates (1.4%), and benzodiazepines (0.7%, for full details see "Dräger sheet" on https://osf.io/a7tmp).

Self-report

Table 1 shows an overview of the self-report data. 97 participants indicated that they had not had any alcohol on the day of testing. 238 participants indicated not having used any substance (other than alcohol), whereas 42 indicated having used one or more substance(s).

Misinformation Paradigm

Primary Analyses

Table 2 displays the summary statistics from the stepwise regression analyses on all DVs, using hours of sleep and number of active substances as predictors. Hours of sleep emerged as the single statistically significant predictor for the memory variables of control false alarms and suggestibility. Inspection of the regression coefficients revealed that number of hours of sleep was negatively related to control false alarms and suggestibility. In other words, more sleep-restricted individuals displayed higher control false alarm and suggestibility rates. However, overall hours of sleep only accounted for 3.9-4.3% of the variance (see Table 2). The model was not statistically significant for the DVs hits, critical false alarms, sensitivity, and response bias.

Exploratory Analyses

For each of the six DVs, hours of sleep was entered in model 1, and the binary predictors specifying drug use (THC, amphetamines, MDMA, cocaine, alcohol) were entered using the stepwise method in model 2. Use of THC and use of amphetamines emerged as the only statistically significant predictors of control false alarms [F (2, 137) = 7.29, $p < .001$, $R^2 = .096$]. Inspection of the regression coefficients showed that both variables were positively related to control false alarms [THC: $\beta = .24$, t (137) = 2.95, $p = .004$; amphetamines: $\beta = .22$, t (137) = 2.66, $p = .009$,] indicating that participants who had been tested positive for THC or amphetamines scored higher on control false alarms. Drug use did not explain any statistically significant portions of the variance in any of the other DVs (all analyses can be retrieved from the OSF: https://osf.io/a7tmp). Table 3 depicts mean scores of each subgroup on all DVs, including the sleep-restricted subgroup for reference.

Table 2

Misinformation/suggestibility primary analyses: stepwise regression

	Descriptives[a]			Model statistics					Coefficients			
Dependent variable	*M*	*SD*	*SE*	*R*	R^2	*Significant predictor*	*t*	*p*	*Unstandardized*	*SE*	*Standardized*	*95% CI*
Hits	0.611	0.132	0.008	0.152	0.023	-	-	-	-	-	-	-
False alarms (critical)	0.265	0.176	0.011	0.000	0.000	-	-	-	-	-	-	-
False alarms (control)	0.077	0.121	0.007	0.196	0.039	Hours of sleep	-3.280	0.001	-0.015	0.004	-0.196	-0.023; -0.006
Suggestibility	2.963	1.51	0.092	0.208	0.043	Hours of sleep	-3.180	0.002	-0.176	0.055	-0.191	-0.284; -0.067
Sensitivity *d'*	1.324	0.566	0.034	0.000	0.000	-	-	-	-	-	-	-
Response bias *c*	0.362	0.354	0.021	0.160	0.026	-	-	-	-	-	-	-

Note.

[a] All based on $n = 270$

Table 3

Misinformation/suggestibility parameters by sub-group [Mean (SD)]

Group (*n*)	Hits	Critical false alarms	Control false alarms	Suggestibility (yield score, 0-5)	Sensitivity	Response bias
Control (64)	.63 (.13)	.27 (.17)	.05 (.09)	2.75 (1.66)	1.43 (.58)	.37 (.36)
MDMA (40)	.63 (.13)	.26 (.18)	.08 (.12)	3.2 (1.24)	1.40 (.57)	.33 (.36)
Amphetamine (11)	.59 (.09)	.21 (.15)	.15 (.13)	2.7 (1.56)	1.22 (.38)	.38 (.31)
Cocaine (9)	.59 (.09)	.28 (.14)	.02 (.06)	3.2 (1.09)	1.30 (.42)	.41 (.28)
THC (10)	.62 (.10)	.27 (.18)	.16 (.16)	3.80 (.79)	1.19 (.57)	.28 (.30)
Alcohol (22)	.58 (.11)	.28 (.16)	.05 (.11)	2.55 (1.60)	1.18 (.36)	.38 (.23)
Sleep-restricted (33)	.61 (.11)	.29 (.16)	.10 (.14)	3.00 (1.68)	1.20 (.51)	0.31 (.29)

Note.

All based on $n = 140$

Implantation Paradigm

N = 6 observations were excluded due to a mismatch in fake news and manipulation conditions, leaving *n* = 271 valid observations. *N* = 132 (48.7%) participants received manipulation A (The Kooks surprise concert), and *n* = 139 (51.3%) received manipulation B (Heineken free beer tent), i.e. they were interviewed about events at Lowlands and it was suggested that they had been at the fake event. Out of these participants, *n* = 139 (51.3%) were exposed to fake news. For manipulation A, 3 (valid percent 3.7%) participants responded yes that they went to the supposed event when initially asked (79, i.e., 96.3% said no, *n* = 50 missing responses[11]). In response to the implantation, 97 (89.0%) maintained a belief score of 1 ("definitely did not happen"), while 12 (11.0%, missing responses *n* = 23) reported an elevated belief score >1. Regarding recollection of the event, 105 (95.5%) reported no memory, while 5 (4.5%) reported a recollection score >1 (missing *n* = 22). It was recorded that 7 (5.3%) people accepted the misinformation (7 unsure, 117 did not accept it, 1 missing), and only 1 person came up with additional detail. For manipulation B, 8 participants (valid percent 5.8%) answered that they went to the event when initially asked, while 131 (94.2%) said no. In response to the implantation manipulation, 101 (84.9%) reported no belief that they went to the event, while 18 (15.1%) had an elevated belief score >1. With regard to recollection, 106 (92.2%) reported no memory of the event at all, while 9 (7.8%) reported a recollection score >1. Six (4.3%) participants were recorded as accepting the misinformation, 10 (7.2%) were recorded as maybe accepting it, and 123 (88.5%) did not accept it. In addition, 6 (4.3%) came up with additional details about the fake event (*n* = 6 missing).

In total (A and B collapsed together), the majority of participants indicated no belief that the suggested event occurred (86.8%, *n* = 44 missing), while 13.2% of those asked had a belief score >1 (*M* = 4.5, *SD* = 2.24). For recollection, the majority did not report any memory of the suggested event (93.8%, *n* = 46 missing), but a proportion of 6.2% indicated an elevated recollection score of >1 (*M* = 6.29, *SD* = 2.02).

For the following analyses, 12 observations were excluded due to failure of the manipulation test. In the series of hierarchical two-way ANOVA, neither of the binary predictors *fake news exposure*,

[11] Large proportions of missing data here are thought to stem from a faulty setting in Qualtrics that was changed after day 1

hours of sleep, and *number of active substances* nor their interaction were statistically significantly associated with false belief or false recollection (all *p*s > .05, see https://osf.io/a7tmp).

Discussion

In this field study, we examined effects of naturally-occurring substance intoxication and sleep deficits on proneness to suggestion-induced false memories, expecting greater memory impairment at high intoxication and sleep restriction levels. Music festival visitors were exposed to a virtual reality eyewitness scenario, and subsequently interviewed with a mix of suggestive and non-suggestive questions about the event. Here, restricted sleep but not the number of substances detected in saliva was associated with increased suggestibility and false responses to non-suggestive questions (control false alarms). Exploratory analyses suggested that some substances especially THC and amphetamine use elevated the risk of false endorsement of non-suggestive questions. Additionally, we aimed to implant false memories of suggested recent festival events, exposing half the participants to fake news of said event. Contrary to our expectation, fake news exposure did not exacerbate false memory formation, and neither did sleep restriction or substance intoxication.

Our most consistent pattern of findings concerned the relationship between sleep restriction and false memory creation. That is, in our misinformation task, sleep restriction was associated with some memory variables but not others. Specifically, reduced sleep predicted a greater tendency to go along with misleading either-or questions ($R^2 = 4\%$), our measure of suggestibility, but not with suggestive questions about non-presented details, our measure of suggestion-induced false memories. Reduced sleep also predicted false alarms for control questions ($R^2 = 4\%$). Our results are partially in line with previous research showing greater levels of false memories and interrogative suggestibility in sleep-deprived individuals (Blagrove, 1996). While sleep restriction only explained a small proportion of variance, it should be noted that in previous research, participants were usually deprived of sleep for an entire night or restricted to a few hours for multiple nights in a row, with most robust effects on false memories detected after total sleep deprivation (i.e., entire night; Blagrove, 1996; Frenda et al., 2014; Lo et al., 2016). In our sample, all participants had had some sleep. Still, our findings add to the growing body of experimentation showing that sleep restriction can amplify false memory creation, the novel feature of this study being that we showed this in a field study.

The number of substances that a participant had recently used did not predict performance on any of the memory variables in the misinformation paradigm. Possibly, lumping substances of different pharmacological mechanisms and effects on cognition together was too crude a measure

of intoxication, thereby nullifying any effects on false memory proneness. Zooming in on single substances indicated that not all substances were equally memory-impairing. Use of THC (main psychoactive compound of cannabis), as well as amphetamines was related to higher levels of control false alarms when compared to a sober control group, even when controlling for levels of sleep restriction. THC administration prior to memory retrieval has been shown to elevate false memories of both neutral and emotional stimuli such as words, pictures, and details from a virtual reality crime, inducing a response bias particularly for unrelated items (Doss, Weafer, Gallo, et al., 2018a; Hart et al., 2010; A. B. Ilan et al., 2004; Kloft et al., 2019; Kloft et al., 2020). Similarly, administration of the prototypic stimulant drug dextroamphetamine prior to retrieval also increased false recall and recognition rates in a word and a picture memory task (Ballard et al., 2014). Our findings underline that intoxication with THC and amphetamines can foster false responding, and that particularly non-suggestive questions about non-presented details seem a sensitive marker of drug influence. Control measures of false alarms are known in memory research as baseline false alarms, and tend to be treated as byproducts in recognition tasks which are used to adjust hit and critical false alarm rates (e.g., Gallo, 2010), but can evidently be informative in itself when it comes to drug intoxication. Liberal responding and intrusions in memory of unrelated words have also been associated to false childhood memory (Qin et al., 2008), indicating their potential relevance to autobiographical memory.

In our implantation paradigm, prior exposure to fake Instagram posts did not exacerbate the likelihood of false beliefs or recollections in response to a suggestion of having experienced a false festival event. Given the short retention interval, provision of a visual cue might have actually backfired and facilitated rejection of the suggested event by enabling participants to rely on their visual memory and distinguish the depicted place from truly visited places. Doctored pictures have also been associated with lower rates of implanted false memories previously, compared to other suggestive techniques (Garry & Wade, 2005; Scoboria et al., 2017).

Overall, low proportions of participants reported believing (13%, $n = 30$) or recollecting (6%, $n = 14$) the fake event to a certain extent, indicating that the manipulation was not overly successful when compared to other implantation studies, in which on average about 30% of subjects create an implanted false memory (Scoboria et al., 2017). However, a crucial difference between our and other studies is that we aimed to implant recent rather than childhood events, with a single suggestive occasion rather than multiple (e.g., Otgaar et al., 2013). Memory of festival

events might have still been too well preserved given their relative recentness and event centrality, as people are less susceptible to suggestion after shorter delays and when information is central rather than peripheral (Loftus et al., 1978; Paz-Alonso & Goodman, 2008).

