

Sampling the self

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Sampling the self

*Investigating and improving self-esteem
in pathways to psychopathology*

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Sampling the self

*Investigating and improving self-esteem
in pathways to psychopathology*

Proefschrift

Ter verkrijging van de graad van doctor aan de Universiteit Maastricht,

Op gezag van de Rector Magnificus, Prof. dr. Pamela Habibovic,

Volgens het besluit van het College van Decanen,

In het openbaar te verdedigen

Op vrijdag 15 juli 2022 om 13.00 uur

door

Maud Daemen

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Let's give this bad boy a read

Abed Nadir

Paranimfen

Nele Volbragt

Lotte Scheres

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CHAPTER 1

General introduction, aims and outline of the thesis

Background

It is a hard reality that a happy, untroubled, and carefree childhood is not for everyone. The roots for developing mental health problems, early or later in life, often lie in childhood. In 2016, mental disorders, including depression, anxiety disorder, and psychosis, affected more than 1 billion people globally, which is about 16% of the world's population. Relative to other illnesses such as cardiovascular diseases, cancer, or diabetes, mental disorders account for about 7% of global disease burden. Furthermore, mental disorders were responsible for 19% of all years lived with disability (1). In middle- and high-income countries, more than half of the general population will develop at least one mental disorder across their lifespan (2). Mental health disorders have a multifaceted phenomenology, a complex aetiology, and many mental disorders first emerge during childhood or adolescence. Therefore, it is crucial to investigate and identify modifiable psychological mechanisms underlying mental disorders, and target these mechanisms with early interventions in youth, to prevent the development of mental disorders later in life.

Childhood adversity

Many different types of childhood adversities have been investigated, for example peer bullying (e.g. physically hurting, name-calling or excluding someone), dysfunction in the household (e.g. parental discord or a parent with mental illness), and childhood trauma including physical abuse (e.g., hitting or beating), emotional abuse (e.g., verbal assaults, intimidation or humiliation), sexual abuse (i.e., any kind of sexual contact), physical neglect (e.g., not enough food, clothing or shelter) and emotional neglect (e.g., consistently ignoring or disregarding the child's affective needs). Unfortunately, exposure to childhood adversity is quite common. No less than 45.3% of a representative sample of children in Dutch elementary schools reported to have been exposed to an adverse childhood experience. More specifically, when looking at the above mentioned five types of childhood trauma, 12.8% reported to be exposed to emotional neglect, 12.3% to emotional abuse, 8.6% to physical abuse, 3.4% to physical neglect, and 2.3% reported being exposed to sexual abuse (3).

Experiencing childhood adversities may all add up to give the victim an impression of low self-worth. In line with this, individuals exposed to childhood adversities, more often report lower levels of self-esteem, compared to those who are not exposed to childhood adversities (4). It has even been demonstrated that childhood trauma has adverse effects on self-esteem (5,

6). Recently, also the effects of peer bullying received more attention in the light of risk factor for developing mental health and psychosocial problems (7). Additionally, numerous studies reported strong associations between childhood trauma and the development of several adult mental disorders (8, 9). Kessler et al. (9) suggested that extinguishing childhood trauma might lead to a 30% reduction of mental disorders in general. More specifically, multiple studies demonstrated that exposure to childhood trauma is associated with psychotic disorder and increased the risk of the development and maintenance of psychotic symptoms later in life (10, 11).

Psychotic disorder

Psychotic disorder, or psychosis, is a condition that affects the way the brain processes information, characterized by losing touch with reality. This might, for example, involve hearing or seeing things that are not really there (hallucinations), or unshakable beliefs in something untrue (delusions). These are positive symptoms. Negative symptoms might involve, for example, cognitive disorganization (disorganized thinking, slow thinking, decreased concentration and mannerisms and posturing), blunted affect (lack of emotional reactivity), anhedonia (inability to feel pleasure) and altered affective experiences (alterations in experiencing emotions or mood).

Experiencing psychotic symptoms are reported across the psychosis continuum (the general population, who might experience some (even if limited in prevalence and intensity) psychotic-like symptoms in daily life (12, 13), on the one end of the continuum, patients with a psychotic disorder, on the other end). Next to that, there is a familial liability for this disorder. This means that the risk for developing a psychotic disorder is increased in first-degree relatives of people with psychosis (14-16), due to shared liability genes and clustering of socio-environmental adversity within families. This is also reflected in an increased prevalence of subclinical psychotic symptoms in siblings of patients with a psychotic disorder (15, 16). Therefore, it is important to investigate which processes and mechanisms operate in patients, individuals with increased familial liability, and the general population, in pathways to psychotic disorders (14, 15). Childhood trauma is a putative risk factor, but also self-esteem might be an important mechanism in these pathways. Low self-esteem has been found to be common in patients with psychotic disorder (17, 18). Moreover, low self-esteem has been

shown to be involved in the development and maintenance of psychotic symptoms (19, 20), and might therefore be an important mechanism to target in early interventions.

Psychopathology

During the 1990s, there was a growing interest for early interventions for psychosis, which led to great efforts to reform psychosis services and treatment approaches. This early psychosis treatment paradigm laid the groundwork for new approaches in preventive strategies in mental health in general (21). Age 12 – 25 is a crucial time point in life for physical, social, emotional and cognitive development (22). The onset of mental disorders might disrupt these critical stages in the development of an individual. Nonetheless, the majority of mental disorders emerge before the age of 25, and as such, the disease burden is higher during emerging adulthood than during any other period of life (23, 24).

In recent years, there is accumulating evidence that symptoms of psychopathology are transdiagnostic in the early stages (25) and might result in a wide range of mental disorder later in life (26, 27). Therefore, early interventions in youth mental health have become of great importance, and recently, the focus has been shifting from specific interventions for different kind of disorders, to early interventions across the full diagnostic spectrum (28).

Self-esteem

Self-esteem is defined as the evaluation of the self, and is related to personal beliefs about abilities, skills, successfulness and worthiness (29, 30). Results of a recent meta-analysis showed that in the general population, self-esteem increases from age 4 to 11, remains stable from age 11 to 15, and then increases strongly until the age of 30 years old. After the age of 30, self-esteem continues to slowly increase until its peak at age 60, then stays constant until the age of 70, where after it slightly starts to decrease (31). This underlines that youth is a critical period for the development of self-esteem. Self-esteem is essential, not only to well-being, but also to mental health per se. Having high levels of self-esteem is related to greater life satisfaction, more happiness and positive affect, and to more subjective vitality (32). On the contrary, several negative life-events, such as childhood adversity, might have detrimental effects on a persons' self-esteem (4). Low self-esteem, in turn, can have a substantial negative impact on mental health outcomes later in life, such as anxiety, depression, self-injury and psychosis (33, 34). Even more so, low self-esteem is shown to have

an important role in the development and maintenance of severe mental health disorders (35). Therefore, targeting low self-esteem in youth exposed to childhood adversity has great potential.

Ecological Momentary Interventions

Not only are current psychological help strategies difficult to access and accept for youth, they also have limited efficacy in real-world conditions (36, 37). Therefore, there is a pressing need for novel approaches. One novel way to provide (early) youth-friendly interventions, and thereby target psychological mechanisms, such as self-esteem, are Ecological Momentary Interventions (EMIs). Using EMIs, easily accessible and real-time interventions can be delivered in daily life, which might prevent adult mental disorder and reduce disease burden (38-41). An EMI – a “therapist in your pocket” – can be provided using mobile devices, such as smartphones, which enable individuals to access specific and individually tailored intervention components immediately in any given moment and any given context (42).

EMIs have demonstrated promising results for multiple mental health conditions, such as anxiety, bipolar disorder, substance use and depression (43). However, little is known about using EMIs that target transdiagnostic psychological mechanisms, such as self-esteem in youth exposed to childhood trauma, in order to prevent mental disorders later in life.

Assessment of self-esteem

Research instruments can include questionnaires, interviews, tests or observation forms. To ensure the psychometrics of the measures, their reliability and validity should be assessed. Self-esteem can be measured with several research instruments, and even though they all are intended to measure self-esteem, they may all measure slightly different aspects of self-esteem. For example, they can measure explicit self-esteem, which is an indicator of how someone perceives his interpersonal value to others (45), they can measure positive and negative aspects of self-esteem (46, 47), and they can measure implicit self-esteem, which is assumed to be automatic and preconscious (51). Another option is to assess (explicit) self-esteem in daily life.

Experience Sampling Method

Research has shown that self-esteem can fluctuate in daily life, and these fluctuations play an important role in the severity of paranoid experiences (13, 52). Momentary self-esteem and its fluctuations (variability and instability) can be measured using the Experience Sampling Method (ESM). The ESM is a diary technique to repeatedly assess moment-to-moment variation in thoughts, feelings and behavior in different contexts, as they naturally occur in daily life (53). Just like EMIs, recent technological developments made it possible to apply the ESM to be delivered by smartphones. The method has been used in numerous studies to examine mental states and psychopathological symptoms at micro-level (54, 55). One key advantage is that the ESM has high ecological validity and limited recall bias due to its momentary nature. Moreover, it allows for generating intensive longitudinal data, which enables us to explore not only fluctuations in subjective experiences of self-esteem, but also temporal relationships between variables, such as self-esteem and psychotic experiences in daily life.

Until now, it remains unclear if and how some of these types of research instruments that measure self-esteem relate to each other. For example, do they measure more or less the same thing, or do they really tap different underlying components of self-esteem, and can we gain a better overall understanding of the concept self-esteem by assessing all these different components of self-esteem?

Aims and outline of this dissertation

The main aim of this thesis was to investigate and target self-esteem in daily life within individuals with mental health problems. This led to the following specific objectives:

In **Chapter 2**, using the ESM, we aimed to investigate both cross-sectional associations and the temporal order of momentary self-esteem and its fluctuations (instability and variability), on the one hand, and psychotic experiences, paranoia, negative symptoms, and negative affect, on the other, within and across patients with psychotic disorder, their first-degree relatives and controls.

Moving beyond that, in **Chapter 3** we also aimed to investigate whether, across the psychosis continuum (i.e., in patients, their first-degree relatives and in controls), prior exposure to childhood trauma (i.e., physical abuse, emotional abuse, sexual abuse, physical neglect and

emotional neglect) modified the cross-sectional and temporal associations between self-esteem and psychotic experiences in daily life.

In **Chapter 4** we aimed to investigate how momentary self-esteem and positive and negative affect combine to increase the intensity of psychotic experiences in daily life, and vice versa, both cross-sectionally and temporally, across the psychosis continuum (e.g., in patients with psychotic disorder, first-degree relatives of patients with psychotic disorder, and in controls).

Chapter 5 delves into several research instruments intended to measure self-esteem, and will provide an overview of the convergent validity of the RSES (the golden standard), the SERS, the BCSS, the IAT, and momentary self-esteem (measured with the ESM). Moreover, the concurrent validity between the self-esteem measurements and momentary negative affect and momentary psychotic experiences will be described.

As there is a pressing need for novel, youth-friendly early interventions, **Chapter 6** describes the protocol of a transdiagnostic EMI (SELFIE) for improving self-esteem in youth exposed to childhood adversity, which aimed to investigate the efficacy of SELFIE. In this large two-arm randomized controlled trial (RCT) 174 individuals aged 12 – 26 with prior exposure to childhood adversity and low self-esteem will be randomly allocated to the experimental condition (SELFIE in addition to treatment as usual (TAU)) or the control condition (TAU only).

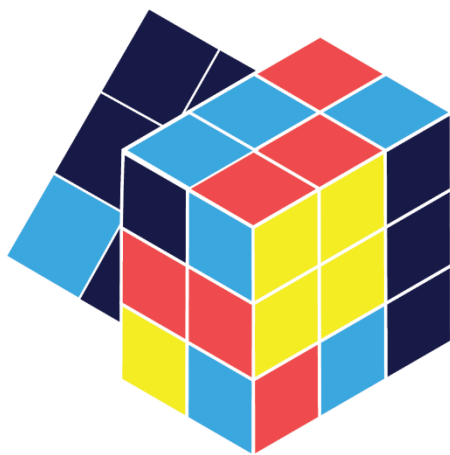
Chapter 7 contains a general discussion in which the main findings, conclusions, directions for future research, and implications for practice of this dissertation will be presented.

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CHAPTER 2

*Self-esteem and psychosis in daily life:
An experience sampling study*

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Abstract

Evidence suggests that self-esteem is an important mechanism in pathways to psychosis. However, whether low or high self-esteem is associated with psychotic experiences remains unclear. Besides, a limited number of studies has investigated fluctuations in state self-esteem in psychotic patients. This study investigated cross-sectional and temporal associations of momentary self-esteem and fluctuations in self-esteem with psychotic symptoms in three groups with different levels of (familial) liability to psychotic disorder. Using the Experience Sampling Method (ESM), momentary self-esteem, fluctuations in self-esteem (i.e., variability and instability), and psychotic experiences, paranoia, negative symptoms (i.e., event anhedonia and social anhedonia), intensity of negative affect and altered affective experiences (instability and variability in negative affect) were assessed in 147 psychotic patients, 131 of their siblings and 113 controls. Lower levels of momentary self-esteem were associated with an increased intensity of psychotic experiences, paranoia and negative affect, with the magnitude of the associations for momentary self-esteem being greatest in patients, followed by relatives. Variability in self-esteem was associated with psychotic and paranoid experiences, the magnitudes were greatest in relatives. Furthermore, we found reciprocal effects between momentary self-esteem and psychotic experiences, paranoia, negative affect, and instability in negative affect. These findings suggest that individuals with familial liability to psychosis (patients and their first-degree relatives) might benefit from targeting momentary self-esteem and variability in self-esteem to decrease the intensity of psychotic experiences, paranoia and negative affect in daily life.

Introduction

There is good evidence that both genetic and socio-environmental factors increase the risk for psychosis (1-4). Several twin and family studies have shown that the risk of developing a psychotic disorder is increased in first-degree relatives of patients with the disorder (3, 4), which suggests a familial liability to psychosis (5). Due to shared liability genes and clustering of socio-environmental adversity within families, the risk of developing psychotic disorder is found to be stronger in relatives of patients compared with the general population (4, 6, 7). This is also reflected at a phenomenologically and temporally early stage in an increased prevalence of subclinical psychotic symptoms in siblings of patients with a psychotic disorder (4, 5). This begs the question which processes and mechanisms operate in individuals with increased familial liability in pathways to psychotic disorders (3, 4).

Several psychological processes have been posited to play an important role in the early stages of psychotic disorder (8-15). More specifically, self-esteem, commonly described as attitudes or beliefs toward the self (16), or as subjective self-evaluations of one's own worth as a person (17), has been implicated as a contributing factor not only in the development and formation (18-21), but also maintenance and severity of psychotic symptoms (18, 22). In a randomized controlled trial conducted by Hall and Tarrrier (23), it was found that by improving self-esteem in patients with psychotic disorder, their positive and negative symptoms and their general psychopathology significantly reduced. Also, Tarrrier (24) indicated that psychotic and affective symptoms can be improved by treatment. However, if self-esteem is not specifically targeted, it will still persist and remain a vulnerability factor for relapse, which indicates that self-esteem is indeed an important factor in the formation of psychotic symptoms. By contrast, some researchers proposed that low self-esteem is a consequence of psychotic experiences (25, 26). Experiencing a psychotic episode may threaten an individual's social importance or ranking and, thereby, have a negative impact on self-esteem (27). Taken together, evidence remains equivocal, and limited in extent, as to whether self-esteem contributes to, and temporally precedes, the development of psychotic experiences, or whether the opposite holds true.

Furthermore, some studies have reported low self-esteem to be more common in individuals with psychosis (11, 19, 28, 29). By contrast, there is also evidence suggesting that the opposite holds true and levels of self-esteem are actually elevated in individuals with psychosis (10, 30). One explanation for these inconsistent findings may be that self-esteem is unstable in

people with psychosis, and thus fluctuates over time (12, 31). The model of self-esteem instability developed by Kernis (32) distinguishes between stable and unstable self-esteem. The model essentially suggests that individuals with stable self-esteem will be relatively unaffected by potential evaluative events (e.g., a non-returned smile to a coworker), whereas individuals with unstable high self-esteem have thoughts about the self that are highly vulnerable to challenge (33, 34).

To date, self-esteem has been most commonly assessed using self-report measures that allow for computing sum or mean scores to index global self-esteem (16). More recently, however, it has also been measured in daily life using the Experience Sampling Method (ESM) (12-15). The ESM is a time-sampling self-assessment diary technique to assess moment-to-moment variation in thoughts, feelings and behaviour as they naturally occur in daily life (35). Key advantages of the ESM are that it allows for generating intensive longitudinal data with high ecological validity and no or very limited recall bias. Therefore, the ESM enables us to better understand the role of psychological processes and mechanisms, such as self-esteem, in daily life (36).

In addition, the ESM also allows for capturing fluctuations in self-esteem (12-14) operationalized as the variability (defined as the within-subject difference between momentary self-esteem and the persons mean across a sampling period) and instability (defined as fluctuations in momentary self-esteem within persons from one moment to the next) in self-esteem over time (10, 12, 33, 34). Ebner-Priemer et al. (37) illustrated the difference between instability and variability using the following example: person 1 goes on a two-week holiday, where it is raining the whole first week, while the sun is shining during the second week. For person 2, who vacations at a different location, it is raining every other day for two weeks. In this example, the weather for person 1 is stable, while the weather for person 2 is unstable. However, the variability for both persons was the same. In their seminal work into fluctuations in self-esteem over time, Thewissen et al. (12) have argued that momentary self-esteem and fluctuations in self-esteem may be more strongly and consistently associated with an increased intensity of psychotic experiences (paranoia in particular) than a global measure of self-esteem (9, 12, 13). In the general population, the intensity of paranoid symptoms has been found to be increased in individuals with lower momentary self-esteem, whereas an increased intensity of other positive symptoms (such as non-paranoid delusions or hallucinations) has been reported to be associated with higher

momentary self-esteem (13). It is also common to investigate negative symptoms in psychosis (38-40). Indeed, psychosis is heterogeneous in its phenomenology. Because of this heterogeneity, some authors have argued to distinguish specific symptoms (38-43), such as paranoia, anhedonia and altered affective experience, in order to identify psychological mechanisms that are linked to these various symptoms. According to cognitive models of psychosis, paranoid experiences are more likely to occur in individuals with low self-esteem. For example, Garety et al. (44) argued that low self-esteem contributes to the development and maintenance of psychosis, and that low self-esteem is specifically associated with paranoia. Moreover, psychotic beliefs may be more persistent if their content is consistent with the conviction of low self-esteem (e.g. the belief to be worthless) (18). Delusions are then seen as confirming low self-esteem further, which, in turn, results in even more persistent delusions (18). Barrowclough et al. (45) advocate that low self-esteem is associated with more severe positive symptoms of psychosis. Also, the model by Bentall et al. (31) states that in paranoid individuals, self-esteem can be boosted and decreased very rapidly by positive or negative events. The function of paranoid experiences is to protect individuals from negative thoughts and feelings about themselves. Therefore, the model predicts that self-esteem would be highly unstable in paranoid patients (31). In line with this, systematic reviews have found support for an association between paranoia and self-esteem instability (46, 47). Chambon et al. (48) proposed that, due to abnormal and unreliable predictions, patients experience difficulties in appreciating social intentions of other people (also known as mentalizing) in social situations. This may result into an increase of instability in self-esteem given self-esteem may represent an interpersonal monitor that alerts an individual to the possibility of social exclusion (49). This theoretical proposition is consistent with the work by Gradin et al. (50), which shows abnormal neural processing of perceived social exclusion in schizophrenia. Momentary manifestations of negative symptoms have been previously operationalized as intensity of negative affect, altered affective experiences (instability and variability in negative affect), anhedonia in events, social anhedonia and asociality (40). Palmier-Claus et al. (9) argued that changes in both positive and negative self-esteem in early stages of psychosis are related to changes in negative symptoms. In contrast, Hermans et al. (40) indicated that negative symptoms in daily life play less of a role during the early stages of psychosis. Negative affect and altered affective experiences are not commonly accepted as negative symptoms. In fact, some ESM studies even found that negative symptoms are

unrelated or inversely related to negative affect in daily life (51). However, altered affective experiences and expressions represent a core feature of psychosis, and they have an important role in negative symptoms, such as blunted affect and anhedonia (52). Thewissen et al. (12) demonstrated that fluctuations in self-esteem covary in people with psychosis with current paranoid symptomatology, with decreasing self-esteem being associated with an immediate increase in paranoia. However, to date, only a small number of studies have investigated momentary and fluctuating self-esteem in people with psychosis, and these studies primarily focused on state paranoia in clinical (12) and non-clinical (13) settings. The association between momentary self-esteem, fluctuations in self-esteem and momentary psychotic symptoms has also never been investigated across different levels of familial liability to psychosis. If specific psychological processes and mechanisms (such as self-esteem) are to be relevant for the development of psychosis, then the association between these processes and psychotic experiences would be expected to be greater in individuals with increased familial liability to psychosis than in controls.

Using experience sampling data from a large multicenter study of patients with psychotic disorder, first-degree relatives of patients with enduring psychotic disorder and controls without a family history of psychotic disorder (i.e., the Genetic Risk and Outcome in Psychosis (GROUP) study) (53), we aimed to investigate whether: 1) self-esteem and fluctuations in self-esteem (variability and instability) will be associated with psychotic experiences, paranoia, negative symptoms, negative affect and altered affective experiences in daily life within patients, first-degree relatives, and controls; 2) the magnitude of associations of self-esteem, and fluctuations in self-esteem (variability and instability) with psychotic experiences, paranoia, negative symptoms, negative affect and altered affective experiences in daily life will be greater in individuals with increased liability to psychosis, i.e., in patients than in controls, in first-degree relatives than in controls, and in patients than in first-degree relatives, and 3) self-esteem and fluctuations in self-esteem (variability and instability) precede psychotic experiences, paranoia, negative symptoms, negative affect and altered affective experiences in daily life, or vice versa, in patients, first-degree relatives, and controls.

Method

Sample

We used data from the GROUP study (53), a large longitudinal multicentre study in the Netherlands and Belgium (see Korver et al. (53) for full details). Patients were identified by clinicians who provided health care for patients with psychotic disorders in selected geographical areas. After obtaining written informed consent, the patients' first-degree relatives (siblings and parents) were contacted. (Unrelated) Controls were recruited by advertisements in local newspapers and by mailing to random addresses in the same geographical areas of patients. Inclusion criteria were: aged between 16-50 years old and sufficient command of Dutch language. Patients had to meet the criterion of being diagnosed with a non-affective psychotic disorder according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria (American Psychiatric 54). The DSM-IV diagnosis was determined using the Comprehensive Assessment of Symptoms and History (CASH) (55).

Controls were only excluded in case of (a family history of) psychotic disorder. A diagnosis of a mental disorder, other than a psychotic disorder, was no exclusion criterion. The study was ethically approved by the Ethical Review Board of the University Medical Centre Utrecht (METC: 04/003- O), and all subjects gave written informed consent. For the current analysis, we only included participants who completed at least one third of the ESM assessments, which is in line with previous ESM studies (56).

Basic sample characteristics

Data on age, gender, ethnicity, level of education (educational levels are adapted from The Dutch Standard Classification of Education (Centraal Bureau 57)), and marital status were collected using a socio-demographic schedule. Illness severity was measured with the Positive and Negative Syndrome Scale (PANSS) (58).

Experience Sampling Method (ESM)

Data on momentary self-esteem and psychotic experiences in daily life was collected using the ESM. Participants received a dedicated digital device (i.e., the PsyMate), which was programmed to beep at semi-random moments within ten 90-minute time blocks a day between 7.30 AM and 10.30 PM for six consecutive days. At each beep, participants were

asked to stop their current activity and to complete the ESM questionnaire, consisting of questions about thoughts, feelings, activity, social context, location, (positive and negative) affect, self-esteem, and psychotic symptoms. Participants were asked to complete self-assessments immediately after each beep. The questionnaire could be accessed until 10 minutes after the beep. Prior to the assessment period, participants received a briefing with detailed instructions. After six days, a debriefing session was scheduled and the PsyMate device was returned, personally or by post.

Table 1. ESM measures of (instability and variability in) self-esteem and psychotic symptoms

Domain	Experience sampling measures
Momentary self-esteem	The mean score of the following two ESM items: "I like myself" and "I doubt myself" (reversed) (59) (within alpha = .24, between alpha = .76).
Fluctuations in self-esteem	<i>Instability:</i> The mean squared successive differences (MSSD) between consecutive reports of the two self-esteem items of each individual person (60, 61). In case of missing time points, no MSSD was calculated. <i>Variability:</i> The (MSSD) between the current time point and the within-person mean of self-esteem on day level across the sampling period (60, 62).
Psychotic experiences	The mean score of eight ESM items was used to assess psychotic experiences: "My thoughts are influenced by others", "I can't get these thoughts out of my head", "I feel unreal", "My thoughts can't be expressed in words", "I feel suspicious", "I hear voices", "I see things that aren't really there", and "I am afraid I will lose control" (within alpha = .66, between alpha = .87). These items have been widely used in ESM studies to measure psychotic experiences with high internal consistency (63-66) and convergent validity with established observer-rated instruments to assess psychotic symptoms such as the Positive and Negative Syndrome Scale (PANSS) (64, 67).
Paranoia	Paranoia was measured with one ESM item: "I feel suspicious" (68, 69).
Event anhedonia	The relationship between the mean score of ESM positive affect items ("I feel cheerful", "I feel relaxed", "I feel satisfied", and "I feel enthusiastic") and the presence of pleasant events (40, 52). Pleasantness of 'the most important event since the last beep' was rated on a bipolar scale ranging from -3 ("very unpleasant") to 3 ("very pleasant").
Social anhedonia	The association between positive affect and the item: "I find being with these people pleasant" (40, 70).
Negative affect	The mean score of the following ESM items: "I feel insecure", "I feel down", "I feel lonely", "I feel anxious", and "I feel annoyed" (within alpha = .67, between alpha = .92).
Altered affective experiences	<i>Instability:</i> The MSSD between consecutive reports of the negative affect items of each individual person (60, 61). In case of missing time points, no MSSD was calculated. <i>Variability:</i> The MSSD between the current time point and the within-person mean of negative affect on day level across the sampling period (60, 62).

ESM measures

Based on the proposed method of Geldhof et al. (71), within- and between-person reliabilities for ESM indices were computed. Momentary negative symptoms were operationalized as event anhedonia and social anhedonia. All ESM items, except for event anhedonia, were measured on a 7-point Likert scale, ranging from 1 (“not at all”) to 7 (“very much”). A detailed description of the ESM measures is shown in Table 1.

Analyses

Using GROUP release number 7.0 and release 1.0 of the ESM data, linear mixed models were fitted in Stata 13.0 (with time points nested within participants and participants nested within families). We fitted nested models using restricted-maximum likelihood estimation (REML) to quantify associations between i) momentary self-esteem, and ii) fluctuations in momentary self-esteem (variability and instability) as the independent variables, and psychotic symptoms (psychotic experiences, paranoia, event anhedonia, and social anhedonia), negative affect and altered affective experiences (instability and variability in negative affect) (all measured with the ESM) as the dependent variables within patients, first-degree relatives, and controls, while controlling for potential a priori confounders (i.e., age, gender, ethnicity, education level, and marital status). For confounders that differed across groups, interaction terms were included for confounding variable \times (fluctuations in) self-esteem (72) (Hypothesis 1).

