

Neural and cognitive determinants of smoking addiction and cessation

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VALORISATION ADDENDUM



This addendum addresses the significance and the impact of the studies described in this dissertation. This is done by outlining in which way our studies are relevant to society, which target groups can benefit from our results, and which activities and products can be derived from our work. In addition, the innovative aspects of our research will be discussed, as well as how knowledge and ideas resulting from our studies have been and can be implemented.

Societal relevance

It is well known that smoking is one of the largest public health threats of current time; in fact, it is the number one preventable cause of death. Worldwide over one billion people smoke tobacco (World Health Organization, 2015), while in the Netherlands this number is close to 3.6 million (Nationaal Expertisecentrum Tabaksontmoediging, 2015). Smoking has serious adverse health effects and can cause life threatening illnesses such as coronary heart disease, chronic obstructive pulmonary disease (COPD), and various forms of cancer. The World Health Organization (WHO) estimates that approximately 6 million people die each year from tobacco-related disease as a result of direct tobacco use or second hand exposure to tobacco smoke (World Health Organization, 2015). In the Netherlands an estimated 20.000 people deacease each year as a consequence of smoking (Nationaal Expertisecentrum Tabaksontmoediging, 2015).

Even though the detrimental consequences of smoking are clear, many smokers continue to smoke because they simply cannot manage to stay abstinent. In fact, a staggering 90% of smokers relapses within the first year after a quit attempt (Nationaal Expertisecentrum Tabaksontmoediging, 2015). Several treatments are available that have been proven effective in prolonging abstinence. However their additional benefit is strikingly low, as one year successful abstinence rates remain well below 50% (Fiore et al., 2008; Rigotti, 2013). Viewing these numbers, it is clear that there is an urgent need for better treatments. In order to treat smoking addiction properly, it is crucial that this phenomenon and its underlying mechanisms are fully and correctly understood. The studies described in this thesis provide new insights in the neural (chapter 2 and 3) and cognitive mechanisms (discussion) underlying attention bias, and its malleability (chapter 4 and 5). The results of these studies provide new insights that can be helpful in the treatment of smoking addiction. We argue that smoking addiction is a complex process sustained by various neural as well as cognitive factors. We also state that targeting one single factor of smoking addiction, for instance eliminating the effects of nicotine by means of

immunotherapy, is not sufficient to help people maintain abstinence as other factors will still assert their influence and trigger addictive behavior. Therefore we suggest that treatments for smoking addiction should target a combination of these various aspects in order to make it easier for ex-smokers to maintain abstinence.

Target groups

The results of the studies discussed in this dissertation are relevant to three distinct target groups. First of all, researchers in the field of smoking addiction or addiction in general can benefit from the new information we have added to the existing knowledge in this field. For example, we have shed a new light on the underlying neural mechanism of attention bias in smokers. Although our findings do not lead to a full and complete understanding of all factors maintaining smoking addiction, we have made a contribution to disentangling this complicated pathology. Researchers could build on these findings as well as the paradigms we have used, when designing new studies in the field. Secondly, (general) physicians and other health care professionals who want to help smokers reach and maintain abstinence could make use of our results when designing a treatment plan. And finally, our findings can be interesting to the general population of smokers who would like to learn more about their addiction and possible ways to quit without relapsing. Particularly, more awareness of the attentional processes underlying cigarette cravings could help smokers gain more control over their smoking habits.

Activities and products

Usually, the process of translating scientific findings in tangible activities, products or services is very slow, with many studies making small contributions to a whole. Similarly, our studies contribute to a better understanding of the processes involved in smoking addiction. Our increased knowledge about these processes can eventually lead to better interventions. We have also investigated two specific interventions, which were mainly aimed at relapse prevention. In the study described in our first chapter we examined the effects of a vaccine which was designed to prevent nicotine from entering the brain. Based on our findings and those from other studies (Esterlis et al., 2013; Hoogsteder, Kotz, van Spiegel, Viechtbauer, & van Schayck, 2014) we suggest that this particular vaccine is not likely to be an effective aid in smoking cessation due to a suboptimal antibody response.

Although this particular vaccine was not sufficiently successful, these findings may contribute to the development of other, more potent vaccines in the near future.