Limitations other than those inherent to field studies are that the substance sub-groups used in our exploratory analyses were small and sometimes included individuals with polysubstance use (both below and above the cut-offs, see https://osf.io/a7tmp for all drug information). Thus, the sub-groups might not always have represented the pure effects of a single substance, which can be better achieved through placebo-controlled experiments. Another limitation was that the implantation required acting on behalf of the experimenter, which was not scripted, therefore introducing extra variability and potentially varying levels of convincingness. Future research on implanting memories for recent events could add, for example, imagination procedures to increase the level of suggestion.

In sum, in this study we attempted to capture effects of everyday sleep deficits and psychoactive drug use on false memory creation and suggestibility. Partially, we observed effects that had previously been studied in lab environments, demonstrating the real-world applicability of those concepts.

Funding and Disclosure

The authors report no conflict of interest. The study was supported by the Lowlands Science initiative.

Acknowledgements

We thank Richard Benning (Maastricht University) for designing the virtual reality scenario, Franc Donkers (Maastricht University) for providing the portable virtual reality setup, and Dräger Safety Germany for collecting and analyzing oral fluid samples, in cooperation with MVZ Labor Dessau GmbH, Dessau, Germany. Further, we are grateful to Lowlands Science for the opportunity to conduct this research. Finally, we thank Natasha Mason, Jessica Bruijel, Nina Tupper, Rosalie Mourmans, Kayley van Uden, Julia Gros, and Frederick Vinckenbosch for collecting data and being a fantastic festival crew.

Author contributions

JR, LK, HO, AB, and KvO designed the research and wrote the Lowlands proposal, JR, LK, SS, and KvO collected the data, LK and SS analyzed the data (LK: memory, SS: drugs), JS provided advice on the statistical methods, and LK wrote the paper with revisions by all co-authors.

Chapter 7

General discussion

The core aim of this dissertation was to investigate the effects of widespread recreational drugs on false memory formation. The importance of elucidating drug effects on false memory formation has its origins from the frequent involvement of intoxicated individuals in legal cases, which can result in dramatic legal consequences such as wrongful convictions and miscarriages of justice (see **Chapter 1**). To that end, a literature review and four experimental studies were conducted to 1) establish the prevalence of intoxicated witnesses, victims, and suspects (**Chapter 2**), 2) examine the acute and delayed effects of cannabis on spontaneous and suggestion-based false memories (**Chapters 3** and **4**), 3) examine the acute and delayed effects of MDMA on spontaneous and suggestion-based false memories (**Chapter 5**), and 4) to review and assess effects of other drugs on false memory formation and suggestibility (**Chapters 2** and **6**). These aims, associated findings and their implications, and future research directions are discussed in turn. An overview of all experimental studies and key findings of this thesis is also presented in Table 1.

Table 1

Summary of Thesis Experimental Findings

Ch.	Substance	Method + Design	Sample	Dose	Paradigm	Memory stage tested	Key findings	Effect size	
3	**Cannabis**	Between-subjects field experiment	*N* = 156; intoxicated vs sober cannabis users vs controls	self-administered	DRM (recognition)	Intoxicated/sober /control at encoding + retrieval	Higher false memory for unrelated but not critical lures in intoxicated and sober cannabis users, compared to controls	$\eta^2_p = 0.11$	(medium - large)
4	**Cannabis**	Double-blind randomized placebo-controlled laboratory experiment, mixed design	*N* = 64 healthy occasional cannabis users	300µg THC/kg	DRM (recognition)[a]	THC at encoding + immediate retrieval, delayed retrieval sober	Immediate: THC increased false memory (related + unrelated); Delayed: THC increased unrelated but decreased critical lure false memory	*d* = 0.58 + 1.0; *d* = 0.38 + 0.27	(medium, large; small)
					Misinformation (2 virtual reality scenarios, suggestive co-witness + suggestive questioning)[b]		Immediate: THC increased several measures of false memory; Delayed: No effect	*d* = 0.54 - 0.86	(medium - large)
5	**MDMA**	Double-blind randomized placebo-controlled laboratory experiment, mixed design	*N* = 60 healthy occasional MDMA users	75mg MDMA	DRM (recognition)[a]	MDMA at encoding + immediate retrieval, delayed retrieval sober	Immediate: MDMA decreased true and increased false memory (related lures only); Delayed: MDMA decreased true and critical lure false memory	*d* = .27 + 0.42; *d* = 0.30 + .30	(small - moderate)
					Misinformation (2 virtual reality scenarios, suggestive co-witness + suggestive questioning)[b]		Immediate: No effect; Delayed: reduced suggestion-based false memory in eyewitness condition	*d* = 0.77	(medium - large)
6	**Naturally occurring substance use**	Field experiment, mixed design	*N* = 277 festival visitors	self-administered	Misinformation (virtual-reality scenario, suggestive questioning)	If substance present, likely onboard at encoding + retrieval	Sleep restriction predicted suggestibility and non-suggested false alarms; THC + amphetamines increased non-suggested false alarms	R^2 = 3.9 - 4.3; η^2 = .12 + .12	(small; inter-mediate)
					Implantation paradigm		False belief and recollection of a suggested festival event were not associated with fake news exposure, sleep restriction, or substances used	-	

Note.
[a] Within-subjects comparisons
[b] Between-subjects comparisons

Prevalence of Intoxicated Witnesses, Victims, and Suspects

A literature review was conducted to demonstrate the importance and magnitude of the issue of intoxication on behalf of a witness, victim, or suspect of crime (Chapter 2). An outline of the prevalence of legal cases was presented that involved substance intoxication in five selected countries with accessible data (Australia, the Netherlands, England and Wales, United States, Indonesia), encompassing data from official national statistics, governmental legal databases, police survey research, case file research, toxicology analysis, and victim surveys. Whereas overall prevalence of legal cases involving substance use was found to range between 1.2 - 4.3%, the incidence of intoxication in violent crime cases tended to be considerably higher: in such cases, the prevalence of intoxicated suspects was found to range from 25-78% for alcohol and from 10-83% for illicit drugs, and for victims from 24-72% for alcohol and 3-66% for other drugs (see Table 1, Chapter 2). Intoxicated eyewitnesses were also frequently reported by police officers, but specific numbers were mostly lacking. The most commonly identified substances in forensic contexts were alcohol, cannabis, and stimulants (e.g., cocaine, MDMA, amphetamines).

These findings illustrate that the number of cases involving substance use across the reviewed countries is non-negligible, and that particularly in cases of violent crime, intoxication on behalf of at least one of the involved seems to be the norm rather than the exception. Alcohol and other drug (AOD) intoxication raises a number of problems for the legal system. The first issue is that AOD intoxication has to be accurately detected. Biological detection methods (e.g., breathalyzer or saliva drug screen) may routinely be employed with suspects of crime, but generally are not used with victims or witnesses (Monds, Quilter, et al., 2019b). In the absence of such relatively objective assessment methods or an individual's own disclosure, police have to rely on their own observational abilities (Crossland et al., 2018), which research suggests are not better than chance, and intoxication detection training appears underdeveloped (Monds, Quilter, et al., 2019b). Consequently, intoxication in legal cases may often go undetected, unreported, and intoxicated individuals be unknowingly questioned (Rubenzer, 2011).

The second illustration is that once detected, AOD intoxication must be adequately handled. Research has shown that jurisdictions lack standard procedures or differ in their recommendations regarding the handling of intoxicated witnesses and suspects, including when to interview them (e.g., Crossland et al., 2018; Evans et al., 2009; Monds, Cullen, Kloft,

Sumampouw, et al., 2020; van Oorsouw & Merckelbach, 2012). In the absence of procedural safeguards, intoxicated individuals may therefore frequently be inappropriately handled (e.g., questioned at an inadequate time), and evidence-based policies are needed to put standardized practices in place. Third, and of central relevance for the current thesis is the concern that intoxication during a criminal event, during questioning, or both, might contaminate memory reports and compromise an individual's ability to provide a complete and accurate account. Research in this thesis and elsewhere has found that this can indeed be the case (e.g., Jores et al., 2019), but that factors such as the used substance, dose, which memory phase was affected, and the timing of the interview play a determining role in how memory reporting is affected. Hence, a nuanced approach is needed in dealing with intoxicated witnesses, victims, and suspects.

Fourth, perceptions surrounding the credibility of intoxicated individuals can impact investigative outcomes and legal decision-making, such as the decision of whether and how to prosecute (Evans & Schreiber Compo, 2010; Flowe et al., 2011; Monds, Cullen, Kloft, Sumampouw, et al., 2020; Monds, Cullen, Kloft, van Golde, et al., 2020). For example, reduced perceptions of credibility by police, legal professionals, or jurors despite the testimony being accurate could potentially increase the risk of a failed investigation or prosecution. Alternatively, if the testimony is perceived as credible but contains inaccuracies, this could potentially obscure the investigation and result in a wrongful conviction. In summary, intoxication in legal cases creates a trajectory in which disadvantages can accumulate and interact throughout the criminal investigative process, ultimately putting society at increased risk for adverse outcomes.

Cannabis

The impact of cannabis on the susceptibility on false memory formation was investigated in a field experiment in Dutch coffeeshops (Chapter 3), a placebo-controlled laboratory experiment (Chapter 4), and to some extent in a field study at a music festival (Chapter 6).

Spontaneous False Memories

In the coffeeshop field study (Chapter 3) the memory performance of three groups was compared, consisting of a group of acutely cannabis-intoxicated cannabis users, a group of sober regular cannabis users, and a group of sober controls without a history of cannabis use. Subjects were asked to study associatively-related word lists (e.g., *bed, rest, dream, tired*) and, after a short

delay, received a recognition test that included old (e.g., *bed*) and new unpresented words (strongly associated, e.g., *sleep*, and unassociated ones, e.g., *table*). These word lists can successfully evoke spontaneous false memories (Deese/Roediger-McDermott, or DRM, paradigm, Deese, 1959; Roediger & McDermott, 1995). It was found that both acutely intoxicated and sober cannabis users had higher false recognition rates of new unrelated words, compared to controls. True recognition of old words and false recognition of critical lure words did not statistically differ between the three groups. We concluded that acute and residual cannabis use likely induced a liberal or 'yes'-saying bias that becomes most apparent when the level of association between studied and tested materials is low. That is, since unrelated words (e.g., *table*) do not bear any relation with the studied items (e.g., *dream, rest, tired, awake*) and since false recognition items were highest for unrelated items in the cannabis groups, it is probable that cannabis led to a yes-saying bias.

The findings from this field experiment were replicated and extended in the lab (Chapter 4) in a double-blind, randomized, placebo-controlled trial, in which healthy participants who were occasional users of cannabis were administered an active dose of medicinal cannabis (13% THC) versus a placebo (inactive substance). The DRM paradigm was administered and recognition was tested in an immediate condition (during acute cannabis intoxication), and again tested one week later (delayed condition). Mirroring what was found in the coffeeshop study, intoxicated participants performed similarly on measures of true recognition as well as false recognition of critical lures, compared to when they were given placebo. However, and once more echoing findings from the coffeeshop study, acute cannabis resulted in elevated false recognition rates of unrelated lures. In addition, cannabis elevated false alarms in response to related lures, a category that we added as part of the recognition test containing new words that bore some level of association to the studied materials (e.g., the word *nap* in relation to a list centered around the critical non-presented word *sleep*). When tests were repeated after a one-week follow-up at which all participants were sober, memory performance still varied between drug conditions: true recognition and false recognition of critical lures were slightly reduced in the cannabis condition, and false alarms of unrelated lures were again increased. The latter effect could not be accounted for by source confusion from the previous retrieval attempt (see supplementary information, Chapter 4 for more details). Overall however false memory effects were most pronounced during acute intoxication, and cannabis at retrieval robustly increased false memory errors in the DRM paradigm, which may play out as false reports in other contexts.