We then added two-way interactions for (fluctuations in) self-esteem \times group (patients, first-degree relatives, and controls) to examine whether the magnitude of associations of i) momentary self-esteem, and ii) fluctuations in momentary self-esteem with the psychotic symptoms was greater in patients than in controls and first-degree relatives than in controls. A Wald test was used to examine interaction effects as well as the ‘lincom’ command to compute linear combinations of coefficients for testing Hypothesis 2.

We next conducted lagged analyses to investigate the temporal order of i) momentary self-esteem, and ii) fluctuations in self-esteem, on the one hand, and the psychotic symptoms, on the other. We generated within-subject lagged variables of momentary self-esteem, fluctuations in self-esteem, and the psychotic symptoms (at t_{n-1} and t_n). We fitted mixed models to investigate whether (fluctuations) in self-esteem precede psychotic symptoms, or vice versa (Hypothesis 3).

In order to correct for multiple testing, and minimize the probability of type 1 error, we applied the Simes' method, as the conducted tests were not independent. This is in line with previous ESM studies (73, 74). The Simes' correction is viewed as an improvement over the Bonferroni procedure, as this method is more powerful (75). Using the Simes' correction, the lowest P-value is tested against $\alpha=.05/n$ (total number of tests), the second lowest P-value is tested against $\alpha=.05/(n-1)$, the third P-value against $\alpha=.05/(n-2)$, and so on.

Results

The full GROUP sample consisted of 1120 patients diagnosed with a non-affective disorder, 1976 first-degree relatives (1057 siblings and 919 parents), and 590 unrelated controls (53). We used the data from the six-year follow-up, and excluded participants who completed less than one third of the ESM assessments, which resulted in a sample of 392 participants, consisting of 147 patients, 131 relatives, and 113 controls. Basic characteristics of the included and excluded participants are compared in Supplementary Table S1. Excluded patients and relatives consisted of more non-Caucasians compared to the included participants.

Basic characteristics of included participants are displayed in Table 2. On average, patients were younger, more often men, not married or divorced, and had a lower education level than first-degree relatives and controls. When looking at symptoms, patients reported substantially higher levels of positive and negative symptoms, and more disorganisation, excitement and emotional distress compared to their first-degree relatives and controls. The average illness duration of patients was 12.29 years and 98,1% of them were currently using antipsychotics. There was no difference between groups in the number of completed ESM assessments.

Aggregate ESM scores in patients, relatives, and controls

Table 3 depicts that, on average, patients reported higher levels of psychotic experiences, paranoia, negative affect, altered affective experiences, and lower levels of self-esteem than relatives and controls. Patients also experienced more event anhedonia (less positive affect related to pleasant events). Instability and variability in self-esteem was higher in patients than in controls. Relatives and controls did not differ in any of these variables. Social anhedonia (less intense positive affect while being in company of others, compared to the level of positive affect while being alone) did not differ between the groups. A similar pattern

of findings was observed after controlling for possible confounding effects of age, gender, ethnicity, education, and marital status (Supplementary Table S2). Only difference was that, after controlling for confounding effects, event anhedonia did not differ significantly between patients and relatives anymore, while levels of instability in self-esteem are now significantly higher in patients than in relatives. Medication use was not controlled for as a confounder, because 98% of the participants showed to currently use medication.

Table 2. Basic Characteristics

	Patients (n=147)	Relatives (n=131)	Controls (n=113)	Test statistics	P
Age (years), mean (SD)	34.3 (8.2)	35.5 (8.7)	40.9 (11.5)	F=16.95, df=2	<0.001*
Gender, n (%)				$\chi^2=42.24$	<0.001*
Men	99 (67.3)	51 (38.9)	33 (29.2)		
Women	48 (32.7)	80 (61.1)	80 (70.8)		
Ethnicity, n (%)				$\chi^2=4.78$	0.092
Caucasian	131 (89.1)	120 (91.6)	109 (96.5)		
Non-caucasian	16 (10.9)	11 (8.4)	4 (3.5)		
Level of education^a, n (%)				$\chi^2=41.06$	<0.001*
Low	34 (23.1)	9 (6.9)	3 (2.6)		
Middle	66 (44.9)	49(37.4)	42 (37.2)		
High	47 (32.0)	73 (55.7)	68 (60.2)		
Marital status, n (%)^c				$\chi^2=83.95$	<0.001*
Not married	110 (74.8)	40 (30.5)	26 (27.1)		
Married/live together	27 (18.4)	86 (65.7)	64 (66.7)		
Divorced	10 (6.8)	5 (3.8)	6 (6.2)		
Illness duration (years), mean (SD)	12.29 (5.9)	-	-		
Current antipsychotic use, n (%)^d	101 (98.1)	-	-		
PANSS^b, mean (SD)					
Positive symptoms^e	12.1 (6.9)	7.2 (0.6)	7.2 (0.7)	F=49.71, df=2	<0.001*
Negative symptoms^f	11.3 (5.1)	8.2 (1.0)	8.1 (0.7)	F=36.51, df=2	<0.001*
Disorganization^g	13.5 (5.2)	10.1 (0.4)	10.1 (0.4)	F=43.59, df=2	<0.001*
Excitement^h	10.2 (3.3)	8.3 (0.7)	8.2 (0.5)	F=35.68, df=2	<0.001*
Emotional distress^g	13.2 (5.0)	9.2 (2.3)	9.2 (1.9)	F=51.09, df=2	<0.001*
No. completed ESM-assessments, mean (SD)	37.5 (9.5)	39.7 (9.2)	42.4 (9.4)	$\chi^2=0.067$	0.967

^a Educational degree adapted from The Dutch Standard Classification of Education (57)

^b PANSS: Positive and Negative Syndrome Scale

Missing values (%): ^c 4.3, ^d 29.9, ^e 10.7, ^f 10.9, ^g 9.9, ^h 10.5

* statistically significant after Simes' correction.

Self-esteem and psychotic symptoms within patients, relatives and controls

Lower levels of momentary self-esteem were associated with higher levels of psychotic experiences and paranoia (Table 4) in all three groups (patients, relatives and controls) (all $P < 0.001$), with negative affect and variability in negative affect only in patients and relatives (both $P < 0.001$), and with instability in negative affect only in relatives, while controlling for confounders. Momentary self-esteem was not associated with event and social anhedonia. There was good evidence for an association between greater variability in self-esteem and more intense psychotic experiences and paranoia in all three groups (all $P \leq 0.001$), but we found no association with any of the momentary negative symptoms, negative affect or altered affective experiences. Last, we did not find associations between instability in self-esteem and any of the symptoms.

Self-esteem and psychotic symptoms between groups

When we evaluated associations between momentary self-esteem and all psychotic symptoms by group (see Table 4), we found evidence for interaction effects of momentary self-esteem \times group on psychotic experiences, paranoia, negative affect and variability in negative affect (all $P < 0.001$). The results indicated that the associations between self-esteem and negative affect were greater in patients than in relatives and controls, and in turn, greater in relatives than in controls. For the associations between self-esteem and psychotic experiences and variability in negative affect there was no difference between patients and relatives, but associations were stronger in patients and relatives than in controls. Associations between self-esteem and paranoia were greater in patients compared to relatives. There was further evidence of an interaction effect of variability in self-esteem \times group on psychotic experiences, paranoia, and both instability and variability in negative affect (all $P < 0.001$), although we did not find an association between variability in self-esteem and negative symptoms, negative affect or altered affective experiences in any of the groups. Greater variability in self-esteem was more strongly associated with more intense psychotic experiences in relatives than in controls. Interestingly, a weaker association between variability in self-esteem and both psychotic and paranoid experiences was found in patients compared with relatives. Finally, we found evidence for an interaction effect of instability in self-esteem \times group on instability and variability in negative affect, although these associations were not statistically significant in any of the groups.

Table 3. Aggregate ESM scores for momentary (instability and variability in) self-esteem and psychotic symptoms in patients, first degree-relatives and controls

	Patients		Relatives		Controls		Patients vs. controls		Relatives vs. controls		Patients vs. relatives	
	Mean (S.D.)		Mean (S.D.)		Mean (S.D.)		B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
Momentary self-esteem	5.32 (1.23)		5.86 (1.01)		6.01 (0.96)		-0.67 (-0.89 – -0.46)	<0.001*	-0.14 (-0.37 – 0.08)	0.193	-0.53 (-0.72 – -0.33)	<0.001*
Fluctuations in self-esteem												
Instability	0.87 (2.23)		0.64 (1.62)		0.60 (1.80)		0.27 (0.10 – 0.45)	0.002*	0.05 (-0.13 – 0.23)	0.595	0.22 (0.06 – 0.38)	0.006
Variability	0.54 (1.39)		0.40 (1.02)		0.37 (1.19)		0.18 (0.07 – 0.28)	0.001*	0.03 (-0.07 – 0.14)	0.559	0.14 (0.05 – 0.24)	0.004
Psychotic experiences	1.51 (0.68)		1.14 (0.39)		1.11 (0.31)		0.43 (0.32 – 0.54)	<0.001*	0.04 (-0.07 – 0.15)	0.496	0.39 (0.28 – 0.49)	<0.001*
Paranoia	1.45 (0.91)		1.09 (0.48)		1.10 (0.50)		0.36 (0.23 – 0.49)	<0.001*	0.00 (-0.14 – 0.14)	0.995	0.36 (0.24 – 0.49)	<0.001*
Negative symptoms												
Event anhedonia	4.58 (0.91)		4.97 (0.73)		5.08 (0.72)		-0.46 (-0.65 – -0.26)	<0.001*	-0.12 (-0.32 – -0.08)	0.238	-0.34 (-0.52 – -0.16)	<0.001*
Social anhedonia	4.67 (1.09)		5.02 (0.68)		5.18 (0.47)		-0.39 (-0.86 – 0.07)	0.100	-0.13 (-0.60 – 0.33)	0.577	-0.26 (-0.53 – 0.01)	0.055
Negative affect	2.07 (1.05)		1.44 (0.77)		1.38 (0.68)		0.62 (0.47 – 0.78)	<0.001*	0.06 (-0.11 – 0.23)	0.475	0.68 (0.51 – 0.85)	<0.001*
Altered affective experiences												
Instability in negative affect	0.57 (1.50)		0.30 (1.41)		0.30 (1.32)		0.30 (0.19 – 0.42)	<0.001*	0.01 (-0.11 – 0.13)	0.855	0.29 (0.18 – 0.41)	<0.001*
Variability in negative affect	0.44 (1.07)		0.23 (1.11)		0.23 (1.05)		0.23 (0.14 – 0.33)	<0.001*	0.00 (-0.09 – 0.10)	0.945	0.23 (0.14 – 0.32)	<0.001*

Note: ESM, Experience Sampling Method; S.D., standard deviation; CI, confidence interval; *, statistically significant after Simes' correction.

Table 4. Momentary (instability and variability in) self-esteem and psychotic symptoms by group^a

	Patients		Relatives		Controls		Wald test for interaction ^b	
	adj. B (95% CI)	p	adj. B (95% CI)	p	adj. B (95% CI)	p	χ^2 (df)	p
Momentary self-esteem	-0.22 (-0.29 – -0.16)	<0.001*	-0.21 (-0.28 – -0.15)	<0.001*	-0.15 (-0.22 – -0.08)	<0.001*	54.79 (2)	<0.001*
Fluctuations in self-esteem			Outcome: Psychotic experiences					
Instability	0.01 (-0.01 – 0.04)	0.363	0.02 (-0.00 – 0.05)	0.097	0.01 (-0.02 – 0.04)	0.372	6.16 (2)	0.046
Variability	0.08 (0.03 – 0.12)	0.001*	0.12 (0.08 – 0.17)	<0.001*	0.09 (0.04 – 0.14)	<0.001*	50.07 (2)	<0.001*
Momentary self-esteem	-0.43 (-0.53 – -0.33)	<0.001*	-0.36 (-0.46 – -0.26)	<0.001*	-0.33 (-0.43 – -0.22)	<0.001*	49.49 (2)	<0.001*
Fluctuations in self-esteem			Outcome: Paranoia					
Instability	-0.00 (-0.05 – 0.04)	0.887	0.02 (-0.03 – 0.06)	0.413	0.01 (-0.04 – 0.05)	0.780	7.80 (2)	0.020
Variability	0.24 (0.17 – 0.31)	<0.001*	0.28 (0.21 – 0.36)	<0.001*	0.27 (0.19 – 0.34)	<0.001*	14.93 (2)	<0.001*
Momentary self-esteem	-0.01 (-0.06 – 0.04)	0.763	-0.01 (-0.06 – 0.04)	0.746	-0.01 (-0.07 – 0.04)	0.639	0.44 (2)	0.801
Fluctuations in self-esteem			Outcome: Event anhedonia					
Instability	-0.01 (-0.03 – 0.01)	0.471	-0.01 (-0.02 – 0.01)	0.545	-0.01 (-0.03 – 0.01)	0.221	3.47 (2)	0.177
Variability	-0.00 (-0.03 – 0.03)	0.871	-0.01 (-0.04 – 0.02)	0.465	-0.02 (-0.05 – 0.01)	0.262	8.98 (2)	0.011
Momentary self-esteem	0.16 (-0.06 – 0.38)	0.143	0.15 (-0.07 – 0.38)	0.181	0.12 (-0.12 – 0.36)	0.326	0.70 (2)	0.706
Fluctuations in self-esteem			Outcome: Social anhedonia					
Instability	-0.08 (-0.24 – 0.08)	0.331	-0.12 (-0.29 – 0.05)	0.182	-0.12 (-0.31 – 0.07)	0.218	1.76 (2)	0.414
Variability	-0.23 (-0.59 – 0.13)	0.209	-0.31 (-0.68 – 0.05)	0.094	-0.37 (-0.74 – 0.01)	0.056	7.22 (2)	0.027
Momentary self-esteem	-0.38 (-0.49 – -0.27)	<0.001*	-0.26 (-0.37 – -0.15)	<0.001*	-0.14 (-0.25 – -0.02)	0.019	169.98(2)	<0.001*
Fluctuations in self-esteem			Outcome: Negative affect					
Instability	0.01 (-0.04 – 0.06)	0.704	0.01 (-0.05 – 0.06)	0.785	-0.01 (-0.07 – 0.05)	0.737	3.95 (2)	0.139
Variability	0.08 (-0.00 – 0.17)	0.062	0.09 (-0.00 – 0.17)	0.052	0.00 (-0.09 – 0.10)	0.916	38.93 (2)	<0.001*

Table 4. (continued)

	Patient		Relatives		Controls		Wald test for interaction ^b	
	adj. B (95% CI)	p	adj. B (95% CI)	p	adj. B (95% CI)	p	χ^2 (df)	p
Momentary self-esteem	-0.18 (-0.32 – -0.04)	0.011	-0.25 (-0.40 – -0.10)	0.001*	-0.11 (-0.27 – -0.04)	0.141	9.25(2)	0.010
Fluctuations in self-esteem			Outcome: Instability in negative affect					
Instability	0.03 (-0.09 – 0.14)	0.627	-0.04 (-0.16 – 0.07)	0.447	-0.14 (-0.26 – -0.02)	0.027	50.16 (2)	<0.001*
Variability	-0.05 (-0.29 – 0.19)	0.673	0.03 (-0.20 – 0.27)	0.783	-0.21 (-0.46 – -0.04)	0.104	37.91 (2)	<0.001*
Momentary self-esteem	-0.25 (-0.36 – -0.14)	<0.001*	-0.29 (-0.40 – -0.17)	<0.001*	-0.13 (-0.24 – -0.01)	0.033	31.72(2)	<0.001*
Fluctuations in self-esteem			Outcome: Variability in negative affect					
Instability	-0.05 (-0.13 – 0.03)	0.275	-0.04 (-0.13 – 0.04)	0.307	-0.10 (-0.20 – -0.01)	0.027	14.48 (2)	<0.001*
Variability	0.06 (-0.08 – 0.19)	0.401	0.08 (-0.05 – 0.22)	0.223	-0.14 (-0.29 – -0.00)	0.046	117.36 (2)	<0.001*
Note: ESM, Experience Sampling Method; CI, confidence interval; *, statistically significant after Simes' correction.								
^a Adjusted for age, gender, ethnicity, education and marital status x the predicting variable								
^b Wald test for psychological mechanism x group interaction; difference in coefficients across groups:								
	Patients vs. controls		Relatives vs. controls		Patients vs. relatives			
	adj. B (95% CI)	P	adj. B (95% CI)	p	adj. B (95% CI)	p		
	Outcome: Psychotic experiences							
Momentary self-esteem	-0.07 (-0.09 – -0.05)	<0.001*	-0.06 (-0.08 – -0.04)	<0.001*	-0.01 (-0.03 – 0.01)	0.252		
Fluctuations in self-esteem								
Variability	-0.01 (-0.03 – 0.00)	0.149	0.03 (0.02 – 0.05)	<0.001*	-0.04 (-0.06 – -0.03)	<0.001*		
	Outcome: Paranoia							
Momentary self-esteem	-0.03 (-0.06 – 0.00)	0.064	-0.11 (-0.14 – -0.07)	0.031	-0.08 (-0.10 – -0.05)	<0.001*		
Fluctuations in self-esteem								
Variability	-0.02 (-0.05 – -0.00)	0.048	0.02 (-0.01 – 0.04)	0.161	-0.04 (-0.06 – -0.02)	<0.001*		
	Outcome: Negative affect							
Momentary self-esteem	-0.24 (-0.28 – -0.20)	<0.001*	-0.12 (-0.15 – -0.09)	<0.001*	-0.12 (-0.15 – -0.08)	<0.001*		
	Outcome: Variability in negative affect							
Momentary self-esteem	-0.12 (-0.17 – -0.07)	<0.001*	-0.16 (-0.22 – -0.10)	<0.001*	-0.04 (-0.01 – 0.09)	0.086		

Temporal order of ESM scores

Findings on temporal associations between momentary (instability and variability in) self-esteem, and psychotic symptoms in patients, relatives and controls are shown in Table 5. We found that self-esteem at t_{n-1} had a temporal effect on paranoia, negative affect and instability in negative affect at the subsequent time point (t_n) in all three groups (all $P \leq 0.001$). Further, self-esteem at t_{n-1} predicted event anhedonia and psychotic experiences at t_n in controls, and variability in negative affect at t_n in relatives only. We also found a temporal effect of variability in self-esteem at t_{n-1} on psychotic experiences t_n in controls, and of instability in self-esteem at t_{n-1} on variability in negative affect at t_n only in the patient group.

Psychotic experiences, paranoia, negative affect, event anhedonia at t_{n-1} were associated with self-esteem at t_n in all three groups (all $P \leq 0.001$). In patients and relatives, variability in negative affect at t_{n-1} predicted self-esteem at t_n as well, and social anhedonia at t_{n-1} was associated with self-esteem at t_n in patients. In controls psychotic experiences at t_{n-1} had a temporal effect on instability in self-esteem at t_n . Variability in negative affect at t_{n-1} was associated with instability in self-esteem at t_n in patients only. Variability in negative affect at t_{n-1} also had an effect on variability in self-esteem at t_n in all three groups, while intensity of negative affect and instability in negative affect at t_{n-1} were associated with variability in self-esteem at t_n only in relatives. Also psychotic experiences at t_{n-1} had an effect on variability in self-esteem at the subsequent time point in controls (all $P \leq 0.001$).

Last, Table 5 shows that the effect of psychotic experiences, paranoia, negative affect, variability in negative affect and social- and event anhedonia at t_{n-1} on self-esteem at the subsequent time point (at t_n) was stronger than the effect of self-esteem at t_{n-1} on the symptoms at t_n in patients and relatives. On contrast, the effect of momentary self-esteem at t_{n-1} on instability in negative affect at t_n was stronger than vice versa.

All analyses were repeated excluding the paranoia item from mean score of psychotic experiences, which showed that these findings were broadly similar (see Supplementary Tables S3, S4 and S5).

Table 5. Effect of (instability and variability in) self-esteem and psychotic symptoms at t_{n-1} on outcome at t_n by group

Psychological mechanism	Patients		Relatives		Controls	
	adj. B (95% CI)	p	adj. B (95% CI)	p	adj. B (95% CI)	p
			Outcome: Psychotic experiences at t_n			
Psychotic experiences t_{n-1}	0.33 (0.30 – 0.35)	<0.001*	0.34 (0.30 – 0.37)	<0.001*	0.33 (0.30 – 0.36)	<0.001*
Momentary self-esteem t_{n-1}	-0.01 (-0.03 – -0.00)	0.053	-0.02 (-0.03 – -0.00)	0.009	-0.03 (-0.04 – -0.02)	<0.001*
Fluctuations in self-esteem						
Instability t_{n-1}	-0.00 (-0.01 – 0.00)	0.153	0.00 (-0.00 – 0.01)	0.626	-0.00 (-0.01 – 0.00)	0.190
Variability t_{n-1}	-0.00 (-0.01 – 0.00)	0.268	0.00 (-0.01 – 0.01)	0.651	-0.01 (-0.02 – -0.01)	<0.001*
			Outcome: Paranoia at t_n			
Paranoia t_{n-1}	0.21 (0.18 – 0.24)	<0.001*	0.26 (0.23 – 0.29)	<0.001*	0.19 (0.16 – 0.22)	<0.001*
Momentary self-esteem t_{n-1}	-0.07 (-0.10 – -0.05)	<0.001*	-0.03 (-0.05 – -0.01)	0.001*	-0.05 (-0.06 – -0.03)	<0.001*
Fluctuations in self-esteem						
Instability t_{n-1}	0.01 (-0.00 – 0.02)	0.095	0.00 (-0.01 – 0.01)	0.607	-0.00 (-0.01 – 0.01)	0.760
Variability t_{n-1}	0.01 (-0.01 – 0.03)	0.197	0.00 (-0.01 – 0.02)	0.547	-0.01 (-0.02 – -0.00)	0.010
			Outcome: Event anhedonia at t_n			
Event anhedonia t_{n-1}	0.22 (0.19 – 0.26)	<0.001*	0.24 (0.20 – 0.27)	<0.001*	0.23 (0.20 – 0.26)	<0.001*
Momentary self-esteem t_{n-1}	0.01 (0.00 – -0.02)	0.007	0.01 (-0.00 – 0.02)	0.201	0.02 (0.01 – 0.03)	<0.001*
Fluctuations in self-esteem						
Instability t_{n-1}	0.00 (-0.00 – 0.01)	0.471	0.00 (-0.00 – 0.01)	0.758	-0.00 (-0.01 – -0.00)	0.017
Variability t_{n-1}	-0.00 (-0.01 – 0.00)	0.472	0.00 (-0.01 – 0.01)	0.950	-0.01 (-0.01 – -0.00)	0.007
			Outcome: Social anhedonia at t_n			
Social anhedonia t_{n-1}	0.93 (0.89 – 0.97)	<0.001*	0.51 (0.44 – 0.58)	<0.001*	0.42 (0.26 – 0.57)	<0.001*
Momentary self-esteem t_{n-1}	0.05 (0.00 – 0.09)	0.047	0.02 (-0.01 – 0.06)	0.113	0.01 (-0.06 – 0.07)	0.819
Fluctuations in self-esteem						
Instability t_{n-1}	-0.00 (-0.04 – 0.03)	0.917	-0.01 (-0.03 – 0.00)	0.150	-0.02 (-0.06 – 0.01)	0.219
Variability t_{n-1}	-0.00 (-0.05 – 0.04)	0.833	-0.00 (-0.03 – 0.02)	0.640	0.02 (-0.04 – 0.08)	0.438
			Outcome: Negative affect at t_n			
Social anhedonia t_{n-1}	0.37 (0.34 – 0.40)	<0.001*	0.33 (0.30 – 0.37)	<0.001*	0.37 (0.34 – 0.40)	<0.001*
Momentary self-esteem t_{n-1}	-0.07 (-0.10 – -0.05)	<0.001*	-0.06 (-0.08 – -0.03)	<0.001*	-0.10 (-0.12 – -0.07)	<0.001*
Fluctuations in self-esteem						
Instability t_{n-1}	0.00 (-0.01 – 0.02)	0.578	-0.00 (-0.01 – 0.01)	0.571	0.01 (-0.00 – 0.02)	0.056
Variability t_{n-1}	0.00 (-0.01 – 0.02)	0.837	-0.00 (-0.02 – 0.02)	0.976	-0.01 (-0.02 – 0.00)	0.055

Table 5. (continued)

	Patients		Relatives		Controls	
	adj. B (95% CI)	p	adj. B (95% CI)	p	adj. B (95% CI)	p
			Outcome: Instability in negative affect at t_n			
Instability in negative affect t_{n-1}	0.18 (0.14 – 0.21)	<0.001*	0.49 (0.44 – 0.54)	<0.001*	0.43 (0.40 – 0.46)	<0.001*
Momentary self-esteem t_{n-1}	-0.18 (-0.23 – -0.14)	<0.001*	-0.14 (-0.20 – -0.08)	<0.001*	-0.11 (-0.16 – -0.06)	<0.001*
Fluctuations in self-esteem						
Instability t_{n-1}	0.03 (0.00 – 0.05)	0.034	-0.01 (-0.05 – 0.02)	0.406	0.02 (0.00 – 0.05)	0.042
Variability t_{n-1}	0.12 (0.08 – 0.16)	<0.001*	0.02 (-0.03 – 0.08)	0.386	0.02 (-0.02 – 0.05)	0.339
			Outcome: Variability in negative affect at t_n			
Variability in negative affect t_{n-1}	0.17 (0.15 – 0.20)	<0.001*	0.24 (0.20 – 0.28)	<0.001*	0.21 (0.18 – 0.24)	<0.001*
Momentary self-esteem t_{n-1}	-0.05 (-0.08 – -0.02)	0.003	-0.10 (-0.14 – -0.06)	<0.001*	-0.05 (-0.09 – -0.01)	0.016
Fluctuations in self-esteem						
Instability t_{n-1}	0.03 (0.01 – 0.04)	0.001*	0.00 (-0.02 – 0.03)	0.766	0.01 (-0.00 – 0.03)	0.155
Variability t_{n-1}	0.01 (-0.01 – 0.04)	0.250	0.03 (-0.00 – 0.07)	0.084	0.02 (-0.00 – 0.05)	0.064
			Outcome: Self-esteem at t_n			
Psychotic experiences t_{n-1}	-0.18 (-0.25 – -0.11)	<0.001*	-0.19 (-0.27 – -0.10)	<0.001*	-0.43 (-0.54 – -0.32)	<0.001*
Paranoia t_{n-1}	-0.07 (-0.10 – -0.03)	<0.001*	-0.12 (-0.19 – -0.06)	<0.001*	-0.26 (-0.33 – -0.20)	<0.001*
Negative symptoms						
Event anhedonia t_{n-1}	0.39 (0.30 – 0.49)	<0.001*	0.31 (0.22 – 0.40)	<0.001*	0.30 (0.22 – 0.39)	<0.001*
Social anhedonia t_{n-1}	0.48 (0.33 – 0.62)	<0.001*	0.19 (0.05 – 0.33)	0.007	0.33 (0.05 – 0.61)	0.021
Negative affect t_{n-1}	-0.15 (-0.19 – -0.12)	<0.001*	-0.22 (-0.27 – -0.17)	<0.001*	-0.21 (-0.25 – -0.17)	<0.001*
Altered affective experiences						
Instability in negative affect t_{n-1}	-0.03 (-0.05 – -0.01)	0.010	-0.03 (-0.06 – -0.00)	0.021	0.00 (-0.02 – 0.02)	0.854
Variability in negative affect t_{n-1}	-0.04 (-0.07 – -0.02)	0.001*	-0.06 (-0.09 – -0.03)	<0.001*	0.01 (-0.02 – 0.03)	0.676
Momentary self-esteem t_{n-1}	0.21 (0.18 – 0.24)	<0.001*	0.20 (0.17 – 0.23)	<0.001*	0.20 (0.17 – 0.24)	<0.001*
Fluctuations in self-esteem						
Instability t_{n-1}	0.02 (0.01 – 0.04)	<0.001*	0.03 (0.02 – 0.05)	<0.001*	0.04 (0.03 – 0.06)	<0.001*
Variability t_{n-1}	0.05 (0.03 – 0.07)	<0.001*	0.12 (0.09 – 0.15)	<0.001*	0.12 (0.10 – 0.14)	<0.001*