For another study we have developed an online training which was aimed at reducing attention bias in smokers (chapter 4). Attention bias causes smokers to focus their attention on craving triggering cues in their environment and has been associated with relapses after a quit attempt (Janes et al., 2010; Powell, Dawkins, West, Powell, & Pickering, 2010; Spiegelhalter et al., 2011; Waters et al., 2003). Decreasing attention bias therefore may contribute to reduced craving and possibly prolonged abstinence. Our study has shown that five sessions of online attention bias modification (ABM) training successfully reduced attention bias in the general population of smokers. Follow-up studies are needed to find out whether the effects of this training are also clinically relevant. It would be very interesting to find out whether decreasing attention bias by means of ABM would also diminish cue-elicited craving and thereby can help prolong abstinence. If this is the case, this type of training is very well suitable to be applied through a mobile application.

Innovation

The research described in this dissertation is innovative in several ways. First, we were the first researchers to test the mechanism of action of nicotine immunization by means of functional magnetic resonance imaging (fMRI). Before the start of our study, other studies had only investigated immunogenicity, safety, and clinical effectiveness of nicotine vaccines (Cerny & Cerny, 2009; Cornuz et al., 2008; Hartmann-Boyce, Cahill, Hatsukami, & Cornuz, 2012; D.K. Hatsukami et al., 2011; Dorothy K. Hatsukami et al., 2005; Hoogsteder et al., 2014; Raupach, Hoogsteder, & van Schayck, 2012). Nevertheless, the hypothesized mechanism of this treatment is that it precludes nicotine from entering and stimulating the brain. Therefore it is critical to assess changes nicotineric stimulation of the brain after treatment in order to understand if and how immunization is effective.

Secondly, the studies in chapter 2 and 3 go beyond univariate fMRI analyses which are traditionally applied in our field. Instead, we made use of more advanced analysis methods such as multi voxel pattern analysis (MVPA) and a multivariate searchlight paradigm. MVPA analysis techniques employ the spatial distribution of neural responses, and thereby are able to pick up information that is too subtle to be discovered by traditional univariate analyses (De Martino et al., 2008). This enabled us to identify subtle differences

in visual processing of smoking related and neutral cues, that could only be detected when smokers were deprived of nicotine but not when they were satiated.

Third, our ABM training was one of the first comprising multiple sessions and is still the only one that is fully web based. Before the start of our study, three studies had applied single session ABM for smokers, with varying results (Attwood, O'Sullivan, Leonards, Mackintosh, & Munafò, 2008; Field, Duka, Tyler, & Schoenmakers, 2009; McHugh, Murray, Hearon, Calkins, & Otto, 2010). We hypothesized that multiple sessions of ABM training would be more successful in robustly reducing attention bias. During the time our study was executed three other studies were published in which multiple sessions of ABM were administered to smokers (Begh et al., 2015; Kerst & Waters, 2014; Lopes, Pires, & Bizarro, 2014). Two of these studies confirmed our hypothesis (Kerst & Waters, 2014; Lopes et al., 2014), as did our own findings. Providing this type of training online has many advantages, for instance it may offer increased convenience, confidentiality, and reduced stigma for smokers (Brown et al., 2014). Moreover, it allowed us to reach a large sample of smokers that well reflects the composition of the general population of smokers.

And finally, we were the first to determine the influence of personal and smoking related characteristics of smokers on the effectiveness of ABM training. In order to bring ABM on the market as an aid for relapse prevention, it is important to understand for whom it will work and for whom it may not. Since attention bias seems to be higher in certain smokers (e.g. males (Littel, Euser, Munafò, & Franken, 2012), heavy smokers (Mogg & Bradley, 2002; Vollstädt-Klein et al., 2011; Zack, Belsito, Scher, Eissenberg, & Corrigan, 2001), light smokers (Hogarth et al., 2003; Mogg et al., 2005) than others, it is possible that ABM is also more effective for certain subgroups of smokers. However our study demonstrated for the first time that ABM was equally successful for all smokers irrespective of age, gender, education, nicotine dependence, or their motivation to quit.

Implementation

We have undertaken and will undertake various efforts to ensure that the knowledge obtained from our studies reaches the target groups. First of all, I have presented most of our findings at several international conferences which are frequented by researchers and clinicians from all over the world. In addition, we aim to publish the research articles that constitute this thesis in various international scientific journals that target both scientific and clinical audiences. Moreover, in order to disseminate our findings to the general public we will also publish an article on a popular scientific website hosted by researchers from

Maastricht University (www.brainmatters.nl). In addition, the findings will be brought to the attention of regional and national media by means of a press release from Maastricht University. Besides knowledge dissemination we are also planning to make our ABM training available to the public through a mobile application. Though, these plans are still in the early stages.

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