Suggestion-based False Memories and Suggestibility

In the placebo-controlled study describe above, the susceptibility to suggestive misinformation in two versions of the misinformation paradigm was also examined (Chapter 4). In comparative treatment (cannabis vs. placebo) conditions, participants experienced two fully immersive virtual reality crime scenarios, once in the role of an eyewitness and once as a perpetrator committing a theft. Misinformation was introduced through a virtual co-witness and through suggestive questions in an interview about the event, in which true and false memory was also assessed. Cannabis-intoxicated participants were more susceptible than controls to incorrect responses (false alarms) to suggestive and non-suggestive questions relating to the eyewitness scenario. Moreover, they showed a greater general tendency to respond 'yes' to interview questions about both true and false details after the perpetrator scenario, compared to the placebo group. Here, false memory effects were only evident during acute cannabis intoxication, and had dissipated at the one-week follow-up, although the latter could be attributed to the placebo group's memory performance worsening over time. These results are also consistent with a response bias driving up false alarms when cannabis affects retrieval. Our results show that memory errors or response bias as observed in more fundamental research also generalize to complex situations of forensic relevance.

Finally, in our Lowlands field study (Chapter 6) we found elevated false alarms in response to non-suggestive questions about a virtual reality crime in participants who tested positive for THC use in saliva. Although these analyses were exploratory and had limitations (e.g., small group size of $n = 10$) this finding adds further evidence to the notion that THC during retrieval can foster false responding, and that particularly non-suggestive questions about non-presented details seem a sensitive marker of cannabis use. Suggestion-based false memory and suggestibility were however not statistically significantly affected by THC in this field study.

Theoretical Implications

Analyzing the observed findings regarding spontaneous false memories from Chapters 3 and 4 in light of other cannabis DRM literature (Ballard et al., 2012; Doss, Weafer, Gallo, et al., 2018a; Riba et al., 2015) and in the context of some of the prominent theories in the false memory literature (associative-activation theory/AAT and fuzzy-trace theory/FTT) the following picture

emerges: impaired processing of targets (presented words) through THC intoxication at encoding seems to reduce associative activation (AAT) or gist-based memory (e.g., of the critical lure). This plays out as classic amnestic effects when tested later during the sober state, resulting in reduced true memory but also reduced false memory of critical lures, which are similar to targets in terms of content (however, see supplementary information in Chapter 4, additional analyses on the confounding effects of repeated and novel test items). Therefore, THC intoxication during encoding seems to decrease memory for the relatedness of presented words, providing partial support for AAT and FTT.

When present during retrieval, cannabis increased false responding in an association-dependent manner, with largest effects for unrelated words. It is difficult to say whether cannabis induced actual false memories in the sense of vivid recollections, or whether criterion shifts were at play, or both. Whereas false alarms for critical or related items are seen as more likely to reflect underlying memory processes representing "actual" false memories (Arndt, 2010), false responding to unrelated items is frequently seen as an indication of response bias (i.e., the general tendency to respond to items in a systematic but potentially false direction, such as a yes-bias, Wright et al., 2008). We and others found evidence for both (Doss, Weafer, Gallo, et al., 2018a).

The fact that cannabis during retrieval induced the highest rates of false memories is difficult to reconcile by the main tenets of AAT and FTT, since both assume that false memories are primarily caused at encoding (e.g., Gallo, 2010). Although it is possible that during retrieval being confronted with targets might cause, for example, associative (re)activation of the lists, a framework with an explicit monitoring component such as the *activation/monitoring theory* (AMT) might be better suited to account for the findings (e.g., Roediger, Watson, et al., 2001). Monitoring refers to the decision process that helps to determine the source of the activated information to discriminate studied from unstudied material (similar to the source-monitoring framework described in chapter 2). This process is a direct reflection of conservative or liberal retrieval criteria, or in other words response bias. We have seen that cannabis likely affects this component at retrieval.

A third effect detected in this thesis was that even when retrieval occurs during the sober state cannabis was associated with an elevated response bias (i.e., increased false recognition of new unrelated words). We demonstrated this in sober regular users of cannabis (Chapter 3) and

sober occasional users who had encoded the lists during intoxication one week prior to the retrieval attempt. Most individuals in the coffeeshop study's sober cannabis group had consumed cannabis the day before the experiment for the last time, indicating that for this group residual THC effects might have played a role, given that THC is a lipid-soluble chemical which is not rapidly eliminated from the body (Huestis, 2007). Residual effects are less likely to play a role in our placebo-controlled study given that the retention interval was 7 days. Given that memory was impaired through THC at encoding and the first retrieval attempt, perhaps a liberal criterion shift was maintained and carried over to the second retrieval attempt. However, in the study by Riba and colleagues, chronic but 4-weeks abstinent cannabis users were more prone to false memory creation (i.e., false recognition of related lures) compared to controls, indicating that also persistent long-term effects on false memory susceptibility can be a consequence of cannabis use.

We have suggested an increase in irrelevant associations as a potential explanation of the liberal responding observed in both intoxicated and non-intoxicated cannabis consumers. Scientific evidence for this notion comes for example from an animal study that showed increased incidental learning due to activation of hippocampal CB1 receptors (Busquets-Garcia et al., 2018). A loosening of associations also parallels observations specified by the liberal acceptance (LA) account of schizophrenia: A plethora of studies have revealed that schizophrenic patients base decisions upon very little evidence, revealing lower decision thresholds, relative to controls (see Moritz et al., 2009). Moreover, problems with source-monitoring and response bias are a common occurrence in schizophrenia patients; for example, hallucination scores have been found to be correlated with an increased bias toward false recognitions of non-presented words (Brébion et al., 2005; Harvey, 1985). This dovetails nicely with the postulated relation between THC and psychosis, i.e., transient induction of psychotic-like symptoms but also increased risk of psychotic disorders after cannabis use (Gage et al., 2016), indicating further similarities between the two in producing cognitive bias. However, it should be noted here that according to recent evidence an appreciable portion of the association between cannabis use and schizophrenia is not causal (Gillespie & Kendler, 2020).

Applied Implications

The most important message from this research is that cannabis exerted a general impact on memory by increasing various types of recollective errors, which can be perilous in

investigative interviewing settings. Although there is debate on whether different types of false memories are related to each other (Ost et al., 2013; Otgaar, Howe, et al., 2016), the findings presented in this dissertation show that intoxicated individuals might be at high risk to form all kinds of memory errors. This was demonstrated using a basic (DRM) and two more applied (misinformation) paradigms of high ecological validity. The more ecologically valid findings confirmed what has been demonstrated in more fundamental research, namely cannabis consistently increases susceptibility to false memories. The results have implications for police, legal professionals, and policymakers with regard to the treatment of cannabis-intoxicated witnesses and suspects and the validity of their statements.

The findings that intoxicated participants were more susceptible to suggestive questions in an eyewitness role and showed higher acquiescence (yes-saying) in a perpetrator role imply that interviewing an individual while they are still intoxicated should be minimized to reduce the risk of false reporting as induced by cannabis. Questioning should be postponed and, if needed, occur as soon as the person has sobered up to prevent memory decay due to time. However, a person under the influence of cannabis during an event, as well as sober-but-frequent cannabis users, might still show a yes-bias towards some new information later. Therefore, findings suggest that intoxicated individuals and potentially also regular cannabis consumers should be categorized as a vulnerable group, similar to child or elderly witnesses and suspects (e.g., Bull, 2010). This means that special safeguards and best practice recommendations such as the use of skilled interviewing techniques should be put in place to ensure that best evidence is achieved (i.e., maximizing accuracy and minimizing error, see Holliday et al., 2012).

Our two studies (Chapters 4 and 6) have been the first and only ones to employ the misinformation paradigm with cannabis, only one of them being placebo-controlled, and thus need replication. In the only other two studies that exampled acute effects of cannabis on eyewitness memory for a mock crime (Vredeveldt et al., 2018; Yuille et al., 1998) intoxicated participants' accounts assessed by free recall tests and open questions were less complete (i.e., provided fewer correct details) but not less accurate (i.e., did not provide more inaccurate details). Therefore, higher potential for false responding in the context of cannabis use thus far has only been demonstrated when *closed* questions and a forced-choice format were used. This underscores the importance of use of adequate interviewing strategies (open, non-leading questions) and use of

reliable and valid interviewing tools (e.g., the cognitive interview, Fisher & Geiselman, 1992; Geiselman et al., 1986) particularly when it comes to interviewing (previously) intoxicated individuals. It could be that under such procedural safeguards individuals who used cannabis can still provide reliable information, but the boundary conditions have to be further elucidated and confirmed.

As for implications beyond the legal realm, an increased susceptibility to false memory formation or to a yes-saying bias can be detrimental in any high-stake situation. For example, obtaining accurate and reliable information is important in clinical contexts, such as psychotherapy. More generally, since it has been demonstrated that especially acute cannabis influence impairs our ability to process information, it might be wise to avoid acute intoxication during situations where it is important that information is processed and remembered correctly; for example, when studying or when watching the news, where attention to nuanced details is needed. Misinformation can come in form of fake news (e.g., Murphy et al., 2019), and a higher yes-bias could encourage people to accept fake news that aligns with their current biases, prejudices and beliefs.

Future Directions

Future research directions can be formulated with a two-fold aim in mind: To advance basic memory research and theoretical understanding, and to obtain further insights within the wider legal-forensic eyewitness and perpetrator memory context. With regard to theoretical advancement, a viable direction will be to evaluate activation-monitoring theory in the context of cannabis and false memory. This could be done using a task that enables disentanglement of the effects of THC on activation vs monitoring (e.g., using an inclusion/exclusion task, Hege & Dodson, 2004; Pierce et al., 2017). Likewise, testing effects of repeated DRM list presentation as in previous research with alcohol and benzodiazepines (Garfinkel et al., 2006; Mintzer & Griffiths, 2001c) could reveal important theoretical insights on how THC affects learning and memory processes (e.g., gist versus verbatim memory, see Mintzer & Griffiths, 2001). Finally, the cognitive mechanisms underlying THC-induced false memory formation (e.g., memory distrust, response bias) deserve greater attention, and future studies could employ measures of metamemory (e.g., confidence, trait subjective memory measures) to provide further clarification (e.g., van Bergen et al., 2010). From a more psychopharmacological perspective, controlled studies on dose-dependent

effects are also essential to establish a relation between the (drug) mechanism and the observed effect; therefore, future studies could evaluate how the false memory effects of THC and potentially other cannabinoids such as CBD vary with dosage.