Table 5. (continued)

	Patients		Relatives		Controls	
	adj. B (95% CI)	p	adj. B (95% CI)	p	adj. B (95% CI)	p
	Outcome: Instability in self-esteem at t_n					
Psychotic experiences t_{n-1}	0.06 (-0.10 – -0.22)	0.431	0.20 (0.01 – -0.38)	0.035	0.46 (0.18 – 0.73)	0.001*
Paranoia t_{n-1}	0.02 (-0.08 – 0.13)	0.691	0.07 (-0.08 – 0.22)	0.388	0.09 (-0.08 – 0.26)	0.306
Negative symptoms						
Event anhedonia t_{n-1}	0.06 (-0.08 – 0.20)	0.434	-0.05 (-0.16 – 0.05)	0.332	-0.06 (-0.19 – 0.06)	0.317
Social anhedonia t_{n-1}	-0.12 (-0.25 – 0.02)	0.100	-0.29 (-0.53 – -0.05)	0.020	-0.08 (-0.56 – 0.39)	0.733
Negative affect t_{n-1}	0.12 (0.03 – 0.22)	0.011	0.13 (0.04 – 0.22)	0.006	0.07 (-0.04 – 0.19)	0.203
Altered affective experiences						
Instability in negative affect t_{n-1}	-0.02 (-0.08 – 0.04)	0.510	0.09 (0.03 – 0.14)	0.002	0.01 (-0.06 – 0.08)	0.731
Variability in negative affect t_{n-1}	0.17 (0.08 – 0.26)	<0.001*	0.11 (0.04 – 0.18)	0.003	0.08 (-0.01 – 0.18)	0.080
Momentary self-esteem t_{n-1}	-0.35 (-0.44 – -0.27)	<0.001*	-0.57 (-0.65 – -0.49)	<0.001*	-0.60 (-0.68 – -0.51)	<0.001*
Fluctuations in self-esteem						
Instability t_{n-1}	0.35 (0.31 – 0.39)	<0.001*	0.38 (0.35 – 0.42)	<0.001*	0.36 (0.33 – 0.40)	<0.001*
Variability t_{n-1}	0.97 (0.90 – 1.04)	<0.001*	0.91 (0.84 – 0.97)	<0.001*	0.80 (0.75 – 0.85)	<0.001*
	Outcome: Variability in self-esteem at t_n					
Psychotic experiences t_{n-1}	-0.07 (-0.02 – -0.15)	0.152	0.14 (0.03 – 0.24)	0.010	-0.41 (-0.58 – -0.24)	<0.001*
Paranoia t_{n-1}	0.02 (-0.04 – 0.08)	0.484	0.12 (0.03 – 0.20)	0.008	-0.25 (-0.35 – -0.15)	<0.001*
Negative symptoms						
Event anhedonia t_{n-1}	-0.01 (-0.10 – 0.08)	0.838	-0.06 (-0.13 – 0.01)	0.088	-0.14 (-0.25 – -0.04)	0.006
Social anhedonia t_{n-1}	-0.13 (-0.24 – -0.03)	0.016	-0.04 (-0.18 – 0.09)	0.533	-0.10 (-0.33 – 0.12)	0.353
Negative affect t_{n-1}	0.07 (0.02 – 0.13)	0.006	0.11 (0.06 – 0.17)	<0.001*	-0.09 (-0.15 – -0.02)	0.014
Altered affective experiences						
Instability in negative affect t_{n-1}	0.03 (-0.01 – 0.06)	0.098	0.07 (0.03 – 0.11)	<0.001*	0.00 (-0.03 – 0.04)	0.862
Variability in negative affect t_{n-1}	0.12 (0.07 – 0.16)	<0.001*	0.11 (0.07 – 0.16)	<0.001*	0.11 (0.07 – 0.16)	<0.001*
Momentary self-esteem t_{n-1}	-0.04 (-0.09 – 0.01)	0.110	-0.05 (-0.09 – 0.00)	0.069	0.18 (0.12 – 0.24)	<0.001*
Fluctuations in self-esteem						
Instability t_{n-1}	-0.03 (-0.06 – 0.00)	0.081	0.02 (-0.01 – 0.04)	0.255	-0.07 (-0.10 – -0.04)	<0.001*
Variability t_{n-1}	0.05 (0.02 – 0.08)	0.004	0.07 (0.03 – 0.10)	<0.001*	0.07 (0.04 – 0.10)	<0.001*

Note: ESM, Experience Sampling Method; CI, confidence interval; *, statistically significant after Simes' correction

Discussion

Principal findings

Findings partly supported the first hypothesis: lower levels of momentary self-esteem were associated with an increased intensity of psychotic experiences, paranoia (in all three groups), negative affect, variability in negative affect (in patients and relatives) and instability in negative affect (in relatives only). We also found evidence for an association of variability in self-esteem with psychotic experiences and paranoia in all three groups. Instability in self-esteem was not associated with any of the symptoms. As for the second hypothesis, we found evidence that the magnitude of associations between lower levels of momentary self-esteem and more intense psychotic experiences and more variability in negative affect was greater in patients and relatives than in controls. Associations between self-esteem as well as variability in self-esteem and paranoia were only greater in patients than in relatives. The magnitudes of associations between momentary self-esteem and negative affect were greater in patients than in relatives, and greater in relatives than in controls. Additionally, the magnitude of associations between variability in self-esteem and psychotic experiences was greater in relatives than in controls, and, interestingly, weaker in patients than in relatives. When looking at temporal associations (hypothesis 3), we found evidence that momentary self-esteem preceded psychotic experiences (in controls), variability in negative affect (in relatives) and paranoid experiences, negative affect and intensity in negative affect in all three groups, but the effect of these symptoms (except for instability in negative affect) on self-esteem at the subsequent time point was stronger. Instability did not seem to have an effect on any of the symptoms.

Methodological considerations

Several limitations should be considered when interpreting findings from this study. First, only participants who completed at least one third of the ESM assessments were included in the analysis. This may have led to selection bias. Some patients may have been less able to complete ESM assessments due to the severity of their illness. However, in our comparison of included and excluded patients we found no evidence that the illness severity in included patients significantly differed from those excluded from the analysis and even showed a longer illness duration in included patients. If anything, this suggests that more patients with an enduring course of illness completed ESM assessments.

Second, ESM measures of (fluctuations in) self-esteem and psychotic symptoms were based on self-report. Social desirableness or cultural norms may have influenced ESM responses (76, 77). However, participants received a detailed briefing of how to perform the ESM, including a simulated sampling moment. Furthermore, one key advantage of the ESM is that recall bias is very limited due to the short time between the signal and the response (76, 77). Also, the ESM has been found to be a feasible, reliable, and valid method in various populations, including people with psychosis (64, 78, 79).

A further consideration is that paranoia was measured with only one item, which may have led to limited construct validity (80). Nevertheless, a recently conducted meta-analysis found no differences in effect sizes when comparing the use of single- and multiple-item measures (81). It has been stated that a more broadly framed item might cover a greater part of the construct domain with fewer, or even one item(s) (82), which offers the advantage of minimizing reactivity to the assessment method. This is of particular relevance in ESM research, where intensive longitudinal data is collected with high sampling frequency throughout the day. The use of single items is not uncommon in ESM research (82), which also results in less burden, and arguably better compliance. In fact, in several previous experience sampling studies paranoia was assessed with only 1 item, for which good concurrent validity has been previously reported (68, 69).

In addition, momentary self-esteem was measured with two items. Using more items might have resulted in more variability. Self-esteem is considered as a diverse concept, involving both positive and negative self-esteem (16, 83). Consistent with previous ESM studies, which focuses on achieving high reliability though assessing a high number of repeated measures (instead of a high number of items) (35), we measured the positive and a negative dimension of self-esteem (10, 59). Due to this heterogeneity in items, the reliability of the momentary self-esteem items is as one would expect it (within alpha = .24, between alpha = .76) (84). Given that we are repeatedly measuring the two momentary self-esteem variables; we compensate for high error variances. Furthermore, to assess the extent to which the two ESM items that measured self-esteem taps the construct of self-esteem, we examined their convergent validity with the Rosenberg Self-esteem Scale (RSES; Rosenberg (16), one of the most widely used measures to assess trait self-esteem, using the intraclass correlation coefficient (ICC). We examined this in a subsample ($n = 103$) as data on the RSES was collected in the Maastricht centre only. Using this data, we found the ICC being 0.41. This indicated that

the convergent validity of momentary self-esteem in daily life measured with the two ESM items and trait self-esteem measured with the RSES was fair (85). However, for future research we recommend to use additional items for measuring momentary self-esteem in order to cover the full breadth of the momentary self-esteem construct (15, 84). We also need to understand more fully how sampling frequency and schedule may be modified to improve momentary (within) reliability. Lastly, in relation to ESM constructs, although the measures of intensity of negative affect and instability and variability in negative affect have been used before (40, 70), we have to take into account that these are crude proxies for altered affective experiences.

Last, several possible confounders were taken into account. Medication use was not taken into account as a confounder, because of the patients for whom it was known whether they used medication or not ($\pm 70\%$), 98% showed to currently use medication and hence including this variable in the analysis would have led to very high collinearity with the status variable. Nevertheless, unmeasured confounding cannot be ruled out, because variables such as direct measures of genes (at the molecular genetic level) or other potential confounders were not controlled for in the analysis.

Comparison with previous research

The associations between (instability and variability in) self-esteem and psychotic symptoms have been investigated before (10, 12, 33, 34), with some researchers having previously used the ESM to examine these associations (9, 13-15). However, to our knowledge, we are the first to look at these (cross-sectional and temporal) associations using the ESM in individuals from different levels of familial liability to psychosis (i.e., patients with a psychotic disorder, their first-degree relatives and controls).

Cognitive models have emphasized the role of self-esteem in psychosis (18, 31, 43, 44). In contrast to previous research suggesting that not low, but high levels of self-esteem are associated with psychosis (10, 30), but echoing findings from previous reports (11, 19, 28, 29), we found that lower levels of self-esteem were not only associated with an increased intensity of psychotic experiences and paranoia, but also with an increased intensity of negative affect in daily life. As some cognitive models have posited, self-esteem is highly unstable in psychotic and paranoid patients (12, 31, 45, 46). In line with this, we found that levels of instability and variability in self-esteem were significantly higher in patients than in relatives and controls.

Although, as expected, we found that the intensity of psychotic experiences, paranoia, negative affect, altered affective experiences and event anhedonia were highest in patients, and lowest in controls, scores in relatives and controls were, on average, rather low with limited variance. We, nonetheless, expected to find associations in controls, as psychotic and paranoid symptoms, even if limited in prevalence and intensity, have been previously found in the general population (6, 86, 87), and reported to be associated with self-esteem (13).

From several longitudinal follow-up studies, it has become clear that treatment and (good compliance to) medication can decrease the number of relapses of psychosis, prolong the time between relapses, and shorten the duration of relapse in patients with psychotic disorder (88, 89). In the current study, patients were recruited via treating clinicians, so all participants in the patient group were, or have been, in receipt of standard mental health care, including antipsychotic medication (98% of the patients was currently using medication). This might explain why, although patients did report higher levels of intensity of psychotic experiences, paranoia, negative symptoms, negative affect and variability in negative affect, overall the intensity of the symptoms (including the variance) was rather low in the patient group.

We did not find any associations between instability and variability in self-esteem, negative symptoms, negative affect and altered affective experiences. Our results showed that associations between momentary self-esteem and instability and variability in negative affect were greatest in relatives. According to Palmier-Claus et al. (2011a) the association of instability in self-esteem and self-esteem with negative symptoms may be viewed as most important in the early stages of disorder. Our findings in patients with enduring psychosis add to this, in that no such association was observed in this population. Our results also showed that there was no difference in momentary social anhedonia between patients, relatives and controls, which may implicate that social anhedonia may play less of a role and manifest in daily life in the patient group.

Findings from previous research further suggest that fluctuations in self-esteem might be better predictors for psychotic and paranoid experiences than global measures of self-esteem (9, 12, 13, 34). We used the term 'fluctuations' to refer to variability and instability in self-esteem, which, in the past, have often been used interchangeably (37, 90). The results from our study highlight the importance of using the terms variability and instability separately from each other. Both variability and instability in self-esteem were highest in patients and

lowest in controls, which is in line with previous research (12, 31, 34), but fluctuations were not as high as we would have expected based on the study by Thewissen et al. (12). In addition, consistent with previous research (13), we hypothesised that fluctuations in self-esteem were associated with momentary psychotic experiences, paranoia and negative symptoms. However, our findings were mixed. Instability in self-esteem was not associated with any of the symptoms, which is in line with results of several non-experience sampling studies (9, 91). Variability in self-esteem was associated with an increase in psychotic experiences and paranoia in all groups, but these associations were greatest in relatives. This broadly suggests that variability in self-esteem may have a greater impact in shaping psychotic and paranoid experiences in individuals with an intermediate level of psychosis liability, an effect that may attenuate as individuals are pushed along pathways to a more enduring and complex course of psychotic disorder, with illness chronicity and exposure to, and dosage of, antipsychotic medication potentially limiting the impact of (instability and variability in) self-esteem on psychotic symptoms over time and, hence, accounting for the absence of evidence on a temporal effect of momentary self-esteem on psychotic experiences in patients in the current study. One side-effect of antipsychotic medication is affective flattening (92). Illness chronicity and medication use may potentially also have a 'flattening' effect on self-esteem, which might also explain why the associations were weaker in patients than in relatives. The effect of antipsychotic medication was only relevant in the patient group, as none of the controls, and only one participant in the relative group reported to be currently using antipsychotic medication.

Further, neurobiological mechanisms underlying psychosis liability may be considered in interpreting our findings. The insular cortex is believed to be involved in regulating (fluctuations in) self-esteem (93, 94). Imaging studies in people with psychosis have shown reduced activity in several brain structures, including the insula (95, 96). It has even been suggested that psychotic patients have insular volume deficits (94). While speculative, this might provide an additional explanation for why associations between (variability in) self-esteem and several psychotic symptoms were found to be greater in relatives than in patients. Similar to our findings suggesting that self-esteem variability may be particularly relevant in first-degree relatives, it has been found that other mechanisms, such as aberrant salience, also play a more prominent role in individuals with an ultra-high-risk state for psychosis (79, 97).

When looking at the temporal order of associations between momentary (instability and variability in) self-esteem and psychotic symptoms, findings from previous research suggest that self-esteem is a predictor for the onset of psychosis (paranoia in particular) (9, 12, 13). Fowler et al. (98) even reported that there is a dominant direction from self-esteem to paranoia, but a state of paranoia can, in turn, also have a negative effect on self-esteem. In the current study, we indeed found reciprocal temporal association effects between self-esteem and psychotic experiences, paranoia, negative affect, and instability in negative affect. However, the findings in our study suggest that the dominant direction is from these symptoms (and also social and event anhedonia) to self-esteem in patients with enduring psychotic disorder, instead of the other way around, which is in line with other studies (25, 26, 31). These inconsistencies do not necessarily exclude each other. Low self-esteem might be a risk factor before the onset, and thus, in the development of psychosis, as had been previously posited (18). When we looked at this at the micro level, in daily life, our results implicate that momentary self-esteem precedes psychotic experiences in controls and, vice versa, in all three groups. The stronger temporal effect of psychotic experiences on momentary self-esteem at the subsequent time point that we found may be accounted for by self-stigma (99) or experiences of losing control of one's inner world in patients. Especially when symptoms are manifested in an overt way, noticed by others, and possibly result in stigmatization by others, this may negatively impact self-esteem (100), in particular in patients with enduring psychotic disorder. However, our findings further suggest that these processes may operate at the level of more subtle, low-level psychotic experiences and become evident in first-degree relatives and to controls.

Moreover, we found a reciprocal effect for self-esteem and paranoia, negative affect, and instability in negative affect in all three groups (and for self-esteem and psychotic experiences in relatives and controls), which may be viewed as corroborating the notion that self-esteem may contribute to the initial development of symptoms, which, once manifest, may be more persistent if their content is consistent with the conviction of low self-esteem (18). Experiencing psychotic symptoms are then seen as confirming low self-esteem further, which, in turn, results in even more persistent symptoms (18).

Conclusion

The findings of this study highlight the relationship between self-esteem and psychotic symptoms in daily life of individuals with increased familial liability in psychosis. We found reciprocal effects between paranoia, negative affect, instability in negative affect and momentary self-esteem; although we found that symptoms had a stronger effect on self-esteem than the other way around. The findings of this study may have clinical implications. We suggest that, in treating psychosis, targeting self-esteem in daily life may be beneficial for both patients and their first-degree relatives in decreasing intensity of psychotic experiences, paranoia and negative affect. What is more, (variability in) self-esteem was found to play a more prominent role in some of the psychotic symptoms in first-degree relatives. This suggests that at-risk individuals, such as relatives, may additionally benefit from targeting self-esteem and variability in self-esteem in daily life to disrupt trajectories to more prominent psychotic symptoms. Hence, the results of this study more broadly indicate that future efforts should focus on interventions that allow us to target self-esteem as a putative momentary mechanism in daily life, like the interventions designed and developed by De Neef (101) or Staring (102). Digital, and particularly, ecological momentary interventions, which are geared to offering micro-interventions just in time when needed most by an individual in a given context outside clinicians' offices and researchers' labs, arguably offer the most promising avenues for targeting several aspects of self-esteem in daily life, and thereby may contribute to public mental health strategies that are tangible and scalable for improving preventive and treatment efforts in psychosis.

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Table S1. Basic characteristics of the excluded participants (participants with less than one third ESM assessments and no CTQ results were excluded)

	Excluded patients (n=48)	Compared to incl. patients	Excluded relatives (n=39)	Compared to incl. relatives	Excluded controls (n=9)	Compared to incl. controls
		Test statistics p		Test statistics P		Test statistics P
Age (years), mean (SD)	32.7 (6.1)	z=0.94 0.349	31.4 (8.1)	z=2.69 0.007	33.2 (9.0)	z=1.77 0.078
Gender, n (%)		$\chi^2=0.20$, df=1 0.652		$\chi^2=0.27$, df=1 0.602		$\chi^2=2.70$, df=1 0.100
Men	34 (70.8)		17 (43.6)		5 (55.6)	
Women	14 (29.2)		22 (56.4)		4 (44.4)	
Ethnicity, n (%) ^a		$\chi^2=14.47$, df=1 <0.001*		$\chi^2=16.11$, df=1 <0.001*		$\chi^2=6.22$, df=1 0.013
Caucasian	30 (65.2)		25 (75.5)		7 (84.6)	
Non-caucasian	16 (34.8)		13 (24.5)		2 (15.4)	
Marital status, n (%) ^c		$\chi^2=1.57$, df=2 0.456		$\chi^2=6.20$, df=2 0.045		$\chi^2=0.59$, df=2 0.745
Not married	37 (77.1)		20 (51.3)		2 (25.0)	
Married/live together	10 (20.8)		17 (43.6)		6 (75.0)	
Divorced	1 (2.1)		2 (5.1)		0 (0)	
Illness duration (years), mean (SD) ^d	10.4 (3.1)	z=2.08 0.038	-	-	-	-
Current antipsychotic use, n ^e	38 (92.7)	$\chi^2=2.77$, df=3 0.429	-	-	-	-
PANSS, mean (SD)						
Positive symptoms ^f	13.5 (8.2)	z=-0.83 0.406	7.4 (1.8)	z=1.09 0.274	7.1 (0.4)	z=0.22 0.826
Negative symptoms ^g	11.9 (5.9)	z=-0.34 0.736	8.4 (1.7)	z=0.12 0.902	8.0 (0.0)	z=0.45 0.652
Disorganization ^g	14.8 (6.4)	z=-1.56 0.117	10.4 (1.3)	z=-1.66 0.097	10.0 (0.0)	z=0.75 0.453
Excitement ^g	10.7 (3.4)	z=-1.65 0.099	8.3 (1.0)	z=-0.02 0.986	8.1 (0.4)	z=-0.09 0.925
Emotional distress ^f	13.7 (5.0)	z=-0.74 0.461	9.6 (2.9)	z=-0.54 0.589	9.0 (1.2)	z=-0.24 0.815

Missing values (%): ^a 3.1, ^b 4.2, ^c 1.0, ^d 20.8, ^e 14.6, ^f 13.5, ^g 14.5

PANSS: Positive and Negative Syndrome Scale

*, statistically significant after Simes' correction

Table S2. Aggregate ESM scores for momentary (instability and variability in) self-esteem and momentary psychotic symptoms in patients, first degree-relatives and controls, adjusted for age, gender, ethnicity, education and marital status.

	Patients vs. controls		Relatives vs. controls		Patients vs. relatives	
	Adj. B (95% CI)	p	Adj. B (95% CI)	p	Adj. B (95% CI)	p
Momentary self-esteem	-0.66 (-0.92 – -0.41)	<0.001*	-0.19 (-0.42 – 0.04)	0.104	-0.47 (-0.70 – -0.25)	<0.001*
Fluctuations in Self-esteem						
Instability	0.33 (0.12 – 0.55)	0.002*	0.05 (-0.14 – 0.24)	0.619	0.29 (0.09 – 0.48)	0.004
Variability	0.25 (0.14 – 0.37)	<0.001*	0.06 (-0.04 – 0.16)	0.256	0.19 (0.09 – 0.29)	<0.001*
Psychotic experiences	0.38 (0.25 – 0.51)	<0.001*	0.05 (-0.06 – 0.17)	0.369	0.33 (0.21 – 0.44)	<0.001*
Paranoia	0.34 (0.19 – 0.50)	<0.001*	0.04 (-0.09 – 0.18)	0.543	0.30 (0.17 – 0.44)	<0.001*
Negative symptoms						
Event anhedonia	-0.40 (-0.63 – -0.17)	0.001*	-0.14 (-0.35 – 0.07)	0.191	-0.26 (-0.46 – -0.06)	0.013
Social anhedonia	-0.47 (-1.03 – 0.08)	0.095	-0.14 (-0.68 – 0.39)	0.599	-0.33 (-0.72 – 0.06)	0.102
Negative affect	0.65 (0.45 – 0.85)	<0.001*	0.09 (-0.09 – 0.27)	0.307	0.56 (0.38 – 0.73)	<0.001*
Altered affective experiences						
Instability in negative affect	0.35 (0.20 – 0.49)	<0.001*	0.01 (-0.12 – 0.14)	0.874	0.34 (0.21 – 0.47)	<0.001*
Variability in negative affect	0.29 (0.17 – 0.40)	<0.001*	0.03 (-0.07 – 0.13)	0.586	0.26 (0.15 – 0.36)	<0.001*

Note: ESM, Experience Sampling Method; CI, confidence interval; *, statistically significant after Simes' correction.

Table S3. Aggregate ESM scores for psychotic experiences (excl. paranoia) patients, first degree-relatives and controls

	Patients		Controls		Patients vs. controls		Relatives vs. controls		Patients vs. relatives	
	Mean (S.D.)	Mean (S.D.)	Mean (S.D.)	Mean (S.D.)	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
Psychotic experiences (excl. paranoia)	1.52 (0.70)	1.15 (0.40)	1.11 (0.29)	1.11 (0.29)	0.44 (0.33 – 0.55)	<0.001*	0.04 (-0.07 – 0.16)	0.422	0.39 (0.29 – 0.49)	<0.001*
Psychotic experiences (excl. paranoia) ^a					0.38 (0.25 – 0.51)	<0.001*	0.06 (-0.06 – 0.18)	0.341	0.32 (0.21 – 0.44)	<0.001*

^a adjusted for age, gender, ethnicity, education and marital status

Note: ESM, Experience Sampling Method; S.D., standard deviation; CI, confidence interval; *, statistically significant after Simes' correction.

Table S4. Momentary (instability and variability in) self-esteem and psychotic experiences (excl. paranoia) by group^a

Psychological mechanism	Patients		Relatives		Controls		Wald test for interaction ^b	
	adj. B (95% CI)	p	adj. B (95% CI)	p	adj. B (95% CI)	p	χ^2 (df)	p
Outcome: psychotic experiences (excl. paranoia)								
Momentary Self-esteem	-0.18 (-0.25 – -0.12)	<0.001*	-0.18 (-0.25 – -0.11)	<0.001*	-0.11 (-0.18 – -0.04)	0.002*	54.61(2)	<0.001*
Fluctuations in Self-esteem								
Instability	0.01 (-0.01 – 0.04)	0.285	0.02 (-0.00 – 0.05)	0.103	0.01 (-0.02 – 0.04)	0.380	4.58 (2)	0.101
Variability	0.01 (0.00 – 0.10)	0.031	0.09 (0.05 – 0.14)	<0.001*	0.06 (0.01 – 0.11)	0.021	47.86 (2)	<0.001*

Note: ESM, Experience Sampling Method; CI, confidence interval; *, statistically significant after Simes' correction.

^a Adjusted for age, gender, ethnicity, education and marital status x the predicting variable

^b Wald test for psychological mechanism x group interaction; difference in coefficients across groups:

	Patients vs. controls		Relatives vs. controls		Patients vs. relatives	
	adj. B (95% CI)	p	adj. B (95% CI)	p	adj. B (95% CI)	p
Outcome: psychotic experiences (excl. paranoia)						
Momentary Self-esteem	-0.07 (-0.09 – -0.05)	<0.001*	-0.07 (-0.09 – -0.05)	<0.001*	-0.00 (-0.02 – 0.01)	0.670
Fluctuations in Self-esteem						
Variability	-0.01 (-0.02 – 0.01)	0.395	0.04 (0.02 – 0.05)	<0.001*	-0.04 (-0.06 – -0.03)	<0.001*

Table S5. Effect of (instability and variability in) self-esteem and psychotic experiences (excl. paranoia), at t_{n-1} on outcome at t_n by group

Psychological mechanism	Patients		Relatives		Controls	
	adj. B (95% CI)	p	adj. B (95% CI)	p	adj. B (95% CI)	p
			Outcome: Psychotic experiences at t_n			
Psychotic experiences t_{n-1}	0.31 (0.28 – 0.34)	<0.001*	0.32 (0.29 – 0.36)	<0.001*	0.32 (0.29 – 0.35)	<0.001*
Momentary self-esteem t_{n-1}	-0.01 (-0.03 – 0.00)	0.122	-0.02 (-0.03 – -0.00)	0.010	-0.03 (-0.04 – -0.02)	<0.001*
Fluctuations in self-esteem						
Instability t_{n-1}	-0.01 (-0.01 – -0.00)	0.036	0.00 (-0.01 – 0.01)	0.636	-0.00 (-0.01 – 0.00)	0.212
Variability t_{n-1}	-0.01 (-0.02 – 0.00)	0.132	0.00 (-0.01 – 0.01)	0.568	-0.01 (-0.00 – -0.01)	<0.001*
			Outcome: Self-esteem at t_n			
Psychotic experiences t_{n-1}	-0.16 (-0.23 – -0.10)	<0.001*	-0.17 (-0.25 – -0.09)	<0.001*	-0.36 (-0.47 – -0.25)	<0.001*
			Outcome: Instability in self-esteem at t_n			
Psychotic experiences t_{n-1}	0.07 (-0.09 – 0.22)	0.411	0.20 (0.02 – -0.38)	0.027	0.50 (0.22 – -0.78)	0.001*
			Outcome: Variability in self-esteem at t_n			
Psychotic experiences t_{n-1}	0.07 (-0.02 – 0.15)	0.137	0.13 (0.02 – 0.23)	0.016	-0.35 (-0.52 – -0.18)	<0.001*

Note: ESM, Experience Sampling Method; CI, confidence interval; *, statistically significant after Simes' correction



CHAPTER 3

*Momentary self-esteem as a putative mechanism
underlying the association between childhood trauma
and psychosis: an experience sampling study*

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Abstract

Background Exposure to childhood trauma is associated with an increased risk of developing and maintaining psychotic symptoms later in life. Self-esteem is a psychological mechanism that has been suggested to be involved in the pathway from childhood trauma to psychosis, but there is only limited evidence to support this claim, especially in daily life.

Objective In the current study, we aimed to investigate whether exposure to childhood trauma (physical, emotional, and sexual abuse, and physical and emotional neglect) modifies the cross-sectional and temporal associations between self-esteem and psychotic experiences in patients with psychotic disorder, first-degree relatives and controls.

Method We assessed momentary self-esteem and psychotic experiences in daily life using the Experience Sampling Method in 139 patients with psychotic disorder, 118 first-degree relatives of patients with psychotic disorder and 111 controls. Childhood trauma was measured with the Childhood Trauma Questionnaire.

Results The association between momentary self-esteem and psychotic experiences in daily life was modified by prior exposure to high vs. low levels of several types of childhood trauma, i.e. physical ($\chi^2=24.90$, $p_{fwe}<.001$) and sexual abuse ($\chi^2=15.86$, $p_{fwe}<.001$) and physical neglect ($\chi^2=116.67$, $p_{fwe}<.001$). Specifically, momentary self-esteem was associated with more intense psychotic experiences in patients exposed to high vs. low levels of physical neglect, in relatives exposed to high vs. low levels of physical abuse, and in relatives and controls exposed to high vs. low levels of sexual abuse. When investigating temporal order, results showed no evidence that childhood trauma modified the temporal associations of self-esteem at t_{n-1} and psychotic experiences at t_n on the one hand, and psychotic experiences at t_{n-1} and self-esteem at t_n , on the other.

Conclusion Self-esteem may be an important underlying psychological mechanism through which childhood trauma (i.e., physical abuse, sexual abuse, and physical neglect) may impact on the intensity of psychotic experiences in daily life.

Introduction

Exposure to childhood trauma can have persistent adverse effects on an individual's wellbeing, social development and physical and mental health (1). Childhood trauma refers to potentially harmful experiences of physical, emotional, and sexual abuse and physical and emotional neglect during childhood (2). There is accumulating evidence that childhood trauma is associated with psychotic disorder (3-6) and increases the risk of developing and maintaining psychotic symptoms later in life (3, 7, 8). A study by Norman, Byambaa (9) showed that the prevalence of childhood trauma in patients with a psychotic disorder is very common: 82 of their 100 participants (patients receiving treatment from an early psychosis clinic) reported exposure to childhood trauma. Similarly, other studies have shown that patients with a psychotic disorder reported having experienced disproportionate levels of childhood trauma (3, 7, 8, 10-12). Furthermore, results of a meta-analysis conducted by Varese, Smeets (3) suggested that one out of three patients might not have developed a psychosis if adversity were to be eliminated as a risk factor (assuming causality), which indicates that childhood trauma plays a prominent role in the development of psychosis. It has also been demonstrated that psychotic symptoms are more severe in those exposed to childhood trauma (9, 13). A prospective cohort-study indicated that the incidence of psychotic experiences decreased significantly when exposure to trauma ceased over the course of the study (14). Lastly, a systematic review revealed that exposure to childhood adversity was associated with persistence of psychotic symptoms in both the general population and clinical studies (15), suggesting that childhood adversity may play an important role in the maintenance of psychotic symptoms in patients with enduring psychotic disorders.

Evidence for familial liability to psychosis (16-18) shows that first-degree relatives of patients with psychosis have an increased risk for developing a psychotic disorder (17, 19). In addition, although exposure to childhood trauma is higher in patients with a psychotic disorder, patients and their siblings share a degree of exposure to childhood trauma (20), as they also share many sociodemographic, parental and developmental characteristics (21).

A number of putative psychological mechanisms have been posited to be underlying the association between childhood trauma and psychosis (22, 23). Self-esteem is one such putative mechanism. A systematic review indicated that exposure to childhood trauma may contribute to low self-esteem (24). Low self-esteem has also been found to be common in patients with psychotic disorders (25-28). Moreover, self-esteem has been shown to be

involved in the development and maintenance of psychotic symptoms (28-32). Lower levels of momentary self-esteem have been found to be associated with an increased intensity of psychotic experiences in daily life (33). Prior exposure to childhood trauma may affect cognition (34), which contributes to the development of a complex system consisting of negative views of one's self, the world and the future (35). Some researchers have suggested that self-esteem is involved in the pathway from negative life events (e.g., childhood trauma) to psychosis, but evidence to support this claim remains limited (29, 36, 37). Only a few studies have investigated the involvement of self-esteem and closely related putative mechanisms such as negative self-schemas, or negative beliefs about self and others in this pathway (38-42).

Self-esteem and psychotic experiences are often assessed using cross-sectional measures, with global scores (38-41). However, another way of collecting data on these variables would be via the Experience Sampling Method (ESM). ESM assesses moment-to-moment variation in thoughts, feelings and behavior in daily life. It generates longitudinal data with very limited recall bias and high ecological validity (43).

Overall, there is limited evidence whether exposure to childhood trauma modifies the association between self-esteem and psychotic experiences, especially in daily life. Considering the important role of childhood trauma in the development and maintenance of psychosis (17, 18, 44, 45), we aimed to investigate whether cross-sectional and temporal associations of momentary self-esteem and psychotic experiences in daily life were modified by prior exposure to childhood trauma (i.e., physical, emotional, and sexual abuse, and physical and emotional neglect) in patients with enduring psychotic disorder, their first-degree relatives and controls. Specifically, using data from the Genetic Risk and Outcome in Psychosis (GROUP) study (46), a large multicenter study of patients with psychotic disorder, first-degree relatives and controls without a family history of psychotic disorder, we aimed to test the following hypotheses:

- 1) Within patients, first-degree relatives and controls, the magnitude of associations of self-esteem and psychotic experiences in daily life (both measured with the ESM) is stronger in individuals exposed to high levels of each type of childhood trauma (i.e., physical, emotional, and sexual abuse, and physical and emotional neglect) vs. those exposed to low levels of childhood trauma (measured with the Childhood Trauma Questionnaire (CTQ)) (H1);

- 2) The difference in magnitude of associations of self-esteem and psychotic experiences in daily life between those exposed to high levels of childhood trauma vs. those exposed to low levels of childhood trauma is (a) stronger in patients than in controls, (b) stronger in relatives than in controls, and (c) stronger in patients than in relatives (H2);
- 3) Within patients, first-degree relatives and controls, the temporal association between (i) self-esteem and psychotic experiences, and (ii) psychotic experiences and self-esteem in daily life (both measured with the ESM) is stronger in individuals exposed to high levels of each type of childhood trauma vs. those exposed to low levels of childhood trauma (measured with the CTQ) (H3);
- 4) The difference in magnitude of temporal associations of (i) self-esteem and psychotic experiences, and (ii) psychotic experiences and self-esteem in daily life, between those exposed to high levels of childhood trauma vs. those exposed to low levels of childhood trauma is (a) stronger in patients than in controls, (b) stronger in relatives than in controls, and (c) stronger in patients than in relatives (H4).

Method

Sample

A sample of patients with a psychotic disorder, first-degree relatives of patients with psychotic disorder, and controls without a family history of psychotic disorder was recruited in the GROUP study (46), a large longitudinal multicentre study in the Netherlands and Belgium. Individuals with a psychotic disorder were recruited from regional psychosis care facilities or academic centers in selected geographical areas. The patients' relatives were contacted after written informed consent was obtained. Controls were recruited by contacting random addresses in the same geographical areas of patients. To be eligible, participants had to be between 16-50 years old and their command of Dutch language had to be sufficient. As an additional criterion, patients had to be diagnosed with a non-affective psychotic disorder according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria (47). In case of a family history of psychotic disorder, controls were excluded. After ethical approval, all subjects gave written informed consent. For the current analyses, only participants who completed the CTQ and, in line with previous ESM studies (48), at least one third (33.3%) of ESM assessments were included.

Data collection

Basic sample characteristics

Using a socio-demographic schedule, data on age, gender, ethnicity, marital status, and educational level (adapted from the Dutch Standard Classification of Education (49)) were collected.

Childhood trauma

The Dutch version of the 25-item Childhood Trauma Questionnaire (Short Version) (2) was used to assess childhood trauma at baseline assessment. The 25 items enquire about five types of trauma in childhood (emotional, physical and sexual abuse, and emotional and physical neglect). All five types of trauma are covered with five items, rated on a 5-point Likert scale (1=Never true; 5=Very often true). The CTQ-SV has shown to be reliable and to provide adequate content coverage. There was also good evidence of criterion validity in both adolescent patients with a psychiatric disorder and individuals from a normative community sample (2). For the analyses, the mean score for each type of trauma was used.

Experience Sampling Method (ESM)

The ESM was used at the 6-year follow-up assessment to collect data on self-esteem and psychotic experiences in daily life. Participants were offered an ESM briefing session providing detailed instructions on the ESM procedure. Participants received a dedicated digital device (i.e., the PsyMate), which emitted a beep at 10 semi-random times a day, within 90-minute time blocks, between 7.30 AM and 10.30 PM for 6 consecutive days. Each time the PsyMate emitted a beep, participants were asked to complete an ESM questionnaire directly after the beep. A debriefing session was scheduled after 6 days. Research has shown that the ESM in samples of patients with psychosis and relatives, is feasible, reliable and valid (50-53).

ESM measures

To assess momentary self-esteem, the mean score of the following two ESM items was used: "I like myself" and "I doubt myself" (reversed) (54) (following the approach by Geldhof, Preacher (55) to analyze multilevel reliability: within-person $\alpha=.22$, between-person $\alpha=.76$). To assess the intensity of psychotic experiences, the mean score of the following eight ESM items was used: "My thoughts are influenced by others", "I can't get these thoughts

out of my head”, “I feel unreal”, “My thoughts can’t be expressed in words”, “I feel suspicious”, “I hear voices”, “I see things that aren’t really there”, and “I am afraid I will lose control” (56, 57) (within-person $\alpha=.64$, between-person $\alpha=.85$). All items were measured on a 7-point Likert scale, ranging from 1 (“not at all”) to 7 (“very much”).

Statistical analysis

For the current analyses, we used release 7.0 of the overall GROUP database and release 2.0 of the ESM data. The ‘mixed’ command in Stata 13.0 was used to fit linear mixed models. Since ESM data include multiple observations within each participant, these were treated as nested within participants, and participants nested within families. Restricted-maximum likelihood estimation (REML) was used to fit the models that estimate the associations between momentary self-esteem as the continuous independent variable and psychotic experiences as the outcome variable. We controlled for the potential confounders age, gender, ethnicity, level of education, and marital status.

We then added two-way (self-esteem \times abuse, self-esteem \times group, abuse \times group) and three-way (self-esteem \times abuse \times group) interaction terms to test whether associations between self-esteem and psychotic experiences were modified by prior exposure to high vs. low levels (mean \pm 1 S.D. of continuous CTQ scores (58, 59)) of each type of childhood abuse and group (patients, relatives, controls). We standardized the continuous ESM and CTQ variables (mean=0, S.D.=1) to interpret significant three-way interaction terms (60). Wald tests were used to test the hypothesis that the interaction effects equal zero. For the three-way interaction models, significance levels of the Wald tests were adjusted to correct for Type-I errors using family-wise error-corrected P values (p_{fwe}), which were computed by multiplying the unadjusted P value by the total number of tests. The ‘lincom’ command was used to compute linear combinations of coefficients to test hypotheses H1 and H2. We next conducted time-lagged analyses to test hypotheses H3 and H4. In order to do so, we generated within-subject lagged variables of self-esteem and psychotic experiences (at t_{n-1} and t_n) and fitted linear mixed models.

Results

The third wave (six-year follow-up) data of the GROUP study was completed by 486 participants (194 patients, 169 relatives and 123 controls). As participants who did not complete the CTQ in the first wave (N=30) and/or a minimum of one third of the ESM assessments in the third wave (N=88) were excluded for the analysis, this resulted in a sample of 368 participants: 139 patients, 118 relatives and 111 controls. The basic characteristics of the excluded participants of the third wave sample were broadly similar to the included participants (as shown in Supplementary table S1). Overall, basic characteristics of included patients, relatives and controls were similar, except that included participants of all three groups were more often white compared to the excluded participants. Compared to relatives and controls, patients were younger and had a lower educational level. The patient group consisted of more men and were more often not married compared to the other two groups. For details see Table 1.

Table 1. Basic Characteristics

	Patients (n=139)	Relatives (n=118)	Controls (n=111)	Test statistics	P
Age (years), mean (SD)	34.5 (8.3)	35.5 (8.7)	41.0 (11.5)	F=15.87, df=2	<0.001
Gender, n (%)				$\chi^2=34.76$	<0.001
Men	88 (65.2)	47 (39.8)	33 (29.7)		
Women	47 (34.8)	71 (60.2)	78 (70.3)		
Ethnicity, n (%)				$\chi^2=5.18$	0.075
White	123 (88.5)	107 (90.7)	107 (96.4)		
Non-white	16 (11.5)	11 (9.3)	4 (3.6)		
Level of education, n (%)				$\chi^2=42.18$	<0.001
Low	35 (25.2)	8 (6.8)	3 (2.7)		
Middle	60 (43.2)	45 (38.1)	42 (37.8)		
High	44 (31.6)	65 (55.1)	66 (69.5)		
Marital status, n (%)^a				$\chi^2=71.14$	<0.001
Not married	101 (72.7)	37 (31.4)	25 (26.9)		
Married/live together	28 (20.1)	76 (64.4)	62 (66.7)		
Divorced	10 (7.2)	5 (4.2)	6 (6.4)		
Current antipsychotic use, n (%)^b	98 (98.0)	-	-		
Childhood trauma, mean, (SD)^{e, f}					
Emotional abuse^c	9.5 (4.2)	7.5 (3.1)	7.1 (3.4)	F=15.51, df=2	<0.001
Physical abuse^c	6.6 (2.9)	5.7 (2.2)	5.5 (1.6)	F=8.53, df=2	<0.001
Sexual abuse^c	6.3 (3.1)	5.6 (2.6)	5.9 (3.0)	F=1.93, df=2	0.147
Emotional neglect^d	11.4 (4.1)	10.6 (4.1)	9.2 (3.9)	F=9.25, df=2	<0.001
Physical neglect	7.2 (2.4)	6.6 (2.5)	6.0 (1.9)	F=9.16, df=2	<0.001

Missing values (%): ^a 4.9, ^b 28.1, ^c 0.5, ^d 0.8

Table 1. (continued)^e Categorical CTQ severity scores by group:

	Patients n (%)	Relatives n (%)	Controls n (%)	Test statistics	P
Emotional abuse				$\chi^2=32.76$, df=6	<0.001
Severe to extreme	13 (9.3)	4 (3.4)	3 (2.8)		
Moderate to severe	19 (13.7)	2 (1.7)	6 (5.5)		
Mild to moderate	34 (24.5)	22 (18.6)	13 (11.9)		
None	73 (52.5)	90 (76.3)	87 (79.8)		
Physical abuse				$\chi^2=15.49$, df=6	0.017
Severe to extreme	8 (5.8)	3 (2.5)	3 (2.7)		
Moderate to severe	11 (8.0)	2 (1.7)	1 (0.9)		
Mild to moderate	7 (5.1)	5 (4.3)	2 (1.8)		
None	112 (81.1)	108 (91.5)	104 (94.6)		
Sexual abuse				$\chi^2=15.51$, df=6	0.017
Severe to extreme	9 (6.5)	4 (3.4)	5 (4.6)		
Moderate to severe	14 (10.0)	2 (1.7)	6 (5.5)		
Mild to moderate	19 (13.7)	11 (9.3)	6 (5.5)		
None	97 (69.8)	101 (85.6)	92 (84.4)		
Emotional neglect				$\chi^2=17.64$, df=6	0.007
Severe to extreme	10 (7.2)	9 (7.6)	6 (5.5)		
Moderate to severe	20 (14.5)	11 (9.3)	4 (3.7)		
Mild to moderate	60 (43.5)	44 (37.3)	35 (32.1)		
None	48 (34.8)	54 (45.8)	64 (58.7)		
Physical neglect				$\chi^2=15.91$, df=6	0.014
Severe to extreme	6 (4.3)	6 (5.1)	2 (1.8)		
Moderate to severe	18 (13.0)	6 (5.1)	4 (3.6)		
Mild to moderate	21 (15.1)	13 (11.0)	9 (8.1)		
None	94 (67.6)	93 (78.8)	96 (86.5)		

^f Differences in in CTQ severity between groups:

	Patients vs. controls		Relatives vs. controls		Patients vs. relatives	
	Adj. B (95% CI)	p	Adj. B (95% CI)	p	Adj. B (95% CI)	P
Emotional abuse	0.67 (0.42 – 0.92)	<0.001	0.09 (-0.14 – 0.32)	0.439	0.58 (0.35 – 0.80)	<0.001
Physical abuse	0.30 (0.09 – 0.51)	0.005	0.05 (-0.14 – 0.25)	0.584	0.25 (0.06 – 0.44)	0.011
Sexual abuse	0.42 (0.19 – 0.66)	<0.001	0.01 (-0.21 – 0.23)	0.917	0.41 (0.20 – 0.63)	<0.001
Emotional neglect	0.51 (0.25 – 0.78)	<0.001	0.30 (0.05 – 0.54)	0.017	0.22 (-0.02 – 0.46)	0.072
Physical neglect	0.26 (0.03 – 0.50)	0.026	0.19 (-0.02 – 0.40)	0.083	0.08 (-0.13 – 0.29)	0.468

Note: CTQ, childhood trauma questionnaire, ESM, Experience Sampling Method; CI, confidence interval, adjusted for age, gender, ethnicity, education and marital status.

Patients reported higher levels of all types of childhood trauma (all $P \leq 0.026$) than controls. Patients also reported higher levels of emotional abuse (adj. $\beta = 0.58$, 95% CI 0.35 to 0.80, $P < 0.001$), physical abuse (adj. $\beta = 0.25$, 95% CI 0.06 to 0.44, $P = 0.011$), and sexual abuse (adj. $\beta = 0.41$, 95% CI 0.20 to 0.63, $P < 0.001$) than the first-degree relatives. Although patients reported higher levels of emotional and physical neglect, the differences between the groups fell short of statistical significance (resp. adj. $\beta = 0.22$, 95% CI -0.02 to 0.46, $P = 0.072$ and adj. $\beta = 0.08$, 95% CI -0.13 to 0.29, $P = 0.468$). Levels of all types of childhood trauma were similar in controls and relatives.

Cross-sectional association between self-esteem and psychotic experiences by childhood trauma and group

As shown in Table 2, after controlling for age, ethnicity, education, and marital status, we found strong evidence that the association between self-esteem and psychotic experiences was modified by exposure to childhood trauma, as indicated by a statistically significant interaction effect of self-esteem \times CTQ total score \times group ($\chi^2=9.04$, $df=2$, $p_{fwe}=.011$). We found statistically significant interaction effects (all $p_{fwe} \leq .001$) of self-esteem \times physical abuse \times group, self-esteem \times sexual abuse \times group, and self-esteem \times physical neglect \times group. However, there was no evidence for interaction effects of self-esteem \times emotional abuse \times group ($\chi^2=5.38$, $df=2$, $p_{fwe}=.068$) and self-esteem \times emotional neglect \times group ($\chi^2=1.78$, $df=2$, $p_{fwe}=.411$).

Within-group comparison (H1)

Lower levels of momentary self-esteem were associated with more intense psychotic experiences in relatives exposed to high levels of childhood trauma in general, compared to those exposed to low levels of childhood trauma (adj. $\beta_{high\ vs.\ low}=-.04$, $P=.025$). There was no evidence that this association was stronger in patients or controls exposed to high vs. low levels of childhood trauma in general. Specifically, in relatives, we found a stronger association between lower self-esteem and more intense psychotic experiences for those exposed to high vs. low levels of physical abuse (adj. $\beta_{high\ vs.\ low}=-.12$, $P<.001$), while we did not find evidence that this association was modified in patients or controls. Further, lower self-esteem was associated with more intense psychotic experiences in relatives and controls exposed to high vs. low levels of sexual abuse (resp. adj. $\beta_{high\ vs.\ low}=-.05$, $P<.001$, and adj. $\beta_{high\ vs.\ low}=.05$, $P=.049$), but not in patients. Lastly, in patients, we found a stronger association between lower self-esteem and more intense psychotic experiences for those exposed to high vs. low levels of physical neglect (adj. $\beta_{high\ vs.\ low}=-.13$, $P<.001$). However, there was no evidence that this association was modified in relatives and controls.

Table 2. Psychological mechanisms (Momentary Self-esteem) underlying childhood trauma in patients, relatives and controls^a

	Patients		Relatives		Controls		Wald test for interaction ^c	
	adj. β (95% CI)	P	adj. β (95% CI)	P	adj. β (95% CI)	P	χ^2 (df)	P_{Ive}
Outcome: Psychotic experiences								
Momentary SE x childhood trauma x group ^b							9.04 (2)	0.011
Level of Childhood trauma								
High (mean+1 SD)	-0.20 (-0.25 – -0.15)	<0.001	-0.29 (-0.32 – -0.27)	<0.001	-0.15 (-0.19 – -0.12)	<0.001		
Average (mean)	-0.17 (-0.20 – -0.14)	<0.001	-0.27 (-0.29 – -0.25)	<0.001	-0.18 (-0.20 – -0.15)	<0.001		
Low (mean-1 SD)	-0.14 (-0.18 – -0.10)	<0.001	-0.25 (-0.28 – -0.22)	<0.001	-0.20 (-0.24 – -0.16)	<0.001		
High vs. low	-0.06 (-0.13 – 0.01)	0.115	-0.04 (-0.08 – -0.01)	0.025	0.05 (-0.00 – 0.10)	0.073		
Momentary SE x emotional abuse x group ^b							5.38(2)	0.068
Momentary SE x physical abuse x group ^b							24.90 (2)	<0.001
Level of physical abuse								
High (mean+1 SD)	-0.16 (-0.22 – -0.10)	<0.001	-0.32 (-0.35 – -0.30)	<0.001	-0.08 (-0.12 – -0.04)	<0.001		
Average (mean)	-0.16 (-0.18 – -0.13)	<0.001	-0.26 (-0.29 – -0.24)	<0.001	-0.11 (-0.14 – -0.08)	<0.001		
Low (mean-1 SD)	-0.16 (-0.21 – -0.11)	<0.001	-0.21 (-0.24 – -0.17)	<0.001	-0.14 (-0.18 – -0.09)	<0.001		
High vs. low	0.00 (-0.09 – 0.09)	0.991	-0.12 (-0.15 – -0.08)	<0.001	0.06 (-0.00 – 0.12)	0.058		
Momentary SE x sexual abuse x group ^b							15.86 (2)	<0.001
Level of sexual abuse								
High (mean+1 SD)	-0.11 (-0.17 – -0.06)	<0.001	-0.29 (-0.32 – -0.27)	<0.001	-0.08 (-0.12 – -0.04)	<0.001		
Average (mean)	-0.15 (-0.18 – -0.13)	<0.001	-0.27 (-0.29 – -0.25)	<0.001	-0.11 (-0.14 – -0.08)	<0.001		
Low (mean-1 SD)	-0.19 (-0.24 – -0.15)	<0.001	-0.25 (-0.28 – -0.22)	<0.001	-0.13 (-0.17 – -0.09)	<0.001		
High vs. low	0.08 (-0.01 – 0.16)	0.066	-0.05 (-0.08 – -0.02)	0.001	0.05 (0.00 – 0.10)	0.049		
Momentary SE x emotional neglect x group							1.78 (2)	0.411

Table 2. (continued)

	Patients		Relatives		Controls		Wald test for interaction ^c	
	adj. β (95% CI)	P	adj. β (95% CI)	P	adj. β (95% CI)	P	χ^2 (df)	p_{five}
Momentary SE x physical neglect x group ^b							116.67 (2)	<0.001
Level of physical neglect								
High (mean+1 SD)	-0.23 (-0.28 -- -0.19)	<0.001	-0.29 (-0.32 -- -0.27)	<0.001	-0.08 (-0.12 -- -0.04)	<0.001		
Average (mean)	-0.17 (-0.20 -- -0.14)	<0.001	-0.28 (-0.30 -- -0.25)	<0.001	-0.11 (-0.14 -- -0.08)	<0.001		
Low (mean-1 SD)	-0.11 (-0.14 -- -0.07)	<0.001	-0.26 (-0.29 -- -0.23)	<0.001	-0.13 (-0.17 -- -0.09)	<0.001		
High vs. low	-0.13 (-0.19 -- -0.07)	<0.001	-0.03 (-0.07 -- -0.01)	0.136	0.05 (-0.01 -- -0.11)	0.107		

SD, standard deviation; df, degrees of freedom; vs., versus; CI, confidence interval; p_{five} , family-wise error-corrected p-values were computed by multiplying the unadjusted p-value by the total number of tests to adjust significance levels of Wald tests for three-way interactions; adj. β , standardized regression coefficients (continuous independent variables were standardized (mean=0, SD=1) for interpreting significant three-way interaction terms and examining the difference in associations between high (mean + 1 SD), average (mean), and low (mean - 1 SD) levels of childhood trauma within and across groups (patients, relatives, controls)).

^a Adjusted for age, gender, ethnicity, level of education, and marital status

^b Three-way interaction as included in the following model (with y_{ij} psychotic experiences as outcome variable): $y_{ij} = \beta_0 + \beta_1(\text{SELF-ESTEEM}) + \beta_2(\text{CHILDHOOD TRAUMA}_j) + \beta_3(\text{GROUP}_j) + \beta_4(\text{SELF-ESTEEM}_{ij} \times \text{CHILDHOOD TRAUMA}_j) + \beta_5(\text{SELF-ESTEEM}_{ij} \times \text{GROUP}_j) + \beta_6(\text{CHILDHOOD TRAUMA}_j \times \text{GROUP}_j) + \beta_7(\text{SELF-ESTEEM}_{ij} \times \text{CHILDHOOD TRAUMA}_j \times \text{GROUP}_j) + \epsilon_{ij}$ (full model not shown and available upon request)

^c Difference in associations between those exposed to high vs. low levels of childhood trauma across groups (Δ high vs. low):

	Patients vs. controls		Relatives vs. controls		Patients vs. relatives	
	adj. β (95% CI)	p	adj. β (95% CI)	p	adj. β (95% CI)	P
Outcome: Psychotic Experiences						
Δ High vs. low childhood trauma across groups	-	-	-	-	-	-
Self esteem						
Δ High vs. low physical abuse across groups	-	-	-	-	-	-
Self esteem						
Δ High vs. low sexual abuse across groups	-	-	-0.10 (-0.16 -- -0.04)	<0.001	-	-
Self esteem						
Δ High vs. low physical neglect across groups	-	-	-	-	-	-
Self esteem						

Between-group comparison (H2)

Next, we examined differences in the magnitude of associations of self-esteem and psychotic experiences between those exposed to high vs. low levels of childhood trauma in general, physical and sexual abuse and physical neglect across groups. These differences in magnitude were only examined if both groups showed significant ($P < 0.05$) within-group associations. When comparing relatives to controls, we found differences in the magnitude of associations between self-esteem and psychotic experiences between those exposed to high vs. low levels of sexual abuse (adj. $\beta_{high\ vs.\ low} = -.10$, $P < .001$), with differences in magnitude being stronger in relatives.