As for more applied future directions, these could pertain to elucidating the boundary conditions of (un)reliable and (in)valid testimony of cannabis-using or intoxicated witnesses and suspects. In real life, interviewees are allowed to provide "I don't know" answers, and research has shown that given such an option, people are able to strategically regulate their testimony and, for example, give highly specific answers only when they deem it highly likely to be correct (i.e., when confidence is high; Weber & Brewer, 2008). This again raises the issue of how metacognition is affected by cannabis: recent research suggests that metacognitive awareness can be generally impaired when acutely intoxicated (Pezdek et al., 2020) but this has only been tested in a face recognition task. Future research could examine how cannabis affects memory reporting in terms of grain size regulation (i.e., when broad vs. specific information is volunteered to police as in Kloft, Hett, et al., submitted) and the cannabis-accuracy relationship for volunteered information. Varying the retention interval between the criminal event and retrieval is also a worthwhile avenue of research (e.g., how is eyewitness memory affected when more than 7 days have passed). Moreover, the effects of repeated interviews in relation to cannabis, eyewitness memory and false memory formation could be investigated as has been done in alcohol research (e.g., Hagsand et al., 2017). Although underpowered, in the pioneering study by Yuille et al. (1998) participants who had experienced a crime under influence of cannabis demonstrated an increase in recall between the first and second interview, resulting in similar recall performance as the placebo group. This is intriguing because research has shown that memory decay can be halted when there are repeated intervening retrieval attempts (e.g., Ebbesen & Rienick, 1998) but potentially errors made during an initial (intoxicated) interview could also carry over. Future studies could test whether repeated interviewing is beneficial for cannabis-intoxicated individuals, and whether memory errors introduced during an intoxicated interview would persist and appear in later interviews.

MDMA

The acute and delayed effects of 3,4-methylenedioxymethamphetamine (MDMA), the main ingredient of ecstasy on spontaneous and suggestion-based false memory formation were

tested in a placebo-controlled study (Chapter 5) using the same design and study procedures as the above-described cannabis study (Chapter 4). MDMA is a stimulant and entactogen that acts as a serotonin releaser.

Spontaneous False Memories

Following the same procedures as in the study described in Chapter 4, participants were once exposed to DRM lists during MDMA intoxication and once during placebo, and recognition was tested immediately as well as one week after (within-subjects comparison). True recognition of presented words was impaired during acute MDMA intoxication but also one week later when sober. This adds to previous findings (e.g., Doss, Weafer, Gallo, et al., 2018b; Kuypers & Ramaekers, 2005) and supports the notion that MDMA intoxication during encoding robustly impairs true memory. In the immediate condition, MDMA did not have a statistically significant effect on false alarm rates for critical or unrelated lures, but did elevate false memories for related lures. When calculating signal detection parameters (i.e., methods of analyzing decision making in the presence of uncertainty), it was found that in the immediate test MDMA reduced overall ability to discriminate between targets and lures (sensitivity) but did not affect overall response bias. At the delayed test one week after encoding MDMA decreased false alarms to critical lures in addition to decreasing hits, but other false alarm measures were unaffected. Signal detection parameters also did not indicate any statistically significant differences between conditions.

Suggestion-based False Memories and Suggestibility

Equivalent to the misinformation procedures in Chapter 4 participants were exposed to a perpetrator and an eyewitness mock crime during comparative drug treatment conditions, and received misinformation about the events through a suggestive eyewitness and through suggestive questions when being interviewed about the event. Between-groups comparisons revealed no statistically significant differences for true or false memory measures during any of the immediate tests. One week later there were also no statistically significant differences detected for the perpetrator scenario, but participants who had undergone the eyewitness scenario during MDMA intoxication were less susceptible to suggestive questions about the event. This was also reflected in a more conservative response bias in the MDMA group. No other signal detection measures were affected by MDMA in any of the conditions. However, equivalence tests conducted to further

explore the null findings (i.e., in the eyewitness immediate and perpetrator immediate and delayed conditions) could not reject the potential presence of a small effect. Therefore, it seems that MDMA did not consistently affect episodic memory in these more applied tasks. Importantly however, susceptibility to external suggestion was not increased in any of the conditions at the observed dose (75 mg) of MDMA intoxication.

In the field study described in Chapter 6 festival visitors were exposed to an eyewitness virtual reality crime and subsequently questioned about the event with a combination of questions tapping into true memory, suggestion-based false memory, suggestibility, and response bias. Using saliva drug screens a group of participants (n = 40) was identified who had non-negligible concentrations of MDMA in their system. A comparison of their memory performance to sober controls, while controlling for hours of sleep during the previous night, revealed no statistically significant between-group differences. A limitation here was that these exploratory analyses did not control for concomitant substance use so MDMA effects might have been confounded or masked with other drug influence.

Theoretical Implications

Small to moderate effects on both true and false memory were detected in the DRM paradigm, with most robust effects on true memory, adding further support to the notion that MDMA primarily interferes with memory encoding (Doss, Weafer, Gallo, et al., 2018b). In terms of the theoretical account of associative-activation theory (AAT), MDMA at encoding, not unlike THC at encoding, might reduce spreading activation, perhaps by impairing the processing of words, so that the result is decreased true memory and decreased critical lure recognition (after a delay). In terms of fuzzy-trace theory (FTT) the findings could be interpreted as MDMA impairing gist-processing but potentially also reducing verbatim processing, given that immediate true memory was also impaired (for similar findings and interpretation with the drug scopolamine see Mintzer & Griffiths, 2001a). In general, the findings are consistent with our prediction made in Chapter 2 that amnesia-producing drugs such as alcohol might indirectly reduce mechanisms of associative activation or gist extraction during encoding, resulting in reduced associative/gist false memory later, thus providing partial support for AAT and FTT. There is now good evidence in the literature that MDMA is such an amnesia-producing drug (Kuypers & Ramaekers, 2005; Kuypers

et al., 2016), although it does not produce periods of complete amnesia as for example sedatives do.

The studies in this dissertation did not assess metamemory but are consistent with some findings by previous studies. Doss and colleagues (2018b) found that MDMA specifically attenuated the *recollection* component of episodic memory, which is characterized by retrieval of specific details of a prior event and relies on the hippocampus (Yonelinas, 2002). In contrast, the other component of episodic memory – *familiarity* – is the feeling of knowing that an event occurred, and is cortically-dependent. Doss et al. (2018b) reported a trend of MDMA at encoding towards enhancement of familiarity. The fact that in the current study MDMA impaired hit rates and critical lures is also indicative of a recollection impairment, whereas the finding that MDMA increased false alarms to related lures could indicate familiarity enhancement: for example, if a few targets can still be remembered, and they are slightly spreading their activation in a particularly ambiguous and perhaps automatic manner, this could explain increased related false alarms through enhanced familiarity. However, this is a strongly speculative explanation. There is however recent indication that the classical psychedelic psilocybin, also a 5-HT_{2A} agonist, produces the same pattern of effects, i.e., impairing recollection while leaving familiarity intact or even tending towards enhancing it (Barrett et al., 2018; see also Doss et al., in preparation). Thus, evidence seems to be accumulating that 5-HT_{2A} agonists impair recollection but may leave familiarity intact or even enhance it (Doss et al., in preparation).

Applied Implications

While MDMA appears to share some effects with THC (as described in the previous sections and in Chapter 4) respective to encoding and true memory, a key difference between the findings from these two studies was that unlike THC, MDMA did not elevate response bias in any of the tasks at any point. Rather, response bias was more conservative after MDMA in one condition, and most importantly, suggestion-based false memories or suggestibility were not increased at any point at the observed doses in the two versions of the misinformation paradigm that were used in Chapters 5 and 6. Moreover, true memory impairment at the dose of 75 mg (Chapter 5) was only detected in the more fundamental DRM task but not in the more applied tasks. These findings are important in light of the issue of intoxicated witnesses and suspects, and also with regard to the current developments regarding MDMA-assisted psychotherapy for the

treatment of post-traumatic stress disorder (PTSD), which recently received the FDA label of breakthrough therapy (Mithoefer et al., 2019). However, the findings described in this dissertation regarding MDMA, false memory formation, and suggestibility are too preliminary to warrant definitive claims and recommendations for applied legal or clinical settings. There is some basis to suspect that MDMA might actually increase suggestibility, such as the finding by Carhart-Harris et al. (2015) that an acute dose of LSD, a classical psychedelic similar to MDMA in its 5-HT_{2A} agonism, enhanced suggestibility in a creative imagination task. Further elucidation of the relationship between MDMA, suggestibility, and false memory formation will be strongly relevant to the legal-psychological and clinical-psychotherapeutic context, and ideas for such are described in the next section.

Future Directions

With actions on numerous neurotransmitter and neural pathways, the entactogen MDMA has a complex neuropharmacological profile that can modulate (emotional) memory and facilitate learning in various ways (see Feduccia & Mithoefer, 2018). There is a dearth of controlled administration studies on MDMA and memory aside from perhaps verbal recall and spatial memory tasks (e.g., Kuypers et al., 2013; Kuypers & Ramaekers, 2007), and the research described here has been the very first to investigate MDMA using different false memory tasks. A wider variety of (false) memory tasks in acute MDMA administration studies is thus called for, both to advance basic memory research and theory as well as to advance applied research on memory and cognition. For example, further studies could aim to replicate the observed DRM effects using study designs that separate the different memory phases. From an applied point of view, future studies could assess 1) whether MDMA affects recall instead of only recognition of a forensically relevant event 2) how MDMA affects strategic memory reporting as in previous alcohol research, and the confidence-accuracy relationship (e.g., Kloft, Hett, et al., submitted) and 3) potentially testing higher doses and dose-response relationships. Finally, employing other suggestibility measures will be a worthwhile research avenue, as for example the Gudjonsson Suggestibility Scale to assess interrogative suggestibility (Gudjonsson, 1997), and imaginative procedures tapping into primary suggestibility (e.g., as used in Carhart-Harris et al., 2015).

Other Drugs

The effects of drugs besides cannabis and MDMA on false memory formation and suggestibility have been reviewed at length in Chapter 2. Furthermore, in the field study at the Lowlands festival, effects of naturally occurring substance use on false memory formation and suggestibility were tested in a misinformation-suggestibility task and an implantation paradigm. Some noteworthy findings and future directions are discussed below.

Reviewing the effects of alcohol on false memory formation and more broadly eyewitness memory (Chapter 2), studies overall indicated that mild and moderate alcohol levels reduced true memory (completeness) but did not elevate the risk to provide inaccurate details in an immediate memory test (Jores et al., 2019). This maps onto some findings from the Lowlands field study described in Chapter 6, in which festival visitors were exposed to an eyewitness virtual reality crime and were subsequently interviewed using a combination of suggestive and non-suggestive questions about true and false event details. Isolating a group of participants (n = 22) who were moderately to highly intoxicated with alcohol (mean breath alcohol concentration = .91) during the crime and the subsequent interview, we detected no statistically significant differences in memory performance when comparing the alcohol group with a sober control group in exploratory analyses. As described in Chapter 2 and supported by some studies, a delay is likely needed before memory is sufficiently degraded through alcohol at encoding so that the susceptibility to false memories and suggestibility becomes elevated. However, some studies have also found elevated suggestibility in an immediate memory test when alcohol levels were high (van Oorsouw et al., 2019; van Oorsouw et al., 2015). Given the applied importance of the question of when very drunk individuals can best be questioned – immediately or after a sobering delay – it would be interesting to aim to replicate findings from the Lowlands study with a higher sample size of highly intoxicated participants in a better controlled setting, using an ecologically valid misinformation method plus adding a delayed condition.