Temporal associations by childhood trauma and group

Findings on temporal associations between momentary self-esteem and psychotic experiences in patients, relatives and controls are shown in Table 3. After controlling for age, ethnicity, education, and marital status, we found no evidence that associations between self-esteem at t_{n-1} and psychotic experiences at t_n , or between psychotic experiences at t_{n-1} and self-esteem at t_n were modified by exposure to any of the types of childhood trauma (i.e., emotional, physical and sexual abuse and emotional and physical neglect) within [H3] and across [H4] groups (i.e., patients, relatives and controls).

DiscussionPrinciple findings

The results of this study, using an experience sampling design, showed strong evidence that associations between momentary (low) self-esteem and increased intensity of psychotic experiences in daily life were modified by several types of childhood trauma, i.e., physical and sexual abuse and physical neglect. For physical abuse, this was only the case for relatives of patients with a psychotic disorder, and for physical neglect this was only the case for patients. Sexual abuse modified the association in relatives and controls, but not in patients. Emotional abuse and emotional neglect did not modify associations between self-esteem and psychotic experiences in any of the groups. When investigating temporal order, we found no evidence that childhood trauma modified the temporal associations of self-esteem at t_{n-1} and psychotic experiences at t_n on the one hand, and psychotic experiences at t_{n-1} and self-esteem at t_n , on the other.

Table 3. Effect of self-esteem and psychotic symptoms at t_{n-1} on outcome at t_n by group modified by childhood trauma ^a

Psychological mechanism	Patients		Relatives		Controls		Wald test for interaction	
	adj. B (95% CI)	p	adj. B (95% CI)	p	adj. B (95% CI)	p	χ^2 (df)	p_{five}
Self-esteem t_{n-1}								
Outcome: Psychotic experiences at t_n								
Emotional abuse								
High (mean+1SD)	-0.04 (-0.10 – 0.03)	0.279	-0.11 (-0.14 – -0.08)	<0.001	-0.02 (-0.07 – 0.03)	0.480	0.07 (2)	0.796
Average (mean)	-0.03 (-0.07 – -0.00)	0.046	-0.13 (-0.16 – -0.11)	<0.001	-0.02 (-0.06 – 0.01)	0.169		
Low (mean-1SD)	-0.03 (-0.08 – 0.02)	0.196	-0.15 (-0.19 – -0.11)	<0.001	-0.03 (-0.07 – 0.02)	0.202		
High vs. low	-0.00 (-0.10 – 0.09)	0.915	0.04 (-0.01 – 0.08)	0.096	0.01 (-0.06 – 0.08)	0.774		
Physical abuse								
High (mean+1SD)	0.01 (-0.07 – 0.09)	0.816	-0.14 (-0.17 – 0.11)	<0.001	-0.02 (-0.06 – 0.03)	0.491	0.58 (2)	0.448
Average (mean)	-0.03 (-0.06 – 0.01)	0.135	-0.12 (-0.14 – -0.09)	<0.001	-0.02 (-0.06 – 0.01)	0.147		
Low (mean-1SD)	-0.06 (-0.11 – -0.00)	0.033	-0.10 (-0.13 – -0.06)	<0.001	-0.03 (-0.08 – 0.01)	0.167		
High vs. low	0.07 (-0.05 – 0.18)	0.247	-0.04 (-0.09 – 0.00)	0.057	0.02 (-0.05 – -0.08)	0.596		
Sexual abuse								
High (mean+1SD)	-0.03 (-0.09 – 0.03)	0.317	-0.12 (-0.14 – -0.09)	<0.001	-0.02 (-0.06 – 0.02)	0.341	0.01 (2)	0.909
Average (mean)	-0.03 (-0.06 – -0.00)	0.046	-0.13 (-0.15 – -0.10)	<0.001	-0.02 (-0.06 – 0.01)	0.143		
Low (mean-1SD)	-0.03 (-0.08 – 0.01)	0.150	-0.14 (-0.17 – -0.10)	<0.001	-0.03 (-0.07 – 0.01)	0.186		
High vs. low	0.00 (-0.08 – 0.09)	0.932	0.02 (-0.01 – 0.05)	0.266	0.01 (-0.04 – 0.06)	0.722		
Emotional neglect								
High (mean+1SD)	-0.02 (-0.07 – 0.02)	0.294	-0.11 (-0.14 – -0.08)	<0.001	-0.02 (-0.07 – 0.03)	0.402	0.04 (2)	0.832
Average (mean)	-0.03 (-0.06 – -0.00)	0.040	-0.13 (-0.15 – -0.10)	<0.001	-0.02 (-0.06 – 0.01)	0.148		
Low (mean-1SD)	-0.04 (-0.08 – 0.00)	0.069	-0.15 (-0.19 – -0.11)	<0.001	-0.03 (-0.07 – 0.02)	0.217		
High vs. low	0.01 (-0.05 – 0.07)	0.641	0.04 (-0.0 – 0.09)	0.107	0.00 (-0.06 – 0.07)	0.885		
Physical neglect								
High (mean+1SD)	-0.02 (-0.07 – 0.03)	0.410	-0.11 (-0.14 – 0.08)	<0.001	-0.03 (-0.08 – 0.02)	0.289	0.18 (2)	0.673
Average (mean)	-0.03 (-0.06 – 0.00)	0.051	-0.13 (-0.15 – -0.10)	<0.001	-0.03 (-0.06 – 0.01)	0.126		
Low (mean-1SD)	-0.04 (-0.08 – 0.00)	0.069	-0.14 (-0.18 – -0.10)	<0.001	-0.02 (-0.07 – -0.02)	0.321		
High vs. low	0.02 (-0.05 – 0.09)	0.601	0.03 (-0.02 – 0.08)	0.276	-0.00 (-0.08 – 0.07)	0.936		

Table 3. (continued)

		Outcome: Self-esteem at t_n					
Psychotic Experiences t_{n-1}							
Emotional abuse							
High (mean+1SD)	-0.09 (-0.22 – 0.05)	0.199	-0.09 (-0.12 – -0.06)	<0.001	-0.13 (-0.27 – 0.00)	0.057	0.472
Average (mean)	-0.09 (-0.14 – -0.04)	0.001	-0.11 (-0.14 – -0.08)	<0.001	-0.08 (-0.15 – -0.02)	0.016	
Low (mean-1SD)	-0.09 (-0.19 – -0.00)	0.046	-0.13 (-0.18 – -0.09)	<0.001	-0.03 (-0.13 – -0.07)	0.512	
High vs. low	0.01 (-0.20 – 0.21)	0.955	0.04 (-0.01 – 0.10)	0.091	-0.10 (-0.29 – -0.10)	0.325	
Physical abuse							
High (mean+1SD)	-0.07 (-0.21 – 0.07)	0.320	-0.10 (-0.13 – -0.07)	<0.001	-0.04 (-0.15 – 0.07)	0.454	0.844
Average (mean)	-0.09 (-0.14 – -0.03)	0.002	-0.10 (-0.13 – -0.08)	<0.001	-0.07 (-0.13 – -0.01)	0.025	
Low (mean-1SD)	-0.10 (-0.20 – -0.01)	0.025	-0.11 (-0.15 – -0.07)	<0.001	-0.10 (-0.20 – -0.00)	0.043	
High vs. low	0.03 (-0.17 – 0.24)	0.751	-0.01 (-0.03 – 0.06)	0.475	0.06 (-0.11 – 0.22)	0.475	
Sexual abuse							
High (mean+1SD)	-0.07 (-0.19 – 0.05)	0.242	-0.10 (-0.13 – -0.07)	<0.001	-0.06 (-0.15 – -0.02)	0.152	0.882
Average (mean)	-0.09 (-0.14 – -0.04)	<0.001	-0.10 (-0.13 – -0.07)	<0.001	-0.07 (-0.13 – -0.01)	0.027	
Low (mean-1SD)	-0.11 (-0.20 – -0.01)	0.025	-0.10 (-0.14 – -0.07)	<0.001	-0.08 (-0.16 – 0.00)	0.055	
High vs. low	0.03 (-0.16 – 0.23)	0.723	0.00 (-0.04 – 0.04)	0.846	0.02 (-0.09 – 0.13)	0.748	
Emotional neglect							
High (mean+1SD)	-0.10 (-0.17 – -0.02)	0.010	-0.10 (-0.14 – -0.06)	<0.001	-0.08 (-0.19 – 0.04)	0.176	0.988
Average (mean)	-0.09 (-0.14 – -0.04)	<0.001	-0.10 (-0.13 – -0.08)	<0.001	-0.07 (-0.14 – -0.01)	0.027	
Low (mean-1SD)	-0.08 (-0.15 – -0.02)	0.014	-0.11 (-0.15 – -0.06)	<0.001	-0.07 (-0.16 – -0.03)	0.180	
High vs. low	-0.02 (-0.12 – 0.08)	0.762	0.01 (-0.05 – 0.07)	0.826	-0.01 (-0.18 – 0.15)	0.871	
Physical neglect							
High (mean+1SD)	-0.09 (-0.16 – -0.01)	0.019	-0.10 (-0.13 – -0.07)	<0.001	-0.00 (-0.19 – 0.18)	0.961	0.490
Average (mean)	-0.09 (-0.14 – -0.04)	<0.001	-0.11 (-0.14 – -0.08)	<0.001	-0.06 (-0.13 – 0.02)	0.123	
Low (mean-1SD)	-0.09 (-0.16 – -0.03)	0.006	-0.12 (-0.16 – -0.07)	<0.001	-0.11 (-0.22 – 0.00)	0.052	
High vs. low	0.01 (-0.09 – 0.11)	0.893	0.02 (-0.03 – 0.07)	0.410	-0.11 (-0.16 – 0.37)	0.431	

SD, standard deviation; df, degrees of freedom; vs., versus; CI, confidence interval; p_{we} , family-wise error-corrected p-values were computed by multiplying the unadjusted p-value by the total number of tests to adjust significance levels of Wald tests for three-way interactions; adj. β , standardized regression coefficients (continuous independent variables were standardized (mean=0, SD=1) for interpreting significant three-way interaction terms and examining the difference in associations between high (mean + 1 SD), average (mean), and low (mean – 1 SD) levels of childhood trauma within and across groups (patients, relatives, controls)).^a Adjusted for age, gender, ethnicity, level of education, and marital status.

Methodological considerations

Several limitations should be taken into account when interpreting the study findings. First, only a selection of the baseline sample made it through the third wave. For our analyses, we had to exclude 118 individuals because they did not complete a sufficient number of ESM assessments, or the CTQ. Possibly, these assessments were too burdensome and, therefore, might have led to selection bias. However, when comparing these groups with the analytic sample in basic sample characteristics of those who participated in the third wave of GROUP assessments, included and excluded participants showed to be comparable to a great extent, except for ethnicity (included participants were more often white in all three groups). Second, the CTQ, which was used to measure exposure to several types of trauma during childhood, is a retrospective self-report measure. It has been argued that the CTQ is prone to recall bias and that the manifestation of psychotic symptoms might affect the ratings on this measure (61, 62). However, Gayer-Anderson, Reininghaus (63) demonstrated accuracy, strength of agreement and convergent validity to be broadly similar between patients with first-episode psychosis and controls. Additionally, all ESM assessments of self-esteem and psychotic experiences were based on subjective self-reports, which might have led to bias. However, the ESM has been found to be a feasible, reliable, and valid assessment method in various populations (43, 50, 64), including patients with psychosis (50, 51, 57).

Moreover, momentary self-esteem was measured with only two items. Using fewer items in ESM research is quite common, since it minimizes the reactivity to the assessment method (65). The construct of self-esteem involves both positive and negative self-esteem (66, 67). Therefore, we used one item that measured the positive, and one that measured the negative dimension of self-esteem, which is in line with previous ESM studies investigating self-esteem (54, 68). Because of this heterogeneity of the self-esteem construct and, hence, ESM items, the internal consistency of the two momentary self-esteem items we used was as expected (within-person $\alpha=.22$, between-person $\alpha=.76$) (69). In previous analyses, we have investigated to what extent the two ESM items adequately tap the construct self-esteem in a subsample of the current sample. We found that the convergent validity between the two momentary self-esteem items and the Rosenberg Self-esteem Scale (RSES; Rosenberg (67)) was fair, with the intraclass correlation coefficient (ICC) being 0.41 (33).

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Next, we controlled for potential *a priori* confounders, such as age, gender, ethnicity, education level and marital status. We did not include medication use as a confounder, as 98% of the patients showed to currently use medication. Nevertheless, unmeasured confounders, such as other childhood adversities, comorbidity, the impact of illness chronicity, and molecular genetic measures, were not taken into account and may have, therefore, influenced the findings.

Last, we standardized the continuous childhood trauma variables, because it allowed us to interpret associations at higher vs. lower levels of childhood trauma (59, 60). Notably, this implies that by using continuous and standardized variables for childhood trauma, no discrete distinction was made between those exposed vs. not exposed but rather those exposed to *higher* vs. lower levels of each type of childhood trauma. Therefore, these results could possibly be an underestimation of the reality.

Comparison to previous research

There is well-established evidence that exposure to childhood trauma is a risk factor for developing a psychotic disorder (3-7, 10-12, 71), and self-esteem has been proposed to be involved in the pathway from childhood trauma to psychosis (38-42). Also, mediation models linking childhood trauma and self-esteem in pathways to psychosis have been previously

proposed and tested (41, 72). However, evidence as to whether prior exposure to childhood trauma (emotional, physical and sexual abuse and emotional and physical neglect) modifies the association of momentary self-esteem and psychotic experiences in daily life remains limited.

As hypothesized (H1), and extending previous findings (33), we found evidence that exposure to physical and sexual abuse and physical neglect modified the association between momentary self-esteem and psychotic experiences in daily life. However, the results also suggested that exposure to emotional abuse and emotional neglect did not modify the association between momentary self-esteem and psychotic experiences in daily life. This is unexpected, as previous studies demonstrated that, when comparing the five types of childhood trauma, emotional abuse and neglect are the types that affect self-esteem the most (73, 74). We would therefore expect that especially these types of trauma would have a particular bearing for the association between self-esteem and psychosis. However, the timing, chronicity and severity of emotional abuse and neglect is related to the extent to which the maltreatment has an impact on developmental trajectories (75). When maltreatment is, for example, less severe, or ends early in childhood, it is possible that its impact might fade with time in some individuals (76, 77). Indeed, our data shows that the vast majority of the participants experienced none or mild to moderate levels of emotional abuse and neglect. Another explanation for these unexpected results might be that cross-sectional modelling of associations between momentary self-esteem and psychotic experiences does not take moment-to-moment variation in these measures into account. However, when we evaluated these associations using time lags, we observed that exposure to childhood trauma did not modify the temporal association of self-esteem with psychotic experiences, and vice versa.

Based on previous literature (38-42), we hypothesized that the effect of exposure to childhood trauma would modify the association of low self-esteem and increased intensity of psychotic experiences in daily life most substantial in patients, followed by relatives. We found that physical neglect modified the association between self-esteem and psychotic experiences in patients, physical abuse modified this association in relatives only, and sexual abuse modified this association in relatives and controls, with the impact being stronger in relatives than in controls. It is possible that controls exposed to childhood trauma may have better coping strategies (78) compared to first-degree relatives of patients with a psychotic

disorder, who have a familial liability to psychosis. Controls might therefore be more resilient to lower levels of self-esteem and psychotic experiences in daily life (78). In line with this, there is also evidence that controls exposed to high levels of childhood trauma were more resilient to daily life stress, compared to first-episode psychosis (FEP) patients, At-Risk Mental State (ARMS) individuals, and help-seeking service users (22, 23). Moreover, previous literature showed that resilience at baseline was lower in individuals who developed psychosis at follow-up, than in those who did not (79), which suggests that resilience is a protective factor in the formation of psychosis (80).

Additionally, relatives have a familial liability to psychosis (16, 18) and they share a degree of exposure to childhood trauma with their siblings with a psychotic disorder (20), which may explain the stronger associations in relatives compared to controls. Patients were all recruited via treating clinicians, which implies that they all received a form of (standard) mental health care, including medication. Treatment, such as psychoeducation, cognitive behavioral therapy and antipsychotic medication, have been shown to reduce symptoms and prevent relapse (81-83). It has been demonstrated that therapy targets distorted beliefs about delusions and hallucinations and, thereby, decreases negative consequences of psychotic symptoms (84). Moreover, results of a meta-analysis showed that the interpretation of these beliefs are addressed during treatment, by taking into account psychological mechanisms that might contribute to the formation and maintenance of psychotic symptoms, such as emotions, arousal, attachment, interpersonal issues, trauma and self-esteem (85). For example, results of a randomized clinical trial showed that treatment, such as Eye Movement Desensitization and Reprocessing (EMDR) and Prolonged Exposure (PE), in patients with psychotic disorder reduced trauma symptoms and psychotic symptoms (86), also at 6-months follow-up. This potentially implies that the influence of trauma of patients might become less impactful over time due to the effects of treatment they have received. Even more so, 98% of the patients currently used antipsychotic medication. One side effect of medication is emotional flattening. Emotional flattening interferes with expressiveness, and this often leads to problems in interpersonal interactions, which in turn leads to more withdrawal from (social) activities (87). Selective perception and selective memory are important features of low self-esteem, and as a consequence, negative convictions about one's self are confirmed over and over again in new situations (88). However, this will not occur that often if patients who are using antipsychotics socially withdraw, and therefore experience fewer social

interactions. Potentially, directly or indirectly, medication use and the effects of illness chronicity might have a flattening effect on self-esteem. Therapy and medication use might limit the impact of exposure to traumatic experiences on the association of self-esteem and psychotic experiences in daily life for patients with enduring psychotic disorder.

Previous research has investigated the temporal order of self-esteem and psychotic experiences in daily life. It was found that self-esteem preceded psychotic symptoms only in controls, and psychotic experiences had a temporal effect on self-esteem in patients with a psychotic disorder, first-degree relatives and controls (33). In the current study, we investigated whether prior exposure to childhood trauma modified the temporal associations between self-esteem and psychotic experiences, and between psychotic experiences and self-esteem. However, the results showed no evidence for this. Nevertheless, we would not rule out the hypothesis of a temporal order entirely, as we now investigated the interaction between prior exposure to childhood trauma, psychotic experiences at t_n , and momentary self-esteem at the previous time point (t_{n-1}), and vice versa. Assessments took place within 90-minute time blocks. It is possible that longer time lags would have yielded different results, as the occurrence of psychosis might be preceded by weeks, months or even years of psychological and behavioral abnormalities (89). Perhaps self-esteem is a mechanism that needs more time to unfold to be succeeded by psychotic experiences.

Conclusion

Taken together, our findings suggest that self-esteem may be a putative underlying psychological mechanism through which childhood trauma may impact on psychotic experiences in daily life. Results showed that this is especially the case in first-degree relatives and, to a lesser extent, in patients with a psychotic disorder. Although we did not find evidence for temporal associations, the cross-sectional results underline the importance of developing and evaluating early, and low-level ecological momentary interventions, that directly target self-esteem, to reduce the intensity of psychotic experiences in daily life. We currently evaluate such an intervention in the SELFIE study (90).

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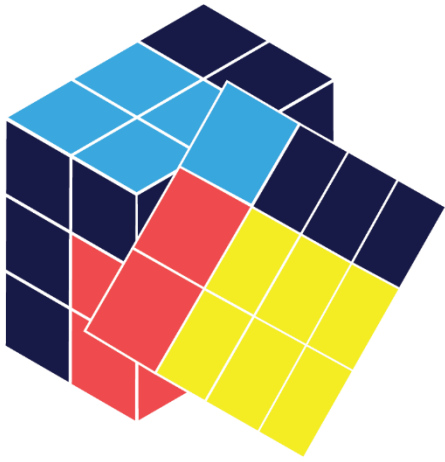
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Supplementary Table S1. Basic characteristics of the excluded participants (participants with less than one third ESM assessments and no CTQ results were excluded)

	Excluded patients (n=55)	Compared to incl. patients	Excluded relatives (n=51)	Compared to incl. relatives	Excluded controls (n=12)	Compared to incl. controls	P
		Test statistics p		Test statistics P		Test statistics P	
Age (years), mean (SD)	32.6 (5.5)	z=1.07 0.284	32.6 (8.2)	z=1.95 0.051	33.5 (9.5)	z=1.95 0.051	
Gender, n (%)		$\chi^2=1.49, df=1$ 0.222		$\chi^2=0.01, df=1$ 0.940		$\chi^2=0.72, df=1$ 0.395	
Men	41 (74.5)		20 (39.2)		5 (41.7)		
Women	14 (25.5)		31 (60.8)		7 (58.3)		
Ethnicity, n (%)^a		$\chi^2=7.99, df=1$ 0.005		$\chi^2=7.98, df=1$ 0.005		$\chi^2=3.98, df=1$ 0.046	
Caucasian	38 (71.7)		37 (72.6)		10 (83.3)		
Non-caucasian	15 (28.3)		13 (27.4)		2 (16.7)		
Level of education, n (%)^b		$\chi^2=2.83, df=2$ 0.243		$\chi^2=0.50, df=2$ 0.779		$\chi^2=0.43, df=2$ 0.805	
Low							
Middle	1 (8.3)		1 (7.1)		0 (0.0)		
High	8 (66.7)		4 (28.6)		1 (25.0)		
	3 (25.0)		9 (64.3)		3 (75.0)		
Marital status, n (%)		$\chi^2=2.37, df=2$ 0.306		$\chi^2=2.19, df=2$ 0.334		$\chi^2=0.90, df=2$ 0.638	
Not married	44 (80.0)		22 (43.1)		3 (25.0)		
Married/live together	10 (18.2)		27 (53.0)		9 (75.0)		
Divorced	1 (1.8)		2 (3.9)		0 (0)		
Current antipsychotic use, n^c	40 (100.0)	$\chi^2= 1.29, df=3$ 0.731	-	-	-	-	

Missing values (%): ^a 2.5, ^b 74.6, ^c 12.7. ESM, experience sampling method, CTQ, childhood trauma questionnaire.



CHAPTER 4

*Modelling the temporal interplay between self-esteem
and positive and negative affect in pathways to
psychosis: an experience sampling study*

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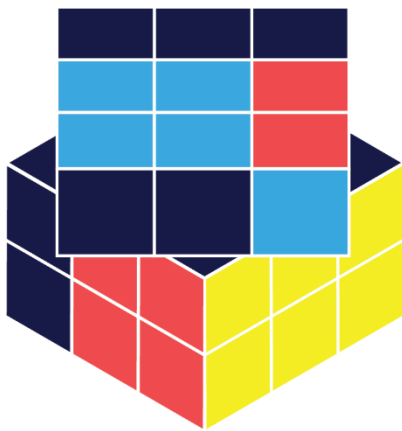
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CHAPTER 5

*Convergent and concurrent validity of explicit, implicit
and momentary self-esteem measurement instruments*

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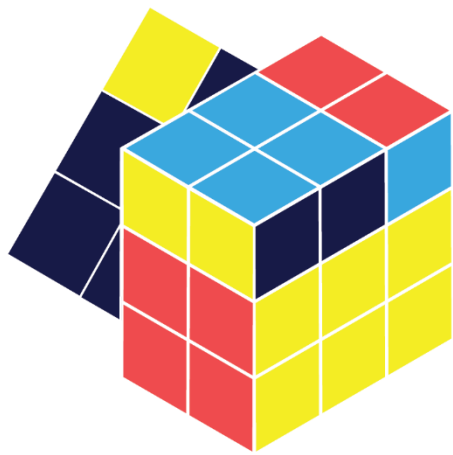
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CHAPTER 6

Efficacy of a transdiagnostic ecological momentary intervention for improving self-esteem (SELFIE) in youth exposed to childhood adversity: study protocol for a multi-centre randomized controlled trial

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Abstract

Background: Targeting low self-esteem in youth exposed to childhood adversity is a promising strategy for preventing adult mental disorder, but psychological help remains difficult to access and accept for youth, calling for novel, youth-friendly approaches. Mobile Health (mHealth) and, most prominently, ecological momentary interventions (EMIs) provide a unique opportunity to deliver youth-friendly, personalized, real-time, guided self-help interventions. The aim of this study is to investigate the efficacy of a novel, accessible, transdiagnostic ecological momentary intervention for improving self-esteem ('SELFIE') in youth with prior exposure to childhood adversity.

Methods/design: In a parallel-group, assessor-blind, multi-centre randomized controlled trial, individuals aged 12–26 years with prior exposure to childhood adversity and low self-esteem will be randomly allocated to SELFIE in addition to treatment as usual (TAU) as the experimental condition or the control condition of TAU only, which will include access to all standard health care. SELFIE is a digital guided self-help intervention administered through a smartphone-based App to allow for interactive, personalized, real-time and real-world transfer of intervention components in individuals' daily lives, blended with three training sessions delivered by trained mental health professionals over a 6-week period. Outcomes will be assessed at baseline, post-intervention, and 6-month follow-up by blinded assessors. The primary outcome will be the level of self-esteem as measured with the Rosenberg Self-Esteem Scale (RSES).

Discussion: The current study is the first to establish the efficacy of an EMI focusing on improving self-esteem transdiagnostically in youth exposed to childhood adversity. If this trial provides evidence on the efficacy of SELFIE, it has significant potential to contribute to minimizing the deleterious impact of childhood adversity and, thereby, preventing the development of mental disorder later in life.

Trial registration number: Netherlands Trial Register, NL7129 (NTR7475); Date of registration: 9 November 2018.

Introduction

The majority of mental disorders first emerge in youth and, as such, contribute substantially to disease burden, which is higher in youth than during any other developmental period (1-5). More specifically, 50% of lifetime cases of mental disorder have started by age 14 years and three quarters by age 24 (2, 6). Mental disorders in youth aged 10-24 years are associated with an immense cost (7-9) and have been found to be the leading cause of disease burden in high-income countries (4, 5). Onset of a mental disorder may disrupt critical age-specific developmental, interpersonal, occupational and educational milestones (10-12) and indicates a need for close scrutiny of the complex interplay between risk and protective factors in childhood and adolescence. Recently, transdiagnostic frameworks have become more prominent (e.g. the Hierarchical Taxonomy of Psychopathology (HiTOP) (13, 14), which broadly posit that symptoms of psychopathology are transdiagnostic in the early stages (15) and might result in a wide range of psychopathology later in life (12, 16). Furthermore, during the ongoing COVID-19 pandemic, measures to control SARS-CoV-2 transmission rates have been shown to have negative effects on mental health, especially in youth (17-19). All this highlights the value of transdiagnostic preventive interventions to improve well-being and resilience in youth and prevent morbidity later in life in order to reduce burden for individuals, families and the wider society (2, 11, 20-22).

Youth referred to mental health services have experienced disproportionate levels of childhood adversity (i.e. abuse, neglect, bullying and household discord) (23-31), which is one of the most pervasive risk factors for developing a range of mental disorders (25, 32, 33). For example, in a nation-wide Dutch study of help-seeking adolescents and young adults with an Ultra High Risk state for Psychosis (UHR), a high prevalence was found for physical (20.9%), sexual (24.8%) and emotional (46.7%) abuse, as well as physical (41.9%) and emotional (66.7%) neglect (29). Also, in a study based on a representative sample drawn randomly from the general population in the Netherlands, it was shown that 29.7% experienced one or more adversities during their childhood (34). Current estimates of attributable risks further suggest that interventions targeted at averting childhood adversity from exerting its adverse effects can prevent a substantial proportion of the incidence of adult mental disorder, and, thereby, have a sizeable public health impact and reduce societal costs (26, 35). While primary prevention of childhood adversity through universal, population-based strategies is of prime importance, it remains difficult to achieve for all, and, hence, interventions targeting the

negative psychological consequences of childhood adversity in youth are a promising selective prevention strategy for adverse outcomes later in life with tangible public health implications (31, 36).

One important psychological mechanism in pathways from childhood adversity to adult psychopathology is low self-esteem (37, 38). Youth is a critical period for the development of self-esteem. Self-esteem is essential to well-being and mental health per se, with a substantial impact on the development and maintenance of severe mental disorders (39). There is now substantial evidence to suggest that exposure to childhood adversity has detrimental effects on self-esteem (40-43). The current evidence further suggests that childhood adversity exerts its detrimental effects on risk of later psychopathology precisely via pathways through low self-esteem (36, 37, 44-47). The prevalence of low self-esteem in help-seeking youth has been reported to be around 45% (48). Taken together, targeting low self-esteem at an early stage in youth exposed to childhood adversity is a promising strategy for preventing mental disorder and reducing societal costs.

Current psychological help, including prevention, however, remains difficult to access and accept for youth and has limited efficacy under real-world conditions, calling for novel approaches (49, 50). While conventional interventions have proven efficacious in reducing psychiatric symptoms via enhancing self-esteem (51), a key next step is to develop and evaluate interventions that are specifically geared toward the specific needs of youth. This is what the current study is designed to achieve. The recent advances in information and communication technologies have led to the development of mobile Health (mHealth) interventions and, most prominently, ecological momentary interventions (EMIs) (52-56). EMIs provide a unique opportunity to deliver youth-friendly, accessible, personalized, real-time, guided self-help interventions targeting candidate psychological mechanisms in daily life and, thereby prevent mental disorder and reduce disease burden. This enables youth to access interventions that are individually adapted to their needs in a given moment and context (e.g., by offering interventions specifically tailored for helping participants in moments of low self-esteem). Recently, the term 'Just-In-Time Adaptive Interventions (JITAs)' has been started to be used by some authors (57, 58), positing that novel characteristics of JITAs are that interventions are initiated by push notifications and dynamically initiated by the app. However, these features have been part of EMIs from the outset, and, hence, if anything JITAs may be used synonymously with EMIs, which have been

proposed at a much earlier point. EMIs are ideally placed for enhancing access to mental health services for youth depending on their needs and preferences by delivering low-threshold interventions by mental health professionals as one component that can be rolled out across child, adolescent and adult mental health services.

Previous studies of conventional interventions suggest that psychiatric symptoms, such as anxiety and depression symptoms, may be reduced through enhancing self-esteem (51). However, these interventions are not tailored toward the specific preferences and needs of youth as naturally occurring in daily life. While EMIs such as the SELFIE intervention provide a unique opportunity to deliver youth-friendly, accessible, personalized, real-time interventions in daily life, robust trial-based evidence on EMIs and other mHealth interventions remains very limited (22, 52, 53, 59-62).

The overall aim of the current study is to test the efficacy of a novel, accessible, transdiagnostic ecological momentary intervention (EMI) for improving self-esteem ('SELFIE') in youth aged 12-26 with prior exposure to childhood adversity in a multi-centre randomized controlled trial (RCT). The SELFIE intervention will be administered in addition to treatment as usual (TAU) (experimental condition) and compared to a control condition of TAU only, which will include (access to) standard health care.

The specific objectives of this study are to:

- 1) Test the efficacy of the SELFIE intervention on improving self-esteem at post-intervention and 6-month follow-up (primary outcome);
- 2) Test the efficacy of the SELFIE intervention on improving momentary self-esteem, positive and negative schematic beliefs of self, resilience, emotional well-being, general psychopathology, functioning, and quality of life at post-intervention and 6-month follow-up (secondary outcomes);
- 3) Establish whether the effects of the SELFIE intervention on primary and secondary outcomes hold at 18-month and 24-month follow-up;
- 4) Examine the cost effectiveness and cost utility of the SELFIE intervention;
- 5) Assess the acceptability, safety, adherence and fidelity of the SELFIE intervention.

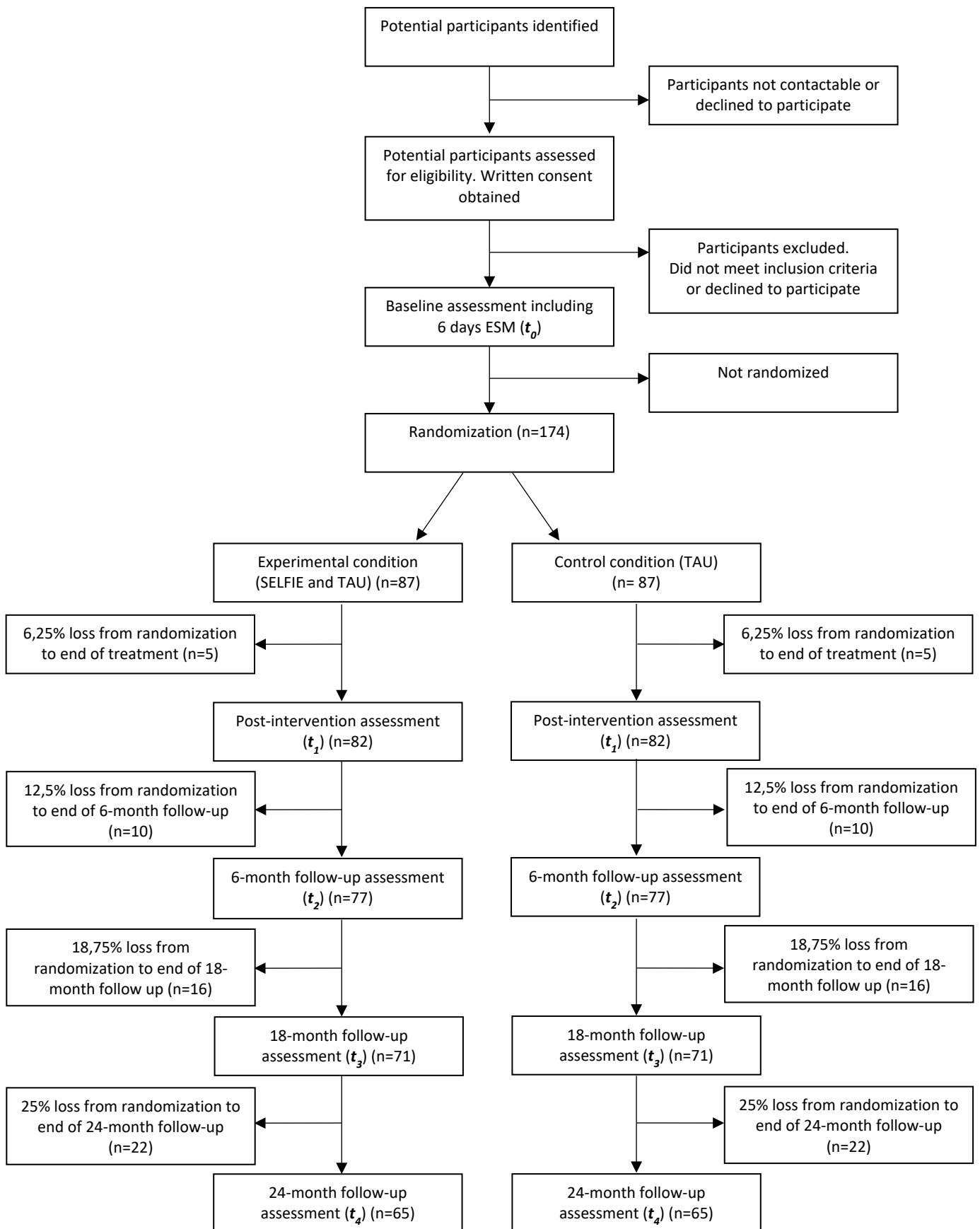


Figure 1. Overview of the study design

Methods

Study design

In a two-arm parallel-group, assessor-blind multi-centre randomized controlled trial, individuals aged between 12 and 26 years with prior exposure to childhood adversity and low self-esteem will be randomly allocated to SELFIE in addition to TAU as the experimental condition or a control condition of TAU only, which includes (access to) standard health care and social services. Participants will be recruited from mental health services in Noord-Holland, Zuid-Holland and Limburg (the Netherlands), and from the general population (e.g., via social media). Outcomes will be measured at baseline (i.e., before randomization), post-intervention (i.e., after the 6-week intervention period), and 6-month, 18-month and 24-month follow-up (i.e., 6, 18 and 24 months after completing the intervention period) by blind assessors (see figure 1 and 2). Randomization will be conducted independently of the research team through a computer-generated sequence, stratified by region of collaborating centres or as external admission. All outcomes will be measured and the statistical analysis will be performed blind to treatment allocation.

Participants

A sample of 174 individuals aged 12-26 with prior exposure to childhood adversity and low self-esteem will be recruited. Participants will be recruited from collaborating mental health services in three regions in the Netherlands: Noord-Holland (Amsterdam University Medical Centers (Location AMC); Levvel), Zuid-Holland (Parnassia Group; Prodeba) and Limburg (Mondriaan; Lionarons GGZ; Koraalgroep). In addition, participants from the general population, who do not seek help from collaborating mental health services, will be recruited e.g. via (targeted adverts on) social media, schools, social services, and flyers at relevant public locations. All individuals presenting to collaborating mental health services will be approached by their treating clinician, who will provide initial information about the study. If the individual is interested in the study, their treating clinician will, in agreement with the potential participant, pass on their contact details to the research team. All potential participants (including those recruited via social media, etc.) will be contacted by the research team and will be fully informed about the study. One week later informed consent will be obtained (if applicable, also from parents/legal guardians), which can be withdrawn by participants at any time and without having any negative consequences for their access to

standard health care). For participants under the age of 16, both parents (or the legal guardian) and participants will receive detailed information about the intervention. In addition, parents (or the legal guardian) and the researcher will consider possible negative reactions of the underage participant to the intervention procedure. Further, it will be determined together with the parents (or the legal guardian) prior to the intervention what the researcher will do in case of reluctance of the underage participant and which behaviour of the participant commonly reflects reluctance. It will be discussed with the parents (or the legal guardian) when the study should be stopped in case of reluctance of their child.

Potential participants will then be asked to complete the screening questionnaires to assess whether they meet the inclusion criteria. Participants aged 16 years or older will be financially compensated for their time, and travel expenses will be fully reimbursed. To minimize loss to follow-up, researchers maintain contact with participants on a regular basis. Also, participants will receive a small additional financial reimbursement for completing all follow-up assessments.

Inclusion criteria

Inclusion criteria are as follows (see table 1 for more detail): 1) aged between 12 and 26 years, 2) exposure to childhood adversity (physical, sexual or emotional abuse, emotional or physical neglect, peer bullying or parental conflict), 3) self-esteem below average measured with the Rosenberg Self-Esteem Scale (RSES) (51, 63, 64), 4) willingness to participate, 5) ability to give informed consent, and 6) parental consent for minors.

Exclusion criteria

Subjects will be excluded if their command of Dutch is insufficient or if their psychiatric symptoms are due to an organic cause.

Table 1. Eligibility criteria

Inclusion criteria
1) Aged between 12 and 26 years old.
2) Adversity: <ul style="list-style-type: none"> a. Childhood trauma: Prior exposure to at least one form of childhood trauma defined as moderate or severe physical (score ≥ 10), sexual (score ≥ 8) and/or emotional (score ≥ 13) abuse, emotional (score ≥ 15) and/or physical (score ≥ 10) neglect, according to established severity categories of the Childhood Trauma Questionnaire (CTQ) (65-67), and/or b. Peer bullying: Exposure to moderate or severe peer bullying, measured with the Retrospective Bully Questionnaire (RBQ) (score of frequency of bullying in one or more ways “sometimes” or more often and/or classified the experience as “quite serious” or “extremely serious”) (68), and/or c. Parental conflict: A score of moderate or severe parental conflict, measured with the Childhood Experiences of Care and Abuse Questionnaire (CECA.Q) section Parental Conflict (frequency score of “regularly” or “often” and/or a severity score of “serious” or “violence”) (69).
3) Self-esteem below average (measured with the Rosenberg Self-Esteem Scale (RSES) (score <26) (51, 64).
4) Willingness to participate in the SELFIE intervention.
5) Ability to give written informed consent.
6) Parental consent for minors.
Exclusion criteria
1) Insufficient command of Dutch
2) Psychiatric symptoms due to an organic cause

Intervention

Control condition: treatment as usual (TAU)

Participants allocated to the control condition will receive treatment as usual (TAU), which will include access to all standard health care and social services. Specifically, this will include all the input from their general practitioner and other providers of health and social services that they would receive if they did not participate in the study, except for manualized treatment that explicitly addresses self-esteem as primary target (e.g., COMET or EMDR (51, 70, 71)) during the intervention period.

Experimental condition: SELFIE + TAU

Participants allocated to the experimental condition will receive the manualized SELFIE intervention within a 6-week period in addition to TAU. The intervention consists of three

face-to-face sessions, each for around 60 minutes, delivered by SELFIE therapists, who will be trained mental health professionals (e.g., psychologists, social workers and mental health *nurse* specialists trained in the SELFIE intervention and receiving regular supervision and inter-*vision* led by a clinical psychologist), three e-mail contacts, and an EMI administered through a smartphone-based App (i.e., the PsyMate® App) for adaptive real-time and real-world transfer of intervention components tailored to person, moment and context, delivered over a 6-week intervention period. Due to the COVID-19 pandemic, some of the face-to-face sessions will be offered through a secure and encrypted video conferencing system. The intervention is based on principles of EMIs (22, 52-56, 62, 71), and a guided self-help approach using principles of cognitive-behavioural therapy (CBT), aimed at modifying cognitive bias inherent to negative self-esteem and developing and practicing a new behavioural repertoire guided by therapists using modeling and shaping as additional important therapeutic techniques (72, 73). Delivering the intervention in individuals' daily lives, and enabling youth to benefit from this intervention in a given moment and context, when most needed (e.g. in moments of low self-esteem) is the key goal of the 6-week SELFIE intervention. Therefore, in the first introductory session, participants will either receive a study smartphone with the App already installed or will be asked to install it on their own smartphone by the SELFIE therapist, who will explain the SELFIE intervention in detail and ask the participant to complete examples of training tasks on the App in order to address the self-selected goals the participant wants to work on in the 6-week intervention period. The App will offer participants 'enhancing', 'consolidating' and 'interactive' tasks (see table 2) (72, 73).

In enhancing tasks, new intervention components will be introduced and practiced, some of which will be modified and extended over the study period. Consolidating tasks will ask participants to practice previously learned components of enhancing tasks on a daily basis. For these tasks, participants will be reminded by the app between 1-3 times per day (varying by intervention week). During the intervention period, the Experience Sampling Method (ESM), a structured diary technique, will be used to assess momentary self-esteem, affect, and pleasantness of activities and events, six times a day, on day 3, 4 and 5 in each of the six intervention weeks using a time-based design with stratified random sampling (i.e., with ESM assessments scheduled at random within set blocks of time) to allow for interactive tasks. Interactive tasks will be provided based on their ESM ratings of (positive and negative) affect, momentary self-esteem and pleasantness of activities and events. For example, (in week 1)

participants will be provided with an interactive task, offering them to add more successes to their positive datalog when they scored high on positive affect, momentary self-esteem and/or pleasantness of activities. Participants can discontinue the intervention at any time upon request without negative consequences.

Outcome measures

After obtaining written informed consent and eligibility assessment, participants will complete a range of self-report, interview-based and computer-based measures to assess primary and secondary outcomes and other study parameters. Participants will complete self-report questionnaires using a smartphone-based App (i.e., the PsyMate® App). Interviews will be conducted using a secure and encrypted video conferencing system. In addition, ESM data will be collected following the protocol from previous ESM studies using the PsyMate® App to measure momentary self-esteem, emotional well-being, stress sensitivity, threat anticipation, and psychotic experiences in daily life for a period of 6 consecutive days (22, 31, 62, 74-76). On each day, participants will be asked eight times per day to complete an ESM, which will be scheduled at random within set blocks of time. At the end of the 6-day baseline ESM period, participants will be asked to complete a short debriefing questionnaire. All the above-mentioned measures will be assessed at baseline (i.e. before randomisation), post-intervention (i.e. after the 6-week intervention period) and 6-month follow-up. Please see Figure 2 (SPIRIT Figure) for details of assessment at each time point. All assessments will be checked for quality and completeness by another member of the research team and an extensive data checking and cleaning will be adhered to as a quality control measure.

Primary outcome

The primary outcome will be global self-esteem, measured with the Rosenberg Self-Esteem Scale (RSES) (63), which is a widely used measure to assess global self-esteem with good reliability and validity (64, 77). The RSES consists of ten items rated on a 4-point Likert scale ranging from 'strongly agree' to 'strongly disagree'. The level of global self-esteem, operationalized as the total score of the RSES, will be compared between the experimental and the control condition at post-intervention and 6-month follow-up (H1).

Table 2. Key components of the SELFIE intervention

		SELFIE intervention (weeks)						
		1	2	3	4	5	6	
Training session	Face-to-face session 1	Face-to-face session 2	Face-to-face session 3	Face-to-face session 3	Face-to-face session 3	Face-to-face session 3	Face-to-face session 3	
Enhancing EMI tasks	Formulating a new positive core belief + Positive datalog (enter daily successes)	Personal positive qualities (integrated in positive datalog) + Tips to identify more positive qualities + One-minute exercise (listing (previously identified) positive qualities)	Overview old behavioral patterns + Development of new behavior patterns	Expanding the positive datalog with successes arising from new behavioral patterns	Strategies to deal with criticism + A critical look at criticism + Cost-benefit analysis of perfectionism + The minimum programme (practicing to perform less than perfect)	Strategies to deal with criticism + A critical look at criticism + Cost-benefit analysis of perfectionism + The minimum programme (practicing to perform less than perfect)	Strategies to deal with criticism + A critical look at criticism + Cost-benefit analysis of perfectionism + The minimum programme (practicing to perform less than perfect)	Writing a positive story about yourself + Maintenance plan (for after the intervention)
Consolidating EMI tasks	Positive datalog + Tips to add more successes in the positive datalog + Rating credibility of the new core belief	Positive datalog + Tips positive datalog + One-minute exercise + Rating credibility of the new core belief	Positive datalog + One-minute exercise + Rating credibility of the new core belief	Positive datalog + One-minute exercise + Expanding new behavior patterns + Rating credibility of the new core belief	Positive datalog + One-minute exercise + A critical look at criticism + Rating credibility of the new core belief	Positive datalog + One-minute exercise + A critical look at criticism + Rating credibility of the new core belief	Positive datalog + One-minute exercise + Rating credibility of the new core belief	
Interactive EMI tasks	Positive datalog (adding successes) Or Positive datalog (viewing previously identified successes)	Positive datalog (adding successes and/or positive qualities) Or Positive datalog (viewing previously identified successes and qualities)	Positive datalog (adding successes and/or positive qualities) Or Positive datalog (viewing previously identified successes and qualities)	Positive datalog (adding successes and/or positive qualities) Or Positive datalog (viewing previously identified successes and qualities)	Positive datalog (adding successes and/or positive qualities) Or Positive datalog (viewing previously identified successes and qualities)	Positive datalog (adding successes and/or positive qualities) Or Positive datalog (viewing previously identified successes and qualities)	Positive datalog (adding successes and/or positive qualities) Or Positive datalog (viewing previously identified successes and qualities)	

Note: see Postma (73) and De Neef (72) for more details.

TIMEPOINT**	STUDY PERIOD							
	Enrolment		Allocation	Post-allocation				
	-t ₁	t ₀ <i>Baseline</i>		t ₁ <i>post-intervention</i>	t ₂ <i>6-month follow-up</i>	t ₃ <i>18-month follow-up</i>	t ₄ <i>24-month follow-up</i>	
ENROLMENT:								
Informed consent	X							
Childhood Trauma Questionnaire (CTQ)								
Parental Conflict (CECA)	X							
Retrospective Bullying Questionnaire (RBQ)	X							
Rosenberg Self-Esteem Scale (RSES)	X							
Screening Questionnaire	X							
Allocation			X					
INTERVENTIONS:								
Experimental condition (SELFIE + TAU)			↔					
Control condition (TAU)			↔					
ASSESSMENTS: Outcome measures								
Ecological Momentary Assessment (EMA) questionnaire		X		X	X	X	X	
EMA briefing questionnaire		X		X	X	X	X	
EMA debriefing questionnaire		X		X	X	X	X	
Self-Esteem Rating Scale (SERS)		X		X	X	X	X	
Rosenberg Self-Esteem Scale (RSES)		X		X	X	X	X	
Brief Core Schema Scales (BCSS)		X		X	X	X	X	
Temperament and Character Inventory (TCI)		X						
Kessler Psychological Distress Scale (K10)		X		X	X	X	X	
Symptom Checklist (SCL-90-R)		X		X	X	X	X	
Positive and Negative Affect Scale (PANAS)		X		X	X	X	X	
Social and Occupational Functioning Assessment Scale (SOFAS)		X		X	X	X	X	
Global Assessment of Functioning (GAF)		X		X	X	X	X	
World Health Organisation Quality of Life Instrument-Brief (WHOQOL-BREF)		X		X	X	X	X	
Brief Psychiatric Rating Scale (BPRS)		X		X	X	X	X	
Trimbos Institute and Institute of Medical Technology Assessment Questionnaire for Costs associated with Psychiatric Illness (TIC-P)		X		X	X	X	X	
EQ-5D 3-level version of the 'EuroQoL' group (EQ-5D-5L)		X		X	X	X	X	
Other study parameters								
Socio-demographic schedule		X						
Composite International Diagnostic Interview (CIDI-B-J-L)		X						
Medication use		X		X	X	X	X	
Treatment Classification (present and past)		X		X	X	X	X	
CECA (social support)		X						
Working Alliance Inventory (WAI)				X				
Debriefing questionnaire: SELFIE Intervention				X				
Debriefing questionnaire: SELFIE Follow-Up					X	X	X	
Qualitative interview (process evaluation)				X				

Figure 2. Standard Protocol Items: Recommendations for Interventional Trial (SPIRIT) Figure. Ecological momentary intervention for improving self-esteem (SELFIE): Schedule of enrolment, interventions and assessments

Secondary outcomes

Secondary outcomes will include the level of momentary, positive and negative self-esteem, resilience, emotional well-being, positive and negative schematic beliefs of self, psychological distress, functioning, subjective quality of life, general psychopathology, clinical symptoms and health-related quality of life, service use (including admission to inpatient services) and cost, which will be compared between the experimental and control condition at post-intervention and at 6-month follow-up (H2). In addition, all secondary outcomes (incl. levels of global self-esteem, operationalized using the total score of the RSES (see previous section)) will be compared between the experimental and control condition and at 18- and 24-month follow-up (H3).

Momentary self-esteem will be assessed with four items, rated on a 7-point scale, using the ESM (78, 79). The mean score will be used for analysis. Positive and negative self-esteem will be measured with the SERS, which is a 20-item rating scale to assess these two dimensions of self-esteem separately with good reliability and validity (80). The total sum score of the positive dimension and the total sum score of the negative dimension will be used in the analysis. Momentary resilience will be assessed with the ESM positive affective recovery from event-related stress in daily life (operationalized as the return to baseline levels of positive affect following event-related stress) (31, 74, 76, 81). We will assess emotional well-being using the Positive and Negative Affect Scale (PANAS) (82) based on the total sum score of the negative affect items, and the total sum score of the positive affect items. Also, a 5-item ESM measure will be used for assessing negative affect and a 4-item ESM measure of positive affect (31, 74, 83). For both measures, a mean score will be used in the analysis. The Brief Core Schema Scale (BCSS) will be used as an established measure of positive and negative schematic beliefs of self and others (84). The following four total scores (all consisting of six items) will be obtained for use in the analysis: negative-self, positive-self, negative-others, positive-others. Psychological distress will be measured with the Kessler Psychological Distress Scale (K10), which is widely used and well-validated in youth (85, 86). A total sum score ranging from 10 to 50 will be used for analysis.

The Social and Occupational Functioning Assessment Scale (SOFAS) (87) and the Global Assessment of Functioning (GAF) scale (88) will be used as a well-validated measure of functioning in youth (86). The overall level of functioning rated by researchers on a scale of 0 to 100 will be used in the analysis.

Subjective quality of life will be measured with the World Health Organisation Quality of Life Instrument-Brief (WHOQOL-BREF) (86, 89). Mean scores of all four domains (physical health, psychological, social relationships, environment) will be used. The revised Symptom Checklist (SCL-90-R) will be used as a reliable and valid measure to assess general psychopathology in youth (86, 90). The measure consists of 90 items, which will be rated on a 5-point scale. The total sum score of the SCL-90-R will be used for analysis. We will use the 24-item version of the Brief Psychiatric Rating Scale (BPRS) (91, 92) as a validated interviewer measure to assess clinical symptoms of psychopathology in youth (86). All items are rated on a 7-point scale and, for the analysis, the BPRS total score will be computed.

The Trimbos Institute and Institute of Medical Technology Assessment Questionnaire for Costs associated with Psychiatric Illness (TiC-P) (93) will be used to collect data on service use (including admission to inpatient services) and cost for cost-effectiveness analysis. Last, data on health-related quality of life will be operationalized by quality-adjusted life years (QALYs), which will be calculated based on the EQ-5D 5-level version of the 'EuroQoL' group (EQ-5D-5L) for cost-utility analysis (94).

Process evaluation

A process evaluation will be performed following the methodology of realist evaluation (95). Initial program theories will be developed based on transcribed data from a focus group with stakeholders as well as expert interviews. Overarching program theory and accompanying context-mechanism-outcome configurations will be tested among intervention users (individual interviews with participants who have completed the SELFIE intervention) as well as those who deliver the intervention (focus group with SELFIE therapists), through iterative data collection. Atlas.Ti will be used as software to support the process of our analyses.

Acceptability, adherence and fidelity

We will carefully assess acceptability, safety, adherence and fidelity of the SELFIE intervention. Participants in the experimental condition will be asked to complete a debriefing questionnaire, which assesses acceptability, satisfaction, and whether or not there were beneficial effects of the EMI tasks and sessions. Also the Working Alliance Inventory (WAI) (96) will be completed by the participant and the SELFIE therapist providing the SELFIE intervention. Adherence to the intervention will be assessed using the implicit EMI adherence

data recorded by the App (e.g. number and duration of completed EMI interactive, enhancing and consolidating tasks). Further, the attended face-to-face sessions will be audio recorded and adherence will be rated on a visual analogue scale (ranging from 0 = 'not at all' to 11 = 'very much') by a clinical psychologist or researchers (supervised by a clinical psychologist).