The Lowlands study (Chapter 6) also demonstrated that poly-drug use is common. The number of psychoactive substances participants had used was not associated with any memory variables in neither task, but some substances were linked to higher false alarms when considered separately (THC, amphetamines). This implies that some substances might affect false memory formation differently or more robustly than others, a conclusion that was also drawn in Chapter 2.

The Lowlands study design was not suited to examine false memory effects of specific drug combinations, and a well-controlled crossover design is needed to evaluate effects of acute co-administration of popular drugs such as alcohol, cannabis, stimulants, and psychedelics. Although drug-drug interactions have sometimes been studied in basic memory research (e.g., THC and MDMA, Dumont et al., 2010), such studies have not focused on false memories, and research on the combined effects of drugs in an applied memory context is entirely lacking.

Summary

In many criminal trials, no forensic technical evidence is available, thus legal decision-making is largely based on testimonies (e.g., Howe et al., 2017). The net result is that there is an inevitable reliance on testimonies given by witnesses, victims, and/or offenders. A factor that may affect the reliability and validity of testimonies is the level of alcohol and/or other drug intoxication. Eyewitnesses, victims, and suspects can be intoxicated during the criminal event or when giving a statement, or both (Evans et al., 2009). Despite the fact that false memories (i.e., memories of events or details that did not happen, e.g., Loftus, 2016; Mazzoni, 2002) are known to have caused wrongful convictions (e.g., Howe et al., 2017), there is sparse knowledge on how intoxication might affect the susceptibility to spontaneous or suggestion-induced false memories. To that end, across a literature review and four experimental studies I 1) established the prevalence of intoxicated witnesses, victims, and suspects (**Chapter 2**), 2) examined the acute and delayed effects of cannabis on spontaneous and suggestion-based false memories (**Chapters 3** and **4**), 3) examined the acute and delayed effects of MDMA on spontaneous and suggestion-based false memories (**Chapter 5**), and 4) reviewed and assessed effects of other drugs on false memory formation and suggestibility (**Chapters 2** and **6**).

In **Chapter 1** I presented a real-life case example in which drug use had likely played a role in distorting memory, thus setting events in motion that ended in the wrongful conviction of an innocent person. Furthermore, a general background of false memory research and memory and drug studies was provided. **Chapter 2** contained a more detailed introduction to the topic of false memories and intoxication, and consisted of three parts: 1) a review of the prevalence of legal cases that involved substance intoxication on the part of an eyewitness, victim, or suspect in order to illustrate the practical importance of this issue; 2) a background of the scientific study of false memories; and 3) a review of the current state of the scientific literature regarding the effects of substance intoxication on false memory formation and suggestibility. Reviewing the prevalence of intoxicated witnesses, victims, and suspects in legal cases, an overall prevalence was found to range between 1.2 - 4.3%, whereas the incidence of intoxication in violent crime cases tended to be considerably higher: in such cases, the prevalence of intoxicated suspects ranged from 25-78% for alcohol and from 10-83% for illicit drugs, and for victims from 24-72% for alcohol and 3-66% for other drugs (see Table 1, Chapter 2). The most commonly identified substances in forensic

contexts were alcohol, cannabis, and stimulants such as MDMA, confirming the importance of our research focus on some of these drugs.

Chapter 3 presented a field experiment in Dutch coffeeshops, in which the memory performance of three groups was compared: acutely cannabis-intoxicated cannabis users, sober regular cannabis users, and sober controls without a history of cannabis use (N = 156). Participants were asked to study associatively-related word lists (e.g., *bed, rest, dream, tired*) and, after a short delay, received a recognition test that included old (e.g., *bed*) and new unpresented words (strongly associated so-called *critical lures*, e.g., *sleep*, and unassociated words, e.g., *table*). This procedure is a highly reliable and common method to evoke spontaneous false memories (Deese/Roediger-McDermott, or DRM, paradigm, Deese, 1959; Gallo, 2010; Roediger & McDermott, 1995). No statistical difference between groups was found for the acceptance of critical lures (i.e., *sleep*), but it was found that both 'high' and sober cannabis users showed an increased likelihood of falsely recognizing completely new stimuli that had no association to the previously studied word list themes. These findings were interpreted as indicative of a cannabis-induced response bias ('yes-saying' bias) that might vary depending on the strength of association between studied and test items.

The results were replicated and extended in the lab (**Chapter 4**). Specifically, in a double-blind, randomized, placebo-controlled trial, healthy volunteers (N = 64) who were occasional users of cannabis were administered an active dose of medicinal cannabis (300 μg THC/kg) versus a placebo (inactive substance). In the active condition, they showed increased false memory levels of stimuli that bore some or no association to previously studied DRM word lists. In addition, the susceptibility to suggestion-based false memories was examined in two virtual reality (VR) based versions of the misinformation paradigm (Loftus, 2005). Cannabis-intoxicated participants were more susceptible than controls to incorrect responses (false alarms) to suggestive and non-suggestive questions after a VR eyewitness scenario and showed a greater general tendency to respond 'yes' to interview questions about both true and false details after a VR perpetrator scenario. Memory tests took place immediately during acute intoxication, and one week later when sober again. False memory effects across all paradigms were mostly restricted to the immediate condition, so when participants were tested during acute intoxication. However, some false memory effects in the DRM were found to persist until the one-week follow-up when participants

were sober again. This study has provided some of the first evidence that using cannabis elevates the risk of creating different types of false memories, and an important implication is that interviewing while an individual is cannabis-intoxicated should be minimized due to elevated risk of false reporting.

In **Chapter 5** the same design and study procedures were used as the above-described cannabis study (Chapter 4) to test the acute and delayed effects of 3,4-methylenedioxymethamphetamine (MDMA), the main ingredient of ecstasy (N = 60). MDMA increased the forgetting of presented words in the DRM paradigm both when participants were tested immediately and one week later. On the immediate test, MDMA increased related but non-critical lures, whereas after a delay MDMA reduced critical lures, as these were similar to old words in content and were to some extent presented on the prior test. Unlike cannabis, however, memory was not affected by acute MDMA intoxication in the two more applied misinformation tasks, and in one condition MDMA even seemed to induce a more conservative responding strategy when memory was tested one week later. Importantly, susceptibility to external suggestion was not increased in any of the conditions with the dose given in this study.

Polysubstance effects on false memory and suggestibility are still unexplored and not always feasible to investigate in a lab setting. Thus, in **Chapter 6** a field study was conducted at the Lowlands music festival to examine the impact of naturally occurring factors on the susceptibility to suggestion: sleep deficits and substance intoxication. In a misinformation-suggestibility task, festival visitors' (N = 277) restricted sleep was associated with increased levels of suggestibility and false alarms to non-suggestive questions related to a virtual reality eyewitness scenario. Recent use of THC or amphetamines was also related to increased false alarms to non-suggestive questions, again confirming that cannabis induces a yes-saying bias and indicating that this category of questions might be a sensitive marker for drug influence. An adapted implantation paradigm was also used in which it was suggested to participants that they experienced an event that recently occurred at the festival. No associations were found between sleep restriction, substance use, nor exposure to fake news and the likelihood to falsely believe or recollect the suggested festival event. However, some people came to falsely believe (13%, n = 30) or falsely remember (6%, n = 14) the false event. This was also the first study that ever used an implantation paradigm to study substance effects.

Finally, in **Chapter 7** the key findings were discussed in a broader context. Namely, it was demonstrated that cannabis intoxication during memory retrieval robustly elevates incorrect responding. Acute cannabis influence was found to increase various types of recollective errors, seemingly inducing a 'yes'-saying response bias, which can be perilous in investigative interviewing settings. The most important recommendation from this dissertation was therefore to avoid questioning of cannabis-intoxicated individuals to minimize false reporting, and rather delay questioning until a sober state is reached. Still, the findings of this dissertation call for the establishment of particular procedural safeguards for situations that involve questioning of individuals who used cannabis during a criminal event, or who use it on a regular basis. It was recommended that cannabis-intoxicated witnesses and suspects be recognized and treated as a *vulnerable* group in legal settings. In contrast, MDMA robustly increased forgetting but further elucidation of false memory effects is needed, particularly in light of future therapeutic applications of MDMA. Further applied studies on suggestibility using, for example, imaginative procedures and potentially investigating higher doses might be a worthwhile target in future research.

Samenvatting

In veel strafzaken is geen forensisch technisch bewijs voorhanden. Dit betekent dat juridische besluitvorming grotendeels toegelegd is op verklaringen van getuigen, slachtoffers, en verdachten (bijv. Howe et al., 2017). Een belangwekkende factor die de betrouwbaarheid en validiteit van verklaringen kan beïnvloeden, is de mate van intoxicatie door alcohol en/of andere drugs. Ooggetuigen, slachtoffers en verdachten kunnen onder invloed zijn tijdens een misdaad of bij het afleggen van een verklaring, of allebei (Evans et al., 2009). Ondanks het feit dat pseudo-herinneringen (d.w.z. herinneringen aan gebeurtenissen of details die niet hebben plaatsgevonden, bv. Loftus, 2016; Mazzoni, 2002) bekend zijn als oorzaak van onterechte veroordelingen (bv. Howe et al., 2017), is er maar weinig bekend over hoe intoxicatie de vatbaarheid voor spontane of door gesuggereerde valse herinneringen zou kunnen beïnvloeden. Daartoe heb ik in een literatuuronderzoek en vier experimentele studies 1) de prevalentie van bedwelmde getuigen, slachtoffers en verdachten vastgesteld (**Hoofdstuk 2**), 2) de acute en vertraagde effecten van cannabis op spontane en op suggestie gebaseerde valse herinneringen onderzocht (**Hoofdstukken 3** en **4**), 3) de acute en vertraagde effecten van MDMA op spontane en op suggestie gebaseerde valse herinneringen onderzocht (**Hoofdstuk 5**), en 4) de effecten van andere drugs op de vorming van pseudo-herinneringen en op suggestibiliteit onderzocht en beoordeeld (H**oofdstukken 2** en **6**).

In **Hoofdstuk 1** presenteerde ik een casus waarin drugsgebruik waarschijnlijk een rol had gespeeld bij het vervormen van het geheugen, en zo gebeurtenissen in gang had gezet die uitliepen op de onterechte veroordeling van een onschuldig persoon. Verder werd een algemene achtergrond gegeven van onderzoek naar pseudo-herinneringen en geheugen- en drugsstudies. **Hoofdstuk 2** bevatte een meer gedetailleerde inleiding op het onderwerp valse herinneringen en intoxicatie, en bestond uit drie delen: 1) een overzicht van de prevalentie van rechtszaken waarin sprake was van intoxicatie door een ooggetuige, slachtoffer of verdachte, om het praktische belang van deze kwestie te illustreren; 2) een achtergrond van het wetenschappelijk onderzoek naar pseudo-herinneringen; en 3) een overzicht van de huidige stand van de wetenschappelijke literatuur betreffende de effecten van intoxicatie door een stof op de vorming van pseudo-herinneringen en op suggestibiliteit. Bij het onderzoek van de prevalentie van bedwelmde getuigen, slachtoffers en verdachten in rechtszaken bleek de algemene prevalentie tussen 1,2 en 4,3% te liggen, terwijl de prevalentie van intoxicatie in geweldszaken aanzienlijk hoger lag: in dergelijke zaken varieerde

de prevalentie van bedwelmde verdachten van 25-78% voor alcohol en van 10-83% voor illegale drugs, en voor slachtoffers van 24-72% voor alcohol en 3-66% voor andere drugs (zie tabel 1, hoofdstuk 2). De stoffen die in de forensische context het vaakst werden geïdentificeerd waren alcohol, cannabis, en stimulerende middelen zoals MDMA, hetgeen bevestigt hoe belangrijk het is dat ons onderzoek zich op sommige van deze drugs concentreert.