Other measures

A socio-demographic schedule will be used to assess basic socio-demographic and clinical characteristics including age, gender, employment status and level of education. Resilience will be assessed with the Temperament and Character Inventory (TCI) (97). Last, other confounders, such as alcohol and substance use (Composite International Diagnostic Interview (CIDI), sections B, J and L) (98), medication use, treatment classification, and social support (Childhood Experience of Care and Abuse (CECA), section social support) (69) will also be assessed.

Sample Size

Previous studies demonstrated that third-wave cognitive behavioral therapy (CBT) (22, 99, 100), including CBT focusing on self-esteem (51, 101), may lead to reductions in symptoms of psychopathology of moderate to large effect size. In line with previous research, the power calculation is based on the primary outcome of level of self-esteem as measured with the RSES (51). Power simulation in the R environment indicated that a sample size of 130 participants (65 per condition) is sufficient to test our primary hypothesis of the effect of condition (SELFIE + TAU vs. TAU) on self-esteem, while controlling for self-esteem at baseline. Specifically, this will allow us to detect an effect size (standardized mean difference (SMD)) of 0.3 (experimental vs. control condition), i.e., a difference that is considered clinically relevant, at (at least) post-intervention or 6-month follow-up with a power of 0.87 (primary hypothesis), and, at long term, (at least) at one of the post-intervention and follow-up time points (6-month, 18-month and 24-month follow-up), with a power of 0.82 when testing at $\alpha=0.05$ using linear mixed modelling. Based on our previous and ongoing work, we will allow for a 25% attrition rate at 2-year follow-up, which will result in a loss to follow-up of around 22 individuals per condition on average (see figure 1). Hence, we will recruit a total sample of 174 participants (87 experimental, 87 control condition) at baseline.

Randomization and blinding

Each participant will be randomized at a 50:50 ratio to the experimental or control condition after completing the baseline assessment. Randomization will be conducted through a computer-generated sequence, stratified by region of a collaborating centre or as external admission. The assessors will be blind to the allocation of subjects when assessing participants at post-intervention, 6-month, 18-months and 24-month follow-up. After random allocation to the experimental condition, the names and contact details of the participants will be passed on to the SELFIE-therapist providing the SELFIE intervention. This will be done through an independent researcher. This researcher will inform the assessors when assessments at post-intervention and follow-up need to take place for each individual participant. The design of this study is single blinded, because SELFIE therapists and patients cannot be masked towards the allocation of patients to the experimental or control condition. Any data specific to the intervention condition (e.g., on treatment fidelity) will be stored in a separate database. Any breaks in masking will be documented in the trial master file and another assessor will be allocated to complete the next set of assessments where possible.

Assessment of safety

Serious Adverse Events (SAE), which include any serious incidents that result in death, persistent or significant disability or incapacity, require (extension of) hospitalization or are life threatening, will be monitored and collected throughout the study period. In case of occurrence, SAEs will be reported to the accredited Medical Ethics Review Committee (MERC), the Data Monitoring and Ethics Committee (DMEC) and the Trial Steering Committee (TSC). Whilst carefully documented, it is not expected that any SAE will occur as a result of the intervention. The DMEC will advise on any ethical or safety concerns, monitor evidence for intervention harm (e.g. SAEs) for the experimental condition and review whether these events are in line with expectations. If deemed necessary, the DMEC can recommend to the Coordinator and TSC for interim analyses to be conducted and the trial to be terminated prematurely. All reported (serious) adverse events will be reported in publications of findings from this study.

Statistical analysis

A full statistical analysis plan will be written and published prior to unblinding of the study and before any analysis is being undertaken. The trial data set will be accessed by the investigators to test the primary hypothesis of an improvement in self-esteem at post-intervention and 6-month follow-up in a priori planned statistical analysis when data collection for assessments at 6-month follow-up has been completed whilst retaining masking of assessors until the last assessment of the last participant at 24-month follow-up. We will use a linear regression model with the primary outcome of self-esteem at post-intervention and 6-month follow-up entered as the dependent variable and self-esteem measured at baseline, condition (SELFIE + TAU vs. TAU), time (as a two-level factor), centre (as a four-level factor), the baseline \times time interaction and a time \times condition interaction term as independent variables, in line with the intention-to-treat principle. All randomized participants will be included in the analysis, and will be analyzed according to the intention to treat principle. Residuals within subjects will be allowed to be correlated with a completely unstructured variance-covariance matrix to take within-subject clustering of repeated measures into account. We will fit the model using Restricted Maximum Likelihood (REML (102)) in Stata 15 (103), which allows for all available data to be used assuming that data is missing at random if all variables associated with missing values are included in the model (104, 105). Therefore, potential bias due to attrition over the study period, differences between centres, or as a function of baseline self-esteem will be minimized by the model. We will make every effort to assess all participants at post-intervention and follow-up. To test the main effect of condition, an omnibus test of no difference between the two conditions at all two time points (Wald-type test with $df=2$ and $\alpha = .05$) will be used. The two time-specific contrasts will be examined if the omnibus test is statistically significant to determine at which time points significant differences are present (each tested at $\alpha = .05$). The two time-specific contrasts (to determine at which time points significant differences are present) will only be examined if the omnibus test is significant and, hence, the family-wise Type I error rate of finding at least one significant difference at the three time points is controlled at $\alpha = .05$. Hypotheses in relation to secondary outcomes of momentary self-esteem, positive and negative schematic beliefs of self, resilience, emotional well-being, general psychopathology, functioning, and quality of life at post-intervention and 6-month follow-up will be tested following the same steps. The investigators will access the trial data set to test hypotheses in

relation to all four time points (i.e., post-intervention, 6-month, 18-month, and 24-month follow-up) in a priori planned statistical analysis when data collection for assessments at 24-month follow-up has been completed. For hypotheses in relation to primary and secondary outcomes at all four time points (i.e., post-intervention, 6-month, 18-month, and 24-month follow-up), the main effect of condition will be tested using, again, an omnibus test of no difference between the two groups at all four time points (Wald-type test with $df=4$ and $\alpha = .05$). The four time-specific contrasts will be examined to determine at which time points significant differences are present (each tested at $\alpha = .05$), if the omnibus test shows to be statistically significant. Since randomization will be performed in blocks, stratified by region of collaborating centre or as external admission, all analyses will include this as a covariate, even though it is not expected this variable will lead to bias. As participants will be randomly assigned to experimental and control condition, no differences across conditions are expected in other study parameters (socio-demographics, alcohol and substance use, medication use, treatment classification, social support and self-compassion). If, however, in contrast to what would be expected, there are significant differences at baseline in any of these parameters across conditions, these will be included as covariate(s) in analyses with primary and secondary outcomes as dependent variable. As ESM data have a multilevel structure, multiple ESM observations (level 1) will be treated as nested within time points (i.e., baseline, post-intervention and 6-month, 18-month, and 24-month follow-up) (level 2) and time points will be treated as nested within subjects (level 3).

Cost-effectiveness analysis (CEA) will be conducted based on service use and cost data collected using the TiC-P. Cost-utility analysis (CUA) will be conducted using quality-adjusted life years (QALYs), which will be calculated based on the EQ-5D-5L. For both CEA and CUA, the incremental cost-effectiveness ratio (ICER) will be calculated, which reflects the extra cost needed (or saved) per one unit increase in self-esteem or QALY gained, respectively.

Descriptive statistics will be used and confidence intervals constructed as appropriate to compute basic sample characteristics and summarize findings on acceptability, safety, and intervention fidelity of, as well as adherence to the intervention.

Interim analyses and stopping guidelines

Since it is not expected that any harm will occur related to participation in this study, there are no predefined stopping guidelines and no a priori planned interim analyses. The DMEC

can recommend to the Coordinator and TSC for interim analyses to be conducted if deemed necessary because of any ethical or safety concerns.

Research governance

Maastricht University is the sponsor of this study. The trial has received ethical approval from the Medical Ethics Review Committee (MERC) at Maastricht University Medical Centre (MUMC), the Netherlands (reference: NL64393.068.17). Amendments to the study protocol will be submitted to the MERC for approval, then communicated to all relevant parties (DMEC, TSC, the sponsor, funder, and collaborating centres) and will be updated in the clinical trial registry. In case of deviations from the study protocol, a breach report form will be used for documentation. The handling of the data will be in compliance with the Dutch and European General Data Protection Regulation (GDPR). If a participant withdraws their consent, all data from that participant will be destroyed. No biological specimens will be collected in this trial. All data will be handled confidentially and will be coded using a number according to the order of entry. In line with the GDPR, all data will be securely stored and personal data will be stored separately from the number-coded data. Consistent with the consortium agreement of this study, the Coordinator will have overall responsibility for the trial and will be responsible for the day-to-day management of the project. The Project Leader advises on, and supports, the Coordinator in the day-to-day management of the project. Each party (i.e., School for Mental Health and Neuroscience, Mondriaan, Level, Academic Medical Centre Amsterdam, Parnassia) appoints its lead scientist on the project as Principal Investigator (PI). The Coordinator and Project Leader will liaise closely with all PIs on recruitment and consent procedures. The Trial Management Committee will meet monthly and includes the Coordinator, the Project Leader and all PIs. It will be chaired by the Coordinator and will manage the day-to-day running of the study, audit the trial conduct, and oversee preparation of reports to the MERC, the TSC and the DMEC. The Coordinator will permit trial-related monitoring, audits and MERC review (conducted by the Clinical Trial Center Maastricht, which is independent from the study sponsor (i.e. Maastricht University)). The TSC will meet at least annually to provide independent overall supervision of the trial, to approve the protocol and any amendments and to monitor progress (e.g. data completion rates and adherence to the protocol). Also, the DMEC will meet at least annually. The DMEC will advise on ethical or safety concerns and, for the experimental condition, monitor evidence for intervention harm

(e.g. SAEs) and review whether these events are in line with expectations. The DMEC can recommend to the Coordinator and TSC to be given access to all trial data as well for interim analyses to be conducted and the trial to be terminated prematurely if deemed necessary.

Discussion

Exposure to childhood adversity may have deleterious effects on self-esteem, which, in turn, has been shown to be an important putative transdiagnostic mechanism in pathways from childhood adversity to adult psychopathology (37, 38), and thus, is a promising target for early intervention. Even though self-esteem is a common target of conventional psychological interventions (51, 71, 72, 101), current psychological help remains difficult to access for youth in real-world service delivery settings (49, 50), and therefore, new approaches are required. The current paper presents the study protocol of a multi-centre RCT to evaluate the efficacy of an EMI (SELFIE) to improve self-esteem in youth exposed to childhood adversity. SELFIE, an intervention that extends beyond or even outside the clinical setting, has been designed to improve the accessibility and efficacy of psychological interventions for youth exposed to childhood adversity (49, 50). The potential effects of the SELFIE intervention may help to minimize the deleterious impact of, and hence, resilience to, childhood adversity by improving self-esteem and, thereby, prevent the development of severe and enduring mental disorder later in life and reduce disease burden. This study contains several unique and novel aspects. To our knowledge, SELFIE is the first transdiagnostic EMI that focuses on improving self-esteem in youth exposed to childhood adversity, which will inform our understanding of self-esteem as a psychological mechanism as well as the growing knowledge of mHealth intervention development and implementation, in particular for EMIs. An advantage of EMIs is that the intervention components are delivered in, and therefore more easily translated to, diverse contexts of daily life (54). In doing so, the SELFIE intervention focuses on positive rather than negative self-esteem, that is, the goal of SELFIE is to build a competing positive self-esteem, without directly targeting more deeply rooted negative self-esteem (72). This makes this low-level intervention suitable as a guided self-help EMI that is easily accessible, individually tailored and offered in daily life. Also, the multi-centre RCT design implemented in different regions of the Netherlands will provide high external validity of findings. Cost effectiveness and cost utility will inform implementation, and the process evaluation on

acceptability, treatment adherence, and treatment fidelity will provide important data on potential barriers, but also on potential facilitators for implementation.

Trial status

The trial has been registered at trialregister.nl (no. NTR 7475) in November 2018, and all study procedures were approved by the MERC at MUMC in August 2018. We are currently working with protocol version 10, originating from February 2021. Recruitment started in December 2018, the first enrollment was in January 2019, recruitment was completed in June 2021 and outcome assessment will continue until December 2022.

Ethics approval and consent to participate

The trial has received ethical approval from the Medical Ethics Review Committee (MERC) at Maastricht University Medical Centre (MUMC), the Netherlands (reference: NL64393.068.17) at August 1st, 2018. Written informed consent will be obtained from all participants before inclusion in the study. A translated version of the informed consent document can be found in the supplementary materials. The Clinical Trial Center Maastricht, which is independent from the study sponsor (i.e. Maastricht University), will conduct trial-related monitoring, audits and MERC review. The sponsor has an insurance that covers for damage to the research participants though injury or death caused by the study, that has become apparent during the study or within four years after the termination of the study.

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SUPPLEMENTARY MATERIAL**Informed Consent Sheet (translated version, participants > 16 years old)****SELFIE**

A new App-driven self-help intervention to increase self-esteem in youth exposed to childhood adversity.

- I have read the information letter and I got the opportunity to ask questions. My questions have been sufficiently answered. I had plenty of time to decide whether I want to participate.
- I know that taking part in this study is voluntary. I also know that I can decide at any time not to participate or to stop participation in the study. I do not have to provide a reason to stop my participation.
- I give permission to inform my primary care provider that I am participating in this study.
- I give permission for the collection and usage of my data to answer the research question in this study.
- I know that some persons have access to my data. These persons are listed in this information letter. I give permission to these persons to access my data.
- I give permission to inform my general practitioner and/or treating specialist about unexpected findings that are (or may be) important for my health.
- I give permission to be contacted by email during the intervention period.
- I know that the study phone may only be used for the research purposes (access to the PsyMate app). I will not use the phone for any other purpose.

Please delete as appropriate for the following questions.

- I *do / do not** give permission to request information from my main practitioner about psychological distress in the past and the use of medication.
- I *do / do not** give permission to record the three SELFIE sessions with the psychologist with a voice recorder.
- I *do / do not** give permission to contact me after this study for a follow-up study.
- I *do / do not** give permission to store my personal data longer to use it for future research in the field of trauma, self-esteem, or to further develop the intervention or the app.

I want to participate in this research.

Name participant:

Signature:

Date : __ / __ / __

I declare that I have fully informed this participant about the study.

If information that could influence the subject's consent becomes apparent during the study, I will inform him/her in time.

Name researcher (or representative):

Signature:

Date: __ / __ / __

Additional information has been provided by:

Name:

Function:

Signature:

Date: __ / __ / __

* Delete as appropriate.

The participant receives a complete information letter, together with a copy of the signed consent form.



CHAPTER 7

General discussion

Purpose of this dissertation

The overall aim of this dissertation was to investigate and target self-esteem in daily life in individuals with mental health problems. Several cognitive models propose self-esteem to presumably be involved in the formation of mental health problems (1-4). The majority of mental disorders emerge before the age of 25, which might disrupt critical stages in the physical, social, emotional and cognitive development of an individual (5, 6). As mental disorders affect a substantial part of the world's population, and contribute to a substantial part of the global disease burden (7), it is crucial to investigate putative psychological mechanisms underlying mental disorders, and target these mechanisms with early interventions in youth, to prevent the development of mental disorders, such as depression, anxiety disorder, and psychosis, later in life.

At first, in order to establish whether self-esteem might be such a relevant mechanism to target in early interventions, we examined (fluctuations in) self-esteem as a putative underlying mechanisms in the intensity of psychotic experiences in daily life across the psychosis continuum (**Chapter 2**), and whether prior exposure to childhood trauma modified these associations (**Chapter 3**). Furthermore, we aimed to investigate how momentary self-esteem, on the one hand, and positive and negative affect, on the other, combine to increase the intensity of psychotic experiences in daily life, and vice versa (**Chapter 4**). In the second part of this thesis we aimed to validate several explicit, implicit and momentary self-esteem measures in youth exposed to childhood adversity (**Chapter 5**). Lastly, we sought to delineate the design of a novel, youth-friendly, transdiagnostic Ecological Momentary Intervention (EMI) for improving self-esteem in youth exposed to childhood adversity, called SELFIE (**Chapter 6**).

In this chapter, the main findings will be summarized, and their implications for scientific and clinical practice will be discussed. Additionally, several methodological considerations and directions for future research will be outlined and discussed.

Strengths and limitations

This thesis has several methodological strengths and limitations which will be discussed next. First, the strengths will be addressed. **Chapters 2, 3 and 4** mainly used the ESM to collect data. The results of **Chapter 5** showed that the ESM is an excellent research instrument to

investigate self-esteem, as it showed good convergent validity with other self-esteem measures, but also showed the best agreement with mental health outcomes. As the ESM assesses self-esteem, psychotic experiences and negative affect repeatedly in daily life, the method allows for generating intensive longitudinal data with high (ecological) validity and reliability with little recall bias due to the short time between the signal and the response (8-10). Furthermore, the ESM has been demonstrated to be a feasible, reliable and valid method in a wide variety of populations, for example in patients with mental disorders, but also in the general population (9, 11-16).

Another strength is that the effects of the EMI SELFIE (**Chapter 6**) are being evaluated in an RCT design, which is considered as 'the gold-standard' for investigating causal relationships (17). **Chapter 5** showed that explicit (RSES, SERS, positive- and negative-self schema scales of the BCSS) and momentary (measured with the ESM) self-esteem measures were complementary to each other. All these measures were used as primary and secondary outcome measures in **Chapter 6**.

As aforementioned, despite the strengths, there are also several limitations throughout the Chapters, that should be considered while interpreting the findings from these studies. In ESM research, it is a rule of thumb to analyze data of subjects that completed at least 33,3% of all the ESM assessments (18). This may have led to selection bias. We compared basic characteristics and illness duration and severity of subjects that were in- and excluded based on 33,3% completion of ESM assessments. Results showed that these groups were comparable to a great extent (except for ethnicity). However, we cannot compare individuals that refused to participate in the studies, as a result, we cannot rule out selection bias.

Second, in order to keep the assessment burden to a minimum, self-esteem (and paranoia) were assessed with few items. This might have led to limited construct validity (19). However, using less items per construct will indeed lead to less burden, and arguably better compliance. Additionally, the results from **Chapter 5** showed good psychometric properties for momentary self-esteem, measured with the ESM. However, this chapter also demonstrated that using multiple self-esteem measurement instruments, could give more comprehensive insights in the self-esteem construct. To be fair, the ESM items used in **Chapters 2, 3 and 4** only used two self-esteem items, while in **Chapter 5**, we used four items. However, a sub-analysis showed that that the convergent validity of momentary self-esteem in daily life measured with the two ESM items and trait self-esteem measured with the RSES was fair.

Last, in **Chapters 2,3 and 4** we investigated research questions regarding temporal priority of our data. Especially **Chapters 3 and 4** provided different results than expected, that is, we found no evidence that childhood trauma modified the temporal associations of self-esteem and psychotic disorder, and vice versa (**Chapter 3**). Furthermore, temporal results in **Chapter 4** only indicated that the effect of self-esteem on psychotic experiences was mediated by negative affect in patients and controls. All these assessments took place within 90-minute time blocks. However, the occurrence of psychosis might be preceded by weeks, months or even years of psychological and behavioral abnormalities (20). In addition, results from Jaya et al. (21) demonstrated that the interplay of self-esteem and negative affect influence each other and build up over the course of 4 to 8 months before they have an impact on psychotic symptoms. Therefore, it is possible that longer time lags would have yielded different results.

Self-esteem as psychological mechanism underlying psychotic experiences in daily life

Self-esteem might be an underlying mechanism in the intensity of psychotic experiences in daily life. In this regard, the results of the study in **Chapter 2** demonstrated that across the psychosis continuum (i.e., in patients with psychotic disorder, first-degree relatives of patients with psychotic disorder, and controls), lower levels of momentary self-esteem and greater variability in self-esteem were associated with an increased intensity of psychotic experiences, paranoia and negative affect in daily life. As some of the associations (e.g., between self-esteem and paranoia and negative affect) were greater in patients, whereas some other associations (e.g., between variability in self-esteem and psychotic experiences and paranoia) were greater in relatives, these findings suggest that variability in self-esteem might have a greater impact in shaping psychotic and paranoid experiences in individuals with an intermediate level of psychosis liability (relatives of patients with psychotic disorder).

Chapter 3 provided some more insight about the role of exposure to high vs. low levels of childhood trauma in the associations between self-esteem and psychotic experiences. There, we found that the association between lower levels of momentary self-esteem and an increased intensity of psychotic experiences in daily life was modified by prior exposure to high vs. low levels of several types of childhood trauma, i.e., physical (in relatives) and sexual (in relatives and controls, with the impact being stronger in relatives than in controls) abuse, and physical neglect (in patients) (**Chapter 3**). Exposure to high vs. low levels of emotional abuse and emotional neglect did not modify these associations.

The results of **Chapter 4** demonstrated that cross-sectionally, the effect of self-esteem on psychotic experiences was mediated by positive affect in patients, and by negative affect in all three groups. The effect of psychotic experiences on self-esteem was mediated by both positive and negative affect in all three groups. Temporal results only indicated that the effect of self-esteem on psychotic experiences was mediated by negative affect in patients and controls.

Taken together, these results suggest that self-esteem may be a putative important underlying psychological mechanism through which childhood trauma may impact on the intensity of psychotic experiences in daily life in individuals across the psychosis continuum. Individuals with familial liability to psychosis (patients and their first-degree relatives), but also from the general population, might benefit from targeting momentary self-esteem and variability in self-esteem to decrease the intensity of psychotic experiences, paranoia and negative affect in daily life.

As symptoms are transdiagnostic in the early stages, often during adolescence (22), and result in a wide range of mental disorder later in life (23), early interventions in youth mental health have become of great importance. Therefore, the focus has been shifting from specific interventions for specific disorders, to early interventions across the full diagnostic spectrum (24).

Targeting self-esteem with Momentary Ecological Interventions

Although youth aged between 12 – 25 years have the highest incidence and prevalence of mental health problems across the lifespan, their access to mental health care is the poorest compared to all other age groups (25). Therefore, novel, youth-friendly approaches are of great importance. Ecological momentary interventions (EMIs), a form of Mobile Health (mHealth), provide a unique opportunity to deliver youth-friendly, personalized, real-time interventions. By delivering the intervention components in daily life, they are more easily translated to, and accepted in, diverse contexts of daily life (26). As demonstrated in **Chapters 2, 3 and 4**, and in previous literature (27, 28), self-esteem has been shown to be an important putative transdiagnostic mechanism in pathways from childhood adversity to adult psychopathology, which makes self-esteem a promising target for early interventions.

We therefore developed an accessible, transdiagnostic EMI for improving self-esteem ('SELFIE') in youth with prior exposure to childhood adversity, for which the protocol is

described in **Chapter 6**. The efficacy of the intervention is being evaluated at the moment, using a randomized controlled trial (RCT) design. The guided self-help EMI SELFIE is administered through a smartphone-based App over a 6-week period, and is accompanied by three face-to-face and three e-mail sessions by a trained SELFIE-therapist. SELFIE aims to modify cognitive bias inherent to negative self-esteem and to develop and practice a new behavioural repertoire. Hence, the key goal is to deliver the intervention in individuals' daily lives, and enable youth to benefit from this intervention in a given moment and context, when most needed (e.g. in moments of low self-esteem).

EMIs have been demonstrated to be effective for multiple mental health conditions, such as anxiety, bipolar disorder, substance use and depression (29). Based on existing literature (27, 28), and **Chapters 2, 3 and 4**, we expect that (assuming the SELFIE intervention proves to be effective) this EMI may help to minimize the deleterious impact of, and hence, resilience to, childhood adversity by improving self-esteem, which in turn prevents the development of severe and enduring mental disorder later in life and reduce disease burden.

Measuring self-esteem

To measure self-esteem, we used the experience sampling method (ESM) in **Chapters 2, 3 and 4**. The ESM is a diary technique to repeatedly assess thoughts, feelings and behaviour, in order to capture the natural occurrence of moment-to-moment variation in daily life (12). Also other research instruments are available to assess different types of self-esteem. In **Chapter 5**, we sought to evaluate the reliability and validity of explicit (Rosenberg Self-esteem Scale (RSES) (30), Self-Esteem Rating Scale (SERS) (31, 32), and Brief Core Schema Scales (BCSS) (33)), implicit (Implicit Association Test (IAT) (34, 35)) and momentary (measured with the ESM (12)) self-esteem measures within a sample of youth, aged between 12 and 26 years, exposed to childhood adversity.

Results showed that the reliability of all self-esteem measures (including positive and negative subscales) ranged between questionable and excellent, and indicated good convergent validity between RSES, SERS, the BCSS positive- and negative-self schema scales, and ESM momentary self-esteem. On the other hand, the IAT was not strongly correlated with the other self-esteem measures. We found evidence for good concurrent validity between all the self-esteem measures, except for the IAT, and momentary negative effect, and between the SERS, the BCSS negative-other schema scale, and the ESM self-esteem scores, and psychotic

experiences. The magnitude of the correlations suggest that the measures are overlapping, but able to capture other nuances and aspects of the self-esteem construct, which indicates that they are complementary to each other. Our results also demonstrated that the ESM has the best amount of agreement with mental health outcomes in daily life (psychotic experiences and negative affect) compared to the other measures. Therefore, it would be recommended to assess self-esteem with multiple measures. However, if that is not feasible, we would recommend the ESM. One disadvantage of the ESM, though, is that it is perceived as demanding and time-consuming (13). Given the amount of agreement of the SERS with mental health outcomes, it would be our second recommendation to assess self-esteem in a sample of youth aged between 12 and 25 years.

The role of ESM and EMI's in future research and clinical practice

ESM

In the past decades, the body of ESM research in psychiatry has been expanding rapidly (36). Most common is to measure positive and negative affect, stress and symptoms, such as psychotic or depressive symptoms, using the ESM (13, 37-39), which is also used in clinical practice. For example, using the ESM for intensive sampling of emotions and context, enables mental health care professionals and patients to enhance resilience (40), to predict and prevent new episodes of depression or psychosis by reacting to rising symptoms (41), or to pick up on early effects of starting or stopping medication, or changing medication (42, 43). Our results indicated that self-esteem might also be an important mechanism to investigate using the ESM. As there is evidence for a transdiagnostic connection between self-esteem and psychopathology (44), self-esteem might also be an important mechanism to research with the ESM. **Chapter 5** has shown that the ESM has great potential to measure self-esteem in future research, as it not only had good concurrent validity with other self-esteem measurement instruments, but also had a great amount of agreement with mental health outcomes, such as negative affect and psychotic experiences. **Chapters 2, 3 and 4** suggested that the intensity of psychotic experiences might potentially be reduced by improving self-esteem.

Furthermore, for the first part of this thesis (**Chapters 2, 3, and 4**), recommendations could be to replicate the findings, and extend them not only using longer time lags, but also using

multiple items to measure both the positive and negative subscales of momentary self-esteem. Using four items in **Chapter 5** showed better internal consistencies for ESM self-esteem, compared to two items that were used in **Chapter 2**. Next to that, it would also be interesting to triangulate momentary ESM measures with explicit and implicit measures of self-esteem to corroborate our findings. This is in line with **Chapter 5**, indicating that several research instruments measuring self-esteem are complementary to each other.