Hoofdstuk 3 presenteerde een veldexperiment in Nederlandse coffeeshops, waarin de geheugenprestaties van drie groepen werden vergeleken: acuut cannabis-intoxicerende cannabisgebruikers, nuchtere regelmatige cannabisgebruikers, en nuchtere controles zonder een geschiedenis van cannabisgebruik (*N* = 156). De deelnemers werd gevraagd associatief-gerelateerde woordenlijsten te bestuderen (b.v. *bed, rust, droom, moe*) en kregen na een korte vertraging een herkenningstest met oude (b.v. *bed*) en nieuwe niet-gepresenteerde woorden (sterk geassocieerde z.g. kritische lokmiddelen, b.v. *slaap*, en ongeassocieerde woorden, b.v. *tafel*). Deze procedure is een zeer betrouwbare en gangbare methode om spontane pseudo-herinneringen op te roepen (Deese/Roediger-McDermott, of DRM, paradigma, Deese, 1959; Gallo, 2010; Roediger & McDermott, 1995). Er werd geen statistisch significant verschil tussen de groepen gevonden betreffende het accepteren van kritische niet-getoonde woorden (d.w.z. *slaap*), maar wel bleek dat zowel "high" als nuchtere cannabisgebruikers een verhoogde kans vertoonden op het ten onrechte herkennen van geheel nieuwe stimuli die geen associatie hadden met de eerder bestudeerde woordlijstthema's. Deze bevindingen werden geïnterpreteerd als een aanwijzing voor een door cannabis veroorzaakte bias (“ja-zeggen” bias), die zou kunnen variëren naar gelang de sterkte van de associatie tussen bestudeerde en test-items varieert.

De resultaten werden gerepliceerd en uitgebreid in het lab (H**oofdstuk 4**). In een dubbelblind, gerandomiseerd, placebogecontroleerd onderzoek kregen gezonde vrijwilligers (*N* = 64), die af en toe cannabis gebruikten, een actieve dosis medicinale cannabis (300 µg THC/kg) tegenover een placebo (inactieve stof) toegediend. In de actieve conditie vertoonden zij verhoogde niveaus van pseudo-herinneringen van stimuli die enige of geen associatie vertoonden met eerder bestudeerde DRM-woordenlijsten. Bovendien werd de vatbaarheid voor op suggestie gebaseerde valse herinneringen onderzocht in twee op virtual reality (VR) gebaseerde versies van het misinformatieparadigma (Loftus, 2005). Cannabis-intoxicerende deelnemers waren na een VR-ooggetuigen-scenario vatbaarder dan controles voor onjuiste antwoorden (valse alarmen) op

suggestieve en niet-suggestieve vragen, en vertoonden een grotere algemene neiging om “ja” te antwoorden op interviewvragen over zowel ware als valse details na een VR-dader-scenario. Geheugentests vonden plaats onmiddellijk tijdens acute intoxicatie, en een week later wanneer men weer nuchter was. De vorming van pseudo-herinneringen in alle paradigma's bleef meestal beperkt tot de onmiddellijke conditie, dus wanneer de deelnemers tijdens de acute roes getest werden. Sommige effecten op pseudo-herinneringen in de DRM bleken echter aan te houden tot de follow-up van een week, wanneer de deelnemers weer nuchter waren. Deze studie heeft voor het eerst aangetoond dat het gebruik van cannabis het risico op het ontstaan van verschillende soorten pseudo-herinneringen verhoogt, en een belangrijke implicatie is dat het afnemen van interviews terwijl iemand onder invloed van cannabis is, geminimaliseerd moet worden vanwege het verhoogde risico op foutieve verklaringen.

In **Hoofdstuk 5** werden dezelfde opzet en studieprocedures gebruikt als de hierboven beschreven cannabisstudie (Hoofdstuk 4) om de acute en vertraagde effecten te testen van 3,4-methyleendioxymethamfetamine (MDMA), het hoofdbestanddeel van ecstasy (N = 60). MDMA vergrootte het vergeten van gepresenteerde woorden in het DRM-paradigma, zowel wanneer de deelnemers onmiddellijk als een week later werden getest. Op de onmiddellijke test vergrootte MDMA pseudo-herinneringen voor verwante maar niet-kritische nieuwe woorden, terwijl na enige tijd MDMA de vorming kritische niet-gepresenteerde woorden verminderde, aangezien deze qua inhoud op gepresenteerde woorden leken en tot op zekere hoogte op de voorafgaande test waren gepresenteerd. In tegenstelling tot cannabis werd het geheugen niet aangetast door een acute MDMA-intoxicatie bij de twee meer toegepaste misinformatietaken, en in één conditie leek MDMA zelfs een conservatievere antwoordstrategie te induceren toen het geheugen een week later werd getest. Belangrijk is dat de gevoeligheid voor externe suggestie in geen van de condities verhoogd werd met de dosis die in deze studie gegeven werd.

De effecten van polysubstanties op pseudo-herinneringen en suggestibiliteit zijn nog niet onderzocht en niet altijd haalbaar om in een laboratorium te onderzoeken. Daarom werd in Hoofdstuk 6 een veldstudie uitgevoerd op het Lowlands muziekfestival om de invloed van slaapgebrek en intoxicatie op de vatbaarheid voor suggestie te onderzoeken. In een misinformatie-suggestibiliteitstaak werd de beperkte slaap van festivalbezoekers (N = 277) in verband gebracht met verhoogde niveaus van suggestibiliteit en vals positieven op niet-suggestieve vragen in

verband met een virtual reality ooggetuigen-scenario. Recent gebruik van THC of amfetamines was ook gerelateerd aan verhoogde vals positieven op niet-suggestieve vragen, wat wederom bevestigt dat cannabis een “ja-bias” induceert en aangeeft dat deze categorie vragen een gevoelige marker voor drugsinvloed zou kunnen zijn. Er werd ook een aangepast implantatieparadigma gebruikt, waarbij aan de deelnemers werd gesuggereerd dat zij een gebeurtenis hadden meegemaakt die onlangs op het festival had plaatsgevonden. Er werden geen associaties gevonden tussen slaapbeperking, middelengebruik, noch blootstelling aan nepnieuws en de waarschijnlijkheid om de gesuggereerde festivalgebeurtenis ten onrechte te geloven of te herinneren. Sommige mensen kwamen echter tot het ten onrechte geloven (13%, n = 30) of ten onrechte herinneren (6%, n = 14) van de fictieve gebeurtenis. Dit was ook de eerste studie die ooit een implantatieparadigma gebruikte om de effecten van stoffen te bestuderen.

Tenslotte werden in **Hoofdstuk 7** de belangrijkste bevindingen in een ruimere context besproken. Er werd namelijk aangetoond dat cannabisintoxicatie tijdens het ophalen van het geheugen incorrect reageren sterk verhoogt. Acute invloed van cannabis bleek verschillende soorten herinneringsfouten te verhogen, en schijnt een “ja"-bias” te induceren, die gevaarlijk kan zijn tijdens het verhoor. De belangrijkste aanbeveling uit dit proefschrift was dan ook om de ondervraging van cannabis-intoxicerende personen te vermijden om de vorming van valse verklaringen te minimaliseren, en liever te wachten met ondervragen tot een nuchtere toestand bereikt is. Toch roepen de bevindingen van dit proefschrift op tot het instellen van bepaalde procedurele waarborgen voor situaties waarin personen worden ondervraagd die cannabis hebben gebruikt tijdens een misdaad, of die het regelmatig gebruiken. Aanbevolen wordt om getuigen en verdachten met cannabis-intoxicatie te erkennen en te behandelen als een kwetsbare groep in juridische settings. Daarentegen deed MDMA het vergeten sterk toenemen, maar verdere opheldering van de effecten op de productie van pseudo-herinneringen is nodig, vooral in het licht van toekomstige therapeutische toepassingen van MDMA. Verdere toegepaste studies naar suggestibiliteit, waarbij bijvoorbeeld mogelijk hogere doses worden onderzocht, zouden een waardevol doel in toekomstig onderzoek kunnen zijn.

Impact Paragraph

The findings in this thesis suggest that popular drugs such as cannabis and MDMA can impact false memory formation, and responding in memory tasks, in different ways. As these drugs are used by many people involved in crime (Evans et al., 2009) but also recreationally by the general population (Winstock, 2019), the findings can have wide societal impact and applied value for a range of target groups, including legal professionals (e.g., lawyers, judges, jurors, police), policy makers, scientists serving as expert witnesses, and clinicians and recreational users.

Potential Impact for Legal Practice, Policy Makers, and Expert Witnesses

The findings in this thesis are of notable legal relevance to all those who collect, use, and evaluate testimonies from eyewitnesses and suspects. In Chapter 2 it was demonstrated that the incidence of intoxication with alcohol, cannabis, and stimulants (e.g., ecstasy, cocaine) was especially high in violent crime cases. This implies that police officers, who are likely to be the first contact between an intoxicated crime-involved individual and the legal system, need to be equipped with appropriate methods of intoxication detection (e.g., formal training, biological detection methods) and be trained in handling (e.g., when and how to question) intoxicated witnesses, victims and suspects. Specifically, the information accumulated in Chapter 2 indicates that at mild to moderate levels of intoxication, alcohol-intoxicated individuals can still provide accurate information while intoxicated and the best strategy is to question them as soon as possible (Jores et al., 2019). At higher alcohol levels and after a delay however, chances of false memories are higher (Evans et al., 2019; van Oorsouw et al., 2019; van Oorsouw et al., 2015).

In contrast, when it comes to cannabis, the information described in Chapters 2-4 specifies that the risk for false memories is highest during acute cannabis intoxication. Therefore, we recommend that when witnesses, victims, and suspects are under the influence of cannabis, interviewing should be minimized to reduce the risk of false reporting that is induced by cannabis. Questioning should be postponed and, if needed, occur as soon as the person has sobered up to prevent memory decay due to time. However, a person under the influence of cannabis during an event, as well as sober-but-frequent cannabis users, might still show a yes-bias towards some new information later. Therefore, findings suggest that intoxicated individuals and potentially also regular cannabis consumers should be categorized as a vulnerable group, similar to child or elderly

witnesses and suspects (e.g., Bull, 2010). This means that special procedural safeguards and best practice recommendations such as the use of skilled interviewing techniques (e.g., using validated tools such as the cognitive interview, Fisher & Geiselman, 1992) should be put in place to ensure that best evidence is achieved (i.e., maximizing accuracy and minimizing error, see Holliday et al., 2012).

The question regarding the reliability and validity of testimonies of intoxicated witnesses/victims/suspects is a relevant one for investigating officers, prosecuting attorneys, expert witnesses, and to judges or jurors ultimately determining a defendant's guilt. This thesis presents a first step to answer this question, and a first investigation into some of the detrimental memory effects of poorly studied but very commonly used drugs. The results presented here will eventually be integrated into the general scientific consensus, and this consensus can be used by expert witnesses to teach juries, legal professionals, and police about memory evidence in crimes that involved alcohol and other drug (AOD) intoxication. Chapter 2 specifically can be a useful resource for experts and legal professionals as it presents an extensive overview and converges findings of studies conducted with AOD in the domain of eyewitness and false memory. Information from Chapters 3, 4, and 6 showed that response bias might be a sensitive marker of drug impairment, and this knowledge could be applied to develop new objective tools to assess response bias in the context of drug use as part of forensic assessment (similar to e.g., Gudjonsson, 1997). This knowledge and general scientific consensus can be utilized by lawyers to defend their clients, by judges to evaluate the appropriateness and probative value of memory evidence, and by jurors to make informed decisions during the legal proceedings. This consensus can also be used to shape evidence-based recommendations to inform public policy and shape police protocols that are specifically designed to support memory functioning and to prevent its contamination. In turn, this increases the chance of obtaining reliable memory evidence, which contributes to the overarching goal in legal-psychological research: preventing miscarriages of justice by maximizing the number of perpetrators rightfully convicted and minimizing the number of innocent people wrongfully convicted.

Potential Impact for Clinicians

Knowledge on the acute, delayed, and long-term consequences of cannabis and MDMA is essential in the context of therapeutic use of these substances. Cannabis is often prescribed to be

used daily (e.g., Hazekamp & Heerdink, 2013), and MDMA-assisted psychotherapy for treatment of post-traumatic stress disorder will become a reality in the coming years (e.g., Mithoefer et al., 2019). Clinicians who are educated about the present findings can on the one hand take the potentially compromised reliability of memory responses by patients receiving these substances into account in their practice. Likewise, they can inform their patients of potentially unwanted side effects. Most important with regard to cannabis is that the risk of exhibiting spontaneous false memory errors, and the risk to go along with leading and non-leading questions is highest during acute cannabis influence. Clinicians should therefore minimize clinical interviews with patients who are under acute cannabis influence, in order to reduce the risk of obtaining unreliable and invalid information. Regular cannabis use however can also result in a general yes-saying bias potentially in the sober state. Clinicians should thus be critical and aware that such general yes-saying tendencies can occur in regular cannabis users. Specific to MDMA, the greatest worry seems to be an increased chance of forgetting events experienced during MDMA intoxication. Clinicians should be aware that patients might be prone to forgetting details from an MDMA-assisted therapy session, which could be counteracted by careful and extensive documentation of the session and later follow-ups, or even recording of sessions.

Potential Impact for Recreational Users

Knowledge on the potential acute, delayed, and long-term memory effects and cognitive consequences of cannabis and MDMA use is relevant to recreational users, who often seek out scientific knowledge to inform their use habits. Elevated tendency to forming false memories and to a yes-saying bias might be viewed as an unwanted side effect of acute or chronic cannabis use. Practically, it is recommended to avoid acute cannabis influence during situations where it is important that information is processed and remembered correctly; for example, when studying or when watching the news, where attention to nuanced details is needed. Misinformation can come in form of fake news (e.g., Murphy et al., 2019), and a higher yes-bias could encourage people to accept fake news that aligns with their current biases, prejudices and beliefs. Similarly, increased forgetting may be seen as an undesirable consequence of an MDMA experience. Recreational MDMA users should consider that certain events experienced during MDMA influence will not be remembered, and appropriate strategies to counteract this (e.g., video recordings, photos) can be chosen if this is desired.

Current Impact

The current findings have been disseminated extensively among scientific audiences and the general public alike, an overview of which is included in the Output section below. The work has been presented at various international academic conferences across both the psychopharmacological and legal psychological fields. Findings have been communicated in lectures to students of various Bachelor and Master programs, and will be integrated as learning material in so-called *problems* in ongoing courses (e.g., of the Forensic Psychology M. Sc. Program) at Maastricht University in accordance with the *Problem-based Learning* system. Additionally, findings have been shared widely across popular social platforms (e.g., Twitter, ResearchGate, Reddit) and have been covered by newspapers from around the world. For example, the paper on cannabis and false memory (Chapter 4) has attained an Altmetric Attention Score of >500 (top 5%) and has widely attracted media attention from news channels and magazines from >20 different countries. Moreover, ample opportunities have been pursued to discuss the current research with the wider public through talks, demos, and podcasts, for example at scientific festivals (Pleasure, Arts, and Science festival, Pint of Science festival), invited talks (Rotterdam Psychedelic Collective, Aha! Event by New Scientist) and workshops on drugs and memory for public prosecutors in NL (invited by Openbaar Ministerie) and for federal police in Sydney, Australia. Similar efforts will be undertaken with the so far unpublished papers in Chapters 2, 5, and 6 to disseminate the findings among the scientific community as well as the general public. A follow-up episode about the MDMA project for the podcast “Drugs and their History in Society” for which I gave an interview earlier this year is already planned. Similarly, findings will be made available in other languages, for example via a blogpost for the German psychology magazine In-Mind as I have done in the past.

Acknowledgements

First and foremost, I would like to thank my wonderful promotors prof. dr. Jan Ramaekers, prof. dr. Henry Otgaar, and prof. dr. Arjan Blokland. I knew that each and every one of your office doors were always open for me if I needed advice or just a chat, and our meetings, besides being extremely fun, always gave me new confidence and left me feeling reassured. Learning from all of you was inspirational and I could not have asked for a better supervisory team. Arjan, thank you for your warm support, both through academic discussions and advice as well as through goofy jokes. Henry, thank you for being a fantastic and caring mentor, for always providing feedback and help at a record speed, and for being an awesome networker at conferences. Your energy and dedication is very admirable and often infectious to those around you. Jan, thank you for being extremely supportive always. Your calm and reflective supervision is very unique, you are always around to listen and confide in, and I just absolutely love being a part of your lab and hope there will be a lot more to work on together.

This thesis has also been written in memory of the late dr. Jordi Riba, whose work on DRM false memory in abstinent cannabis users sparked the idea for this PhD research project. I am glad to have met Jordi in person, having had the chance to discuss our research on multiple occasions, and will remember him fondly.

I would also like to thank the Nederlandse Organisatie voor Wetenschappelijk Onderzoek (NWO) for putting their trust in our team and fund this PhD project.

Many thanks also goes to the members of the assessment committee, prof. dr. Wim Riedel, prof. dr. Marko Jelicic, dr. Eef Theunissen, prof. dr. Letitia Paoli, and prof. dr. Robbert-Jan Verkees, for accepting to read and assess my dissertation.

For the thesis cover design I want to thank the creative Jackson Tupper – the design turned out beyond my wildest dreams, looking more like a cool record cover than a boring dissertation!

Further, I would like to express my appreciation to all the people at UM who made this thesis research possible: to Richard Benning for creating the virtual reality scenarios and explaining IT things on a level that made sense to me, to dr. Cees van Leeuwen for screening countless participants and being a cheerful and trustworthy medical supervisor, and to Annemie

Jeukens for making sure that the administrative aspects are in order and that participants get paid ☻. For coming to the rescue all those times that I could not get a blood sample from a participant I would like to heartily thank Anita van Oers, Laura Borghans, Eliza de Sousa Fernandes Perna, Nadia Hütten, and Johannes Reckweg. Thank you also to all the research assistants, internship students, Marble students, research practical students, and to the Lowlands festival crew, who have all been a huge help in running these studies, and of course to all the participants for their participation. Owing to the nature of these studies, I am glad we could share many enjoyable moments: be it a participant who got overly giggly while intoxicated, who got overly excited by their role as a virtual reality perpetrator, therefore running away and ripping out the entire computer, or who had to be calmed down by having German fairytales read to them.

I was lucky to get to spend eight months of my PhD collecting data in Sydney, Australia, in 2018. Thus, I would like to thank the cannabis memory team from the Langton Center: Sarah Hutchinson for supporting our study as a research manager, for the warm welcome and great tips for TV-shows; Consuelo Rivas for supporting the study as a research nurse and providing me with tips on the best make-up sales in town; and Maria Bravo for being a great pal during my time in Sydney and for the after-work breaks in the pub ☻. Moreover, I am grateful to dr. Celine van Golde and dr. Helen Patterson from the University of Sydney for allowing me to visit the Forensic Psychology lab meetings and meeting many great colleagues and new collaborators. Finally, I would like to express my deep gratitude to my Sydney supervisor dr. Lauren Monds – thank you Lauren for putting me under your wing at Langton as a newbie to drug research in Australia. I have really appreciated you as an additional supervisor and my time in Sydney has had a lasting positive impact on my approach to research, thanks to you. Great to have so many ongoing interesting projects with you, which hopefully we can continue some day even in Sydney again.

To all the colleagues from the NP + PP department, thank you for making it a pleasure to come to work at UNS40 every day. I love thinking back to all our fun times during the department days and Christmas events, playing the mole game, doing the Arjan-style dance, birthday vlaai, and just having food and a drink (or a few) together. I hope there are many more to come. I am especially grateful for the friendships that were built throughout these times with Eliza, Malin, Pablito, Johannes, and Tom and Gabi – you guys are all very, very special and dear to my heart.

Next to NP + PP I was also lucky to be an affiliate member of the Forensic Psychology section, in which I could attend the weekly coffee meetings and yearly retreats. Having my former teachers from the Forensic Psychology Master program now as colleagues was intimidating at first but fast became a brilliant experience. I am grateful for all the fun gatherings and the opportunities that it brought for academic exchange and new collaborations.

I would also like to thank the members of the CELL lab at KU Leuven for having me as a visiting member. Hopefully we will see more of each other in the future!

This PhD could not have been completed without the support of my amazing office mates Natasha Mason, Jessica Bruijel, and Frederick Vinckenbosch. Struggling together through four years of PhD has really bonded us together, and the fact that we are still able to share an office now during our post-docs is really incredible and I hope it will still stay like this for a while (minus Corona). The four of us just make a great team, resulting in the most creative birthday gift creations (sorry Natasha we never went to the trampoline park but at least we jumped around the office for you), and unspoken techniques to deal with annoying office visitors (taking turns is the key). I will miss sharing stories and laughing with you guys, and also our dear office plant Juan (hope he is in good hands at Freddy's house). Jojo (Speedy), you are basically an office mate by association, and our trip to Paris with Jessica and Natasha is unforgettable!

A huge thank you of course goes to my two lovely paranymphs, Nina Tupper and Natasha Mason. Nina, it's amazing that I first had you as a housemate, then a colleague, and now as my paranymph, and we have been close friends throughout this whole time since 2015. You always have my back and cheered me up in tough times with wine, cherry beer and Haribo ☻. Thank you for providing guidance and support throughout the PhD, and for sharing my nerdy love for fantasy books. Tashy, I really loved getting to spend so much time with you during the PhD both as a colleague and a close friend. It has been so helpful to have you around for work and life advice and I don't know how I would have survived all the conferences without you. Enjoying the food in Crete, seeing a naked painter in Berlin, listening to Dieter Koblenz at the Dutch Neuroscience meeting, getting coughed on by a food tour guide and getting pizza in our fancy hotel room in Nice would all not have been half as fun without you.

Finally, I would like to thank the most important people in my life - my family and my fiancée. Liebe Mama, lieber Papa, Ihr habt mir ein außergewöhnliches, großartiges Leben geschenkt und ermöglicht; durch Eure bedingungslose Unterstützung und Euer Vertrauen habe ich immer alles geschafft, was ich erreichen wollte (und wenn nicht, dann war es auch nicht schlimm und eine bessere Möglichkeit hat sich ergeben). Euch und Lenni bin ich sehr dankbar für die Liebe und den Halt, die Ihr mir spendet. Lieber Jonas, ob in Sydney oder in Maastricht, ob zusammen an einem Ort oder tausende Kilometer weit voneinander entfernt warst Du die ganze Zeit meine absolut größte und wichtigste Stütze. Du hast mir immer wieder neuen Mut gemacht und mich aufgebaut und angefeuert, wenn ich das brauchte (was nicht selten war!). Zusammen können wir immer wieder neue Abenteuer erleben, bald hoffentlich sogar zu viert ☻. Danke, dass Du so ein toller Partner bist.

Curriculum Vitae

Lilian Kloft was born on November 20th, 1990, in Bonn, Germany. She completed her high school education in Bonn-Bad Godesberg in North Rhine-Westphalia, Germany. Her academic development in psychology started in 2011, when she enrolled in the English Bachelor of Science Psychology program at the University of Groningen (RUG) in the Netherlands. Her bachelor's thesis was written on the topic of memory impairment in dissociative identity disorder. After spending a semester abroad at the University of Limerick (UL) in Ireland, she graduated Cum Laude in 2014. Subsequently she was accepted to the highly selective Master program Forensic Psychology at Maastricht University (UM). As part of this two-year program, she was able to gain empirical knowledge about but also obtained hands-on training in forensic assessment, therapy, and expert witness skills. In addition, in the second year she completed a clinical internship in a forensic hospital (Lüneburg, Germany), and a research internship in a research-based clinic for children with behavioral disorders (CBRC Sydney, Australia).

During the Master's, she discovered her interest in psychopharmacology, and together with her promotors Prof. Johannes Ramaekers and Prof. Henry Otgaar obtained the Research Talent Grant by the Dutch Research Organization NWO to fund her PhD project on the effects of drugs on false memory formation. In November 2016, she began her PhD at the department of Neuropsychology and Psychopharmacology under supervision of Prof. Dr. Ramaekers, Prof. Dr. Otgaar, and Prof. Dr. Blokland. In an effort to bridge the fields of psychopharmacology and forensic/legal psychology she has employed a multi-method approach to investigate drug effects on memory through field research, literature reviews, surveys, and psychopharmacological experiments. During the course of her PhD project, she spent 8 months at The University of Sydney, Australia, where she was appointed as a Honourary Research Associate to run one of the first non-therapeutic cannabis trials in Australia at a Sydney Drug and Alcohol Clinic (The Langton Center) under the supervision of Prof. Dr. Nicholas Lintzeris and Dr. Lauren Monds.

Output

List of Publications

As Part of this Dissertation:

Kloft, L., Monds, L. A., Blokland, A., Ramaekers, J. G., & Otgaar, H. Hazy memories in the courtroom: a review of alcohol and other drug effects on false memory and suggestibility. Accepted pending minor revisions at *Neuroscience and Biobehavioral Reviews.*

Kloft, L., Otgaar, H., Blokland, A., Garbaciak, A., Monds, L. A., & Ramaekers, J. G. (2019). False memory formation in cannabis users: a field study. *Psychopharmacology*, 1-12. doi:10.1007/s00213-019-05309-w

Kloft, L., Otgaar, H., Blokland, A., Monds, L. A., Toennes, S. W., Loftus, E. F., & Ramaekers, J. G. (2020). Cannabis increases susceptibility to false memory. *Proceedings of the National Academy of Sciences*, 201920162. doi:10.1073/pnas.1920162117

Kloft, L., Otgaar, H., Blokland, A., Toennes, S. W., & Ramaekers, J. G. (submitted). Remembering Molly: immediate and delayed false memory formation after acute MDMA exposure. Under review at *European Neuropsychopharmacology*.

Kloft, L., Otgaar, H., Blokland, A., van Oorsouw, K., Schepers, J., Steinmeyer, S., & Ramaekers, J.G. False memories in the field: impact of substance intoxication and sleep restriction on false memory formation. *In submission*.

Not as Part of this Dissertation:

Flowe, H. D., Colloff, M. F., **Kloft, L**., Jores, T., & Stevens, L. M. (2019). *Impact of alcohol and other drugs on eyewitness memory*. In R. Bull & I. Blandón-Gitlin (Eds.), The Routledge International Handbook of Legal and Investigative Psychology (pp. 149-162). London and New York: Routledge.

Jores, T., Colloff, M. F., **Kloft, L**., Smailes, H., & Flowe, H. D. (2018). A meta-analysis of the effects of acute alcohol intoxication on witness recall. *Applied Cognitive Psychology*. doi:10.1002/acp.3533

Monds, L. A., Cullen, H., **Kloft, L.,** Sumampouw, N., Van Golde, C., Harrison, A., & Otgaar, H. (2020). Police perceptions of eyewitness memory impairment due to alcohol and other drug use: a cross-cultural comparison. https://doi.org/10.31234/osf.io/c2htb

Monds, L. A., Cullen, H., **Kloft, L**., van Golde, C., Harrison, A., & Flowe, H. (2020). Memory and Credibility Perceptions of Alcohol and Other Drug Intoxicated Witnesses and Victims of Crime. https://doi.org/10.31234/osf.io/3afvq

Monds, L. A., **Kloft, L**., Sauer, J. D., Honan, C. A., & Palmer, M. A. (2019) No evidence that alcohol intoxication impairs judgments of learning in face recognition. *Applied Cognitive Psychology*. doi:10.1002/acp.3534

Conference Proceedings - Abstracts/Presentations/Posters:

Kloft, L., Hett, D., Butt, M., Monds, L., Catanho, R. ,& Flowe, H.D. (2020). Retention Interval and Acute Alcohol Intoxication During Encoding on the Accuracy and Informativeness of Memory Reports. Presentation at Virtual Psychonomics, November 2020.

Kloft, L. (2020). Remembering Molly: immediate and delayed false memory formation after acute MDMA exposure. Presentation at online conference: Talking about research on memory and cognition (TARMAC), June 2020. See recorded talk https://www.appliedmemorylab.co.uk/tarmac

Kloft, L., Otgaar, H., Blokland, A., Monds, L., & Ramaekers, J. (2020). Hazy memories: cannabis vaping amplifies the creation of false memory. European Neuropsychopharmacology, 31(S1), S37-S38. https://doi.org/10.1016/j.euroneuro.2019.12.051. Conference abstract and poster, both published in February 2020 in conjunction with the ECNP Workshop on Junior Scientists in Europe - Nice, France, 5-8 March 2020

Kloft, L., Otgaar, H., Blokland, A., Garbaciak, A., Monds, L. A., & Ramaekers, J. G. (2019). False memory formation in cannabis users: a field study. Poster presentation at the Dutch Neuroscience Meeting in June 2019 in Lunteren, Netherlands

Kloft, L. (2019). False memory formation in cannabis users: a field study. Research presentation at the Society of Applied Research on Memory and Cognition (SARMAC) conference in Cape Cod, Massachusetts in June 2019

Monds, L., **Kloft, L**., Arkell, T., Rivas, C., Mills, Z., & Lintzeris, N. (2018). Setting up Medical Cannabis Vaporising Research in Alcohol and other Drug Clinics in Australia: Issues and Key Learnings. Drug and Alcohol Review, 37, S53-S53. https://doi.org/10.1111/dar.12862

Kloft, L. (2018). Effects of drug intoxication on false memories in a legal context. Project presentation at the Society of Applied Research on Memory and Cognition (SARMAC) regional meeting Down Under in February 2018 in Adelaide, Australia

Kloft, L. (2017). Drug effects on false memories in a legal context. Pitch presentation at the EURON Workshop “Psychopharmacology: From Laboratory to Clinic” in October 2017 in Crete, Greece

Kloft, L. (2017). Drug effects on false memories in a legal context. Elevator pitch at the European Association for Psychology and Law (EAPL) conference in May 2017 in Mechelen, Belgium

Invited Presentations and Lectures

Intoxicants and Memory with Lilian Kloft (2020). Invited interview on the podcast "Drugs and their History in Society": https://historyofdrugsinsociety.podbean.com/e/intoxicants-and-memory-with-lilian-kloft

Cannabis Intoxication and False Memory (2019). Research presentation held at the Criminological and Experimental Legal Psychology Lab, KU Leuven, Belgium.

Drugs and Memory – A Forensic Perspective (2019). Talk at *Aha! Event* by New Scientist NL at Oedipus Brewery, Amsterdam, the Netherlands.

Psychedelics and Cognition: Drugs and Memory – A Forensic Perspective (2019). Talk presented at: Psychedelic Science Collective, Rotterdam, the Netherlands.

The good, the bad, and the intoxicated (2019). Symposium at Pint of Science, Maastricht, the Netherlands.

False Memory Formation in Cannabis Users – A Field Study (2019). Presentation held at the Research day, Neuropsychology and Psychopharmacology, Maastricht University, the Netherlands.

Polydrug Use Effects on False Memory - A Field Study (2018). Project presentation at Forensic Psychology Lab, The University of Sydney, Australia.

Effects of drug intoxication in a legal context (2017, 2018, 2019). Lecture held for M.Sc. Research Master in Cognitive and Clinical Neuroscience, Maastricht University, the Netherlands.

Psychopharmacology and the Law (2017). Guest lecture at University of Leuven, Belgium.

Multiple laboratory tours of the Virtual Reality lab (2017-2019) for new Master students at Maastricht University, the Netherlands.

Virtual Reality in Crime Research (2017). Presentation/practical demonstration: at the Pleasure, Art and Science (PAS) Festival in Maastricht

*Effects of drug intoxication in a legal context (*2017). Pitch presentation: at FPN Research Day, Maastricht University, the Netherlands.

Acute effects of cannabis on false memory - A Field Study (2017). Presentation at Forensic Psychology Retreat, Maastricht University, the Netherlands.

Workshops

Drugs & Memory – Can we rely on intoxicated witnesses and suspects of crime? (2020). Online workshop held for Jong OM, Openbaar Ministerie, the Netherlands.

Who can we believe? Recognising, assessing, and dealing with intoxicated suspects, victims and witnesses of crime (2018). Workshop for Australian Federal Airport Police in Sydney, Australia.

Blogs

Kloft, L. & Sauerland, M. (2020). Cannabis könnte Menschen anfälliger für Pseudoerinnerungen machen. In-Mind Blogpost, https://de.in-mind.org/blog/post/cannabis-koennte-menschen-anfaelliger-fuer-pseudoerinnerungen-machen

Grants and Awards

Student Travel Grant. Received in July 2019 to attend *Society of Applied Research on Memory and Cognition* (SARMAC) conference in Cape Cod, Massachusetts.

Open Science Prize. Received in February 2018 at the *Society of Applied Research on Memory and Cognition* (SARMAC) *Regional Meeting Down Under*, Adelaide, Australia valued at 250 USD, sponsored by the Center for Open Science.

NWO Research Talent Grant. Received in July 2016 to fund a PhD position at Maastricht University, the Netherlands, valued at 215k

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