EMI

The recent advances in information and communication technologies have led to the development of mobile Health (mHealth) interventions and, most prominently, ecological momentary interventions (EMIs) (9, 26, 45-47). EMIs extend beyond or even outside the clinical setting (9, 26), and have been proven to be useful in the treatment of numerous health-related areas, such as smoking, diabetes, weight loss, or asthma (48). Although in its relative infancy, EMIs are also proven to be feasible and effective in psychiatry. Some examples of EMIs are depressed outpatients receiving personalized feedback from mood profiles using the ESM (49), support in coping and illness management to individuals with schizophrenia (FOCUS (50)), personalized self-monitoring of early warning signs and symptoms in patients with bipolar disorder (PRISM (51)), training of psychological skills acceptance and commitment therapy (ACT) in daily life in individuals with Ultra-High Risk for Psychosis (UHR) or a first-episode of psychosis (FEP) (ACT-DL (52)), and improving resilience in youth with current distress (EMICOMPAS (53)). To our knowledge, the SELFIE Intervention (**Chapter 6**) is the first transdiagnostic EMI that focuses on improving self-esteem in youth exposed to childhood adversity. The future results of the SELFIE study will inform our understanding of self-esteem as a psychological mechanism as well as the growing knowledge of mHealth intervention development and implementation, in particular for EMIs. If the SELFIE-intervention proves to be effective, it will be of importance to further investigate which of the intervention components were most effective, in order to potentially adjust and improve the intervention. Additionally, the cost effectiveness and cost utility will inform implementation, and the process evaluation on acceptability, treatment adherence, and treatment fidelity will provide important data on potential barriers, but also on potential facilitators for implementation.

Concluding remarks

Prevention and treatment in mental health care are crucial in order to reduce the burden of mental disorders. The results of this thesis indicated that self-esteem might be an important psychological mechanism to target in early interventions. The EMI SELFIE has the potential to contribute to minimizing the deleterious impact of childhood adversity and, thereby, preventing the development of mental disorder later in life, and reduce burden on the healthcare system.

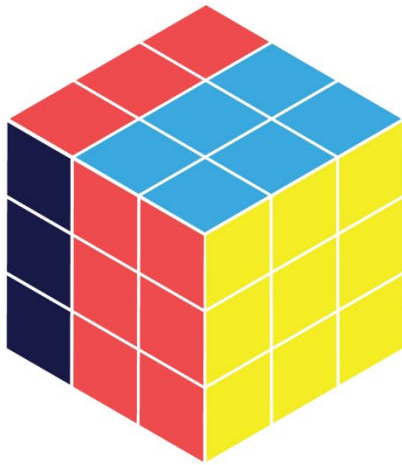
Results also provided recommendations for future research and for clinical practice concerning the use of self-esteem measurement instruments in transdiagnostic youth exposed to childhood trauma, based on the investigated psychometric properties of the measures and on their amount of agreement with several mental health outcomes.

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ADDENDUM

Impact paragraph

Summary

Samenvatting

About the author

Publications and presentations

Dankwoord

Impact paragraph

The aim of this thesis was to investigate and target self-esteem in daily life within individuals with mental health problems. This paragraph reflects on how the obtained knowledge from this thesis is valuable for (future) scientific, clinical and societal use.

Key findings

The burden of having mental disorders is high. In order to reduce the impact of mental disorders on the individual and society, it is crucial to target modifiable psychological mechanisms that underlie these disorders in prevention and early intervention strategies. This might possibly even prevent the development of mental disorders later in life.

One of the aims of this thesis was to investigate whether self-esteem in daily life, i.e., momentary self-esteem, might be one of these psychological mechanisms that underlie mental disorders, such as psychosis, as a potential target by early interventions. We found that lower levels of momentary self-esteem and greater variability in self-esteem were associated with an increased intensity of psychotic experiences and paranoia in patients with psychotic disorder, first-degree relatives of patients with psychotic disorder, and controls. In patients and relatives, lower levels of self-esteem were also associated with increased intensity of negative affect. The magnitudes of these associations were greater in patients and first-degree relatives compared to controls. Moreover, we found that the association between lower levels of momentary self-esteem and an increased intensity of psychotic experiences in daily life was modified by prior exposure to high vs. low levels of several types of childhood trauma, i.e. physical (in relatives) and sexual (in relatives and controls) abuse, and physical neglect (in patients). Additionally, we found that the effects of momentary self-esteem on psychotic experiences, and vice versa, were mediated by positive and negative effect.

These results demonstrate that self-esteem might be an important underlying psychological mechanism through which childhood trauma may impact on the intensity of psychotic experiences in daily life in individuals across the psychosis continuum. Individuals with familial liability to psychosis (patients and their first-degree relatives), but also from the general population, might benefit from targeting momentary self-esteem and variability in self-

esteem to decrease the intensity of psychotic experiences, paranoia and negative affect in daily life.

As there is accumulating evidence that symptoms of psychopathology are transdiagnostic in the early stages (1), and might result in a wide range of mental disorder later in life (2), early interventions in youth mental health have become of great importance. Recently, the focus has been shifting from specific interventions for specific disorders, to early interventions across the full diagnostic spectrum (3).

Psychological help is difficult to access and accept for youth, which calls for novel, youth-friendly approaches (4). Mobile Health (mHealth) and, most prominently, ecological momentary interventions (EMIs) provide a unique opportunity to deliver youth-friendly, personalized, real-time, guided self-help interventions. We therefore developed an accessible, transdiagnostic ecological momentary intervention for improving self-esteem ('SELFIE') in youth with prior exposure to childhood adversity, for which the protocol is described in this thesis.

Last, we validated several self-esteem measurement instruments in youth exposed to childhood adversity, which provided implications for future research and for clinical use.

Relevance

Mental disorders, such as depression, anxiety disorders, and psychosis, affect more than a billion people worldwide, account for about 7 percent of all global disease burden (5), and are responsible for about 20 percent of all years lived with disability (5). About half of the general population will develop at least one mental health disorder across their lifespan (6). Moreover, mental disorders are associated with unemployment, absence due to sickness, and loss of productivity, which leads to an high economic burden (7). Additionally, mental disorders are not only disabling for patients themselves, but can also take a tremendous toll on family members.

Prevention and treatment in mental health care are crucial in order to reduce the burden of mental disorders. Chapters 2, 3 and 4 have demonstrated that momentary self-esteem may be an important underlying mechanism that may impact on the intensity of mental health problems such as negative affect and psychotic experiences, and that associations of momentary self-esteem and more intense psychotic experiences were modified by exposure to high vs. low levels of several types of childhood trauma. The SELFIE intervention, which we

have developed, is currently being evaluated (Chapter 6). The SELFIE study is a large randomized controlled trial, in which 174 individuals aged between 12 and 26 years with prior exposure to childhood adversity and low self-esteem are allocated to the experimental condition (SELFIE in addition to treatment as usual) or the control condition (treatment as usual). SELFIE is a guided self-help intervention administered through a smartphone-based App to allow for interactive, personalized, real-time and real-world transfer of intervention components in individuals' daily lives. The digital intervention is blended with three training sessions delivered by trained mental health professionals over a 6-week period. If this trial provides evidence on the efficacy of SELFIE, it has significant potential to contribute to minimizing the deleterious impact of childhood adversity in youth and, thereby, preventing the development of mental disorder later in life.

Additionally, in chapter 5 we investigated psychometric properties of different types of self-esteem measurement instruments, and their predictive value of mental health outcomes in youth exposed to childhood adversity. This knowledge is of high relevance from both a clinical as a scientific point of view, as we could make recommendations on which research instruments showed good and poor psychometric properties, and might or might not be appropriate to use for this particular target group. We also investigated to what extent these questionnaires can predict mental health outcomes, such as negative affect and psychotic experiences, which make the results both clinically and scientifically highly relevant.

Target Audience

The results of this thesis are relevant for several target groups. First, not only mental health care professionals, but also individuals who are at risk for, or currently dealing with, mental health problems, might benefit from the increased insight of the role of momentary self-esteem in the intensity of psychotic experiences (and negative affect) in individuals exposed to childhood trauma. As symptoms of psychopathology are transdiagnostic in the early stages, and youth is a critical period for self-esteem development (8), targeting self-esteem in mental health care in youth exposed to childhood trauma seems a logical inference. If the randomized controlled trial will prove the efficacy of the SELFIE intervention, we can provide a novel youth-friendly, easy accessible, ecological momentary intervention that is easy implementable within mental health care, but also in earlier stages, for example via schools or GP practices. By building a competing positive self-esteem, we might minimize the

deleterious impact of childhood adversity, which might reduce burden on the healthcare system by reducing waiting lists.

Second, the general public might benefit from the results of this thesis, as self-esteem is not only relevant for mental health, but also to well-being in general. High levels of self-esteem is related to greater life satisfaction, more happiness and positive affect, and to more subjective vitality (9). Our results showed that low levels of momentary self-esteem and greater variability in self-esteem were associated with more intense psychotic experiences and paranoia, not only in patients with psychotic disorder and their first degree relatives, but also in controls. As more than 45% of the children in Dutch elementary schools reported to have been exposed to an adverse childhood experience (10), it might be useful to raise more awareness in the general population about the role of self-esteem in mental health issues.

Third, the results might be of great interest to insurance companies and policy makers. Mental health problems are associated with great direct (e.g. medication, clinic visits, or hospitalization), and indirect (productivity loss, unemployment) costs (11). When policy makers involved in mental health care regulations invest in early prevention and intervention strategies focused on targeting self-esteem, for example, like the youth-friendly and easy accessible SELFIE intervention, this might possibly prevent the development of mental disorders later in life, and, thus, contribute to a decrease in direct and indirect costs that are associated with mental health problems, and to better mental health within the population. For the SELFIE intervention, this will be elaborated by conducting a cost-benefit analysis.

Last, the findings of this thesis have led to implications and recommendations for researchers. For example, we validated several self-esteem measures in youth exposed to childhood adversity. We examined psychometric properties, and provided information on the value of these questionnaires and showed that several measures are complementary to each other. Next to that, some of the chapters also raised new questions, which could be implemented as research questions in future research. Also some of our findings might be replicated and extended.

Activity

Although we already took some steps in involving and informing the target audience for our research, there are still plans for future dissemination of the achieved knowledge by this thesis.

Participants of the SELFIE study and involved mental health centres were and will be updated by annual newsletters, and by social media updates. Moreover, a Dutch role-model, known for her acting roles in youth television series, is an ambassador for the SELFIE study, resulting in her doing several podcasts on mental health and the SELFIE study, and regularly posting our research updates to her 27.5k social media followers. Items on SELFIE were published in local free available magazines, such as 'Hecht' (magazine for all employees of Maastricht University Medical Centre (MUMC)), 'Gezond Idee' (magazine from the MUMC that is delivered to all home addresses in South-Limburg), 'Observant' (independent university magazine of Maastricht University), and 'FOLIA' (independent medium of the University of Amsterdam).

Furthermore, we presented our work at collaborating mental health care institutions, and during centre specific symposia (for example 'Mondriaan Referaat' in 2019, and 'Koraal Onderzoekt' in 2020) throughout the Netherlands. We also presented our work, including a workshop on the SELFIE intervention, to mental health care professionals, experiential experts, and other professionals, at the annual conference for child- and adolescence psychiatry (Jaarcongres Kinder- en Jeugdpsychiatrie) in 2019, and the Spring conference (Voorjaarscongres) organized by the Nederlandse Vereniging voor Psychiatrie (NVvP) in 2020, which enabled us to have discussions with professionals on how to implement the results into clinical practice. Interdisciplinary collaborations, for example with mental health services, will also contribute to the circulation, and perhaps implementation of the achieved knowledge.

To reach the scientific research community, Chapters 2, 3, 4, 5, and 6 were or will be shared via (open access) scientific publications in peer-reviewed journals. Results of the thesis were (and will be) presented at several national and international scientific congresses and symposia (for example, at the International Association of Youth Mental Health (IAYMH) in 2019, Brisbane (Australia), the Society of Ambulatory Assessment (SAA) in 2019, Syracuse, New York (USA), the SAA in 2021, Zurich (Switzerland, online), and the European Society for child and Adolescent Psychiatry (ESCAP), Vienna (Austria)).

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Summary

The overall aim of this thesis was to investigate and target self-esteem in daily life in individuals with mental health problems. At first, in order to lay a theoretical background, we investigated the role of (fluctuations in) self-esteem, childhood trauma and negative affect in the pathways to psychotic experiences in daily life. In **Chapter 2**, we applied the Experience Sampling Method (ESM), a diary technique that can be used to assess thoughts, mood, self-esteem, and context in daily life to investigate the association between momentary self-esteem and its fluctuations (instability and variability) on the one hand, and psychotic experiences, paranoia, negative symptoms, and negative affect and on the other. These associations were investigated across the psychosis continuum (the general population, who might experience some (minor) psychotic-like symptoms in daily life, on the one end of the continuum, patients with a psychotic disorder, on the other end, and relatives of patients with psychotic disorder, who have a familial liability for psychotic disorder, in between). Results showed that lower levels of momentary self-esteem and greater variability in self-esteem were associated with an increased intensity of psychotic experiences, paranoia and negative affect in daily life. Moreover, the findings suggested that variability in self-esteem might have a greater impact in shaping psychotic and paranoid experiences in individuals with an intermediate level of psychosis liability (relatives of patients with psychotic disorder).

Next, **Chapter 3** investigated the role of exposure to high vs. low levels of childhood trauma in the associations between self-esteem and psychotic experiences across the psychosis continuum, using the ESM. Results indicated that the association between lower levels of momentary self-esteem and an increased intensity of psychotic experiences in daily life was modified by prior exposure to different (high vs. low) levels of several types of childhood trauma, i.e., physical (in relatives) and sexual (in relatives and controls, with the impact being stronger in relatives than in controls) abuse, and physical neglect (in patients). However, results of this chapter did not provide enough evidence to support that these associations of interest were modified by exposure to different levels of emotional abuse and emotional neglect did not modify these associations.

In **Chapter 4**, the results of another ESM study demonstrated that the effect of self-esteem on psychotic experiences was mediated by positive affect in patients, and by negative affect in all three groups (i.e., patients with psychotic disorder, first-degree relatives and controls). Furthermore, the effect of psychotic experiences on self-esteem was mediated by both positive and negative affect in all three groups. Looking further at longitudinal effects, results indicated that only the effect of self-esteem at a previous time point on psychotic experiences at the current time point was mediated by negative affect in patients and controls.

To sum up, **Chapters 2, 3 and 4** laid a theoretical background, and suggested that self-esteem might be an important underlying psychological mechanism through which childhood trauma may have an impact on the intensity of psychotic experiences in daily life in individuals across the psychosis continuum. As a result, Individuals with familial liability to psychosis (patients and their first-degree relatives), as well as individuals from the general population, may gain a benefit from targeting momentary self-esteem and variability in self-esteem to decrease the intensity of psychotic experiences, paranoia and negative affect in daily life.

As more research on self-esteem is needed, it is also important to investigate the reliability (the internal consistency of different items in a measure), convergent validity (the amount of agreement between different self-esteem measures) and concurrent validity (predictive value for mental health outcomes) of several self-esteem research instruments that measure self-esteem. **Chapter 5**, therefore, presented an evaluation of the reliability and validity of the Rosenberg Self-esteem Scale (RSES), Self-Esteem Rating Scale (SERS), Brief Core Schema Scales (BCSS), Implicit Association Test (IAT) and momentary self-esteem (measured with the ESM), within a sample of youth, aged between 12 and 26 years, exposed to childhood adversity. Results demonstrated that the reliability of all self-esteem measures ranged between questionable and excellent, and indicated good convergent validity between all measures, except for the IAT, which was not strongly correlated with the other self-esteem measures. We found evidence for good concurrent validity between all the self-esteem measures (except for the IAT) and momentary negative affect, and between several of the self-esteem measures and psychotic experiences. Although the magnitude of the correlations suggest that the measures are overlapping, they are able to capture other nuances and

aspects of the self-esteem construct, which indicates that they are complementary to each other.

Symptoms of mental health disorders are transdiagnostic in the early stages. Moreover, the age between 12 and 25 is not only a crucial time point in life for physical, social, emotional and cognitive development, it is also the age in which the majority of mental disorders emerge. In sum, it is of great importance to develop, test and implement easy accessible and youth-friendly prevention and intervention strategies focusing on improving self-esteem in youth exposed to childhood trauma in order to prevent mental health problems later in life.

Due to recent rapid technological developments, new opportunities have emerged to extend interventions beyond the clinical setting into individuals' daily life. These interventions are also referred to as Ecological Momentary Interventions (EMIs). In this context, **Chapter 6** described the study design of a randomized controlled trial to evaluate an accessible, transdiagnostic daily life EMI for improving self-esteem ('SELFIE') in youth with prior exposure to childhood adversity. The efficacy of the intervention is being evaluated at the moment. The guided self-help EMI SELFIE is administered through a smartphone-based App over a 6-week period, and is accompanied by three face-to-face and three e-mail sessions by a trained SELFIE-therapist. SELFIE aims to modify cognitive bias inherent to negative self-esteem and to develop and practice a new behavioural repertoire. Hence, the key goal is to deliver the intervention in individuals' daily lives, and enable youth to benefit from this intervention in a given moment and context, when most needed (e.g. in moments of low self-esteem).

Overall, this thesis demonstrated that self-esteem might be an important psychological mechanism to target in early interventions. It also provided a protocol for an EMI focused on improving self-esteem in youth exposed to childhood trauma. Finally, **Chapter 7** presents a discussion of the main findings, strengths and limitations and implications for future research and clinical practice.

Samenvatting

Het overkoepelende doel van dit proefschrift was het onderzoeken en verbeteren van het zelfbeeld in het dagelijks leven bij personen met psychische problemen. Om een theoretische achtergrond te schetsen onderzochten we eerst de rol van het meemaken van ingrijpende gebeurtenissen in de kindertijd, (veranderingen in) zelfbeeld en negatief affect in het ontstaan van psychotische ervaringen in het dagelijks leven. De Experience Sampling Methode (ESM) is een gestructureerde dagboektechniek die wordt gebruikt om gedachten, stemming, zelfbeeld en context in het dagelijks leven te meten. In **Hoofdstuk 2** is de ESM toegepast om het verband te onderzoeken tussen (instabiliteit en variabiliteit van) zelfbeeld en psychotische ervaringen. Deze verbanden werden onderzocht over het hele psychosecontinuüm. Aan het ene uiteinde van het continuüm bevindt zich de algemene bevolking, ook wel controles genoemd. Deze controles kunnen in het dagelijks leven enkele (lichte) psychotisch-achtige symptomen ervaren. Aan het andere uiteinde bevinden patiënten met een psychotische stoornis. Daartussenin bevinden zich directe familieleden van patiënten met een psychotische stoornis. Zij hebben een familiair risico op het ontwikkelen van psychotische stoornissen). De resultaten toonden aan dat zowel een laag zelfbeeld als een grotere variabiliteit in het zelfbeeld geassocieerd waren met een verhoogde intensiteit van psychotische ervaringen in het dagelijks leven. Bovendien suggereerde de resultaten dat variabiliteit in zelfbeeld van grote invloed zou kunnen zijn op het ontstaan van psychotische en paranoïde ervaringen bij personen met een verhoogd risico op het ontwikkelen van psychotische stoornissen (familieleden van patiënten met een psychotische stoornis).

Vervolgens onderzochten we in **Hoofdstuk 3** met behulp van de ESM de associaties tussen zelfbeeld en psychotische ervaringen binnen het psychosecontinuüm. Hierbij keken we of een lage ten opzichte van een hoge mate van blootstelling aan trauma in de kindertijd invloed had op deze associaties. De resultaten gaven aan dat het verband tussen een laag zelfbeeld en een verhoogde intensiteit van psychotische ervaringen in het dagelijks leven werd beïnvloed door blootstelling aan een hoge ten opzichte van een lage mate van fysiek misbruik (bij familieleden), seksueel misbruik (bij familieleden en controles), en fysieke verwaarlozing (bij

patiënten). De resultaten van dit hoofdstuk leverden echter onvoldoende bewijs om te stellen dat deze associaties werden beïnvloed door blootstelling aan verschillende mate van emotioneel misbruik en emotionele verwaarlozing.

De resultaten in **Hoofdstuk 4** laten zien dat het effect van zelfbeeld op psychotische ervaringen gemedieerd werd door positief affect bij patiënten, en door negatief affect in alle drie de groepen (patiënten, familieleden en controles). Bovendien werd het effect van psychotische ervaringen op zelfbeeld gemedieerd door zowel positief als negatief affect in alle drie de groepen. Kijkende naar de longitudinale effecten, dan lieten de resultaten zien dat het effect van zelfbeeld op een eerder moment op psychotische ervaringen op een later moment werd gemodificeerd door negatief affect bij patiënten en controles.

Samengevat boden **Hoofdstukken 2, 3 en 4** een theoretische achtergrond en de resultaten impliceerden dat zelfbeeld een belangrijk onderliggend psychologisch mechanisme kan zijn dat in combinatie met het meemaken van trauma's in de kindertijd, invloed kan hebben op de intensiteit van psychotische ervaringen in het dagelijks leven bij individuen over het hele psychosecontinuüm. Dit houdt in dat personen met een familiale aanleg voor psychose (d.w.z. patiënten met een psychotische stoornis en hun directe familieleden), evenals personen uit de algemene bevolking, baat kunnen hebben bij het verbeteren van hun zelfbeeld om zo de intensiteit van psychotische ervaringen en negatief affect in het dagelijks leven te verminderen.

Aangezien er meer onderzoek naar zelfbeeld nodig is, is het ook belangrijk om de betrouwbaarheid (de interne consistentie van verschillende items in een meetinstrument), de convergente validiteit (de mate van overeenstemming tussen verschillende zelfbeeld meetinstrumenten) en de concurrent validiteit (de mate van samenhang met psychische gezondheidsuitkomsten) te onderzoeken van verschillende meetinstrumenten die zelfbeeld meten. **Hoofdstuk 5** bevat daarom een evaluatie van de betrouwbaarheid en validiteit van de Rosenberg Self-esteem Scale (RSES), Self-Esteem Rating Scale (SERS), Brief Core Schema Scales (BCSS), Implicit Association Test (IAT), en zelfbeeld in het dagelijks leven (gemeten met de ESM), bij jongeren tussen de 12 en 26 jaar die zijn blootgesteld aan een of meerdere

ingrijpende gebeurtenissen in de kindertijd. De resultaten toonden aan dat de betrouwbaarheid van alle zelfbeeld meetinstrumenten varieerde tussen twijfelachtig en uitstekend. Verder vonden we goede convergente validiteit tussen alle maten, behalve de IAT. Deze was niet sterk gecorreleerd met de andere meetinstrumenten. Daarnaast vonden we bewijs voor een goede concurrent validiteit tussen alle zelfbeeld meetinstrumenten (behalve de IAT) en negatief affect, en tussen verschillende van de meetinstrumenten en psychotische ervaringen. Hoewel de sterkte van de correlaties suggereerde dat de zelfbeeld meetinstrumenten elkaar overlappen, zijn ze in staat om andere nuances en aspecten van zelfbeeld te meten, wat aangeeft dat de meetinstrumenten complementair aan elkaar zijn.

In het vroege stadium van veel mentale stoornissen zijn symptomen transdiagnostisch. Daarnaast is de leeftijd tussen 12 en 25 jaar niet alleen een belangrijk moment in het leven voor de lichamelijke, sociale, emotionele en cognitieve ontwikkeling, het is ook de leeftijd waarop de meeste psychische stoornissen ontstaan. Kortom, om geestelijke gezondheidsproblematiek op latere leeftijd te voorkomen, is het van groot belang om laagdrempelige en jeugd vriendelijke preventie- en interventie strategieën die gericht zijn op het verbeteren van het zelfbeeld bij jongeren die ingrijpende gebeurtenissen hebben meegemaakt in de kindertijd te ontwikkelen, te testen en te implementeren.

Door recente snelle technologische ontwikkelingen zijn er nieuwe mogelijkheden om interventies buiten de klinische setting uit te breiden naar het dagelijks leven. Deze interventies worden ook wel *Ecological Momentary Interventions* (EMIs) genoemd. In deze context beschrijft **Hoofdstuk 6** de opzet van een gerandomiseerde studie naar een toegankelijke transdiagnostische EMI ter bevordering van het zelfbeeld (SELFIE) bij jongeren die zijn blootgesteld aan ingrijpende gebeurtenissen in de kindertijd. De effectiviteit van deze interventie wordt op dit moment nog geëvalueerd. De begeleide zelfhulp interventie SELFIE wordt aangeboden via een smartphone-gebaseerde app gedurende een periode van zes weken, en wordt begeleid dooreen getrainde SELFIE-therapeut. Het belangrijkste doel van SELFIE is om de interventie toe te passen in het dagelijks leven van jongeren, zodat zij het geleerde kunnen toepassen op momenten en in contexten waar dat het meest nodig is (bijv. op momenten dat ze een laag zelfbeeld ervaren).

Samenvattend toont dit proefschrift aan dat zelfbeeld een belangrijk psychologisch mechanisme kan zijn om aan te pakken in interventies in een vroeg stadium. Een voorbeeld van een interventie die het zelfbeeld verbetert bij jongeren die zijn blootgesteld aan ingrijpende levensgebeurtenissen, is de EMI SELFIE, waarvoor het protocol in dit proefschrift staat beschreven. Ten slotte presenteert **Hoofdstuk 7** een discussie van de belangrijkste bevindingen, sterke punten en beperkingen en implicaties voor toekomstig onderzoek en voor de klinische praktijk.

About the author



Maud Daemen was born on May 21, 1990 in Stein, the Netherlands, where she grew up until she moved to Sittard at the age of 11. After completing her pre-vocational secondary education (VMBO) she continued with a post-vocational secondary education (MBO) programme Social Pedagogic Work, with a specialization as teaching assistant. She did several internships in special education for children with behavioural problems. After completion, Maud then obtained her propaedeutic certificate for the higher vocational education programme Pedagogy. Following on that, she started her bachelor studies in Health Sciences at Maastricht University with a major in mental health. Next to mental health, she also had a great interest in criminology, and therefore Maud decided to do a minor in (criminal) law, and furthermore wrote her bachelor's thesis on the reliability of autistic eyewitness statements. Subsequently, she obtained a Master of Laws degree by completing the master Forensics, Criminology and Law at Maastricht University and a Master of Science degree by completing the master Criminology at VU Amsterdam. During the master at Maastricht University she also participated in a Cold Case project, a collaboration between Team Cold Case Police Limburg, the Limburg Public Prosecution Service and Maastricht University. After completing both masters, she started her PhD project at Maastricht University, under the supervision of Prof. dr. Therese van Amelsvoort and Prof. dr. Ulrich Reininghaus. During her PhD, Maud has also been a visiting scientist at the Central Institute of Mental Health in Mannheim, which is part of Heidelberg University. Currently, Maud is transitioning into the role of research coordinator at the Department of Psychiatry and Neuropsychology.

Publications and presentations

International publications in peer-reviewed journals

Daemen, M., Postma, M.R., Lindauer, R., Hoes-van der Meulen, I., Nieman, D., Delespaul, P., Breedvelt, J.J.F., van der Gaag, M., Viechtbauer, W., Schruers, K., van den Berg, D., Bockting, C., van Amelsvoort, T., & Reininghaus, U. (2021). Efficacy of a transdiagnostic ecological momentary intervention for improving self-esteem (SELFIE) in youth exposed to childhood adversity: study protocol for a multi-center randomized controlled trial. *Trials*, 22(1):641.

Daemen, M., van Amelsvoort, T., GROUP investigators, & Reininghaus, U. (2022). Self-esteem and psychosis in daily life: An experience sampling study. *Journal of Psychopathology and Clinical Science (Formerly Journal of Abnormal Psychology)*, 131 (2), 182-197.

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Daemen, M., van Amelsvoort, T., GROUP investigators & Reininghaus, U. Momentary self-esteem as a putative mechanism underlying the association between childhood trauma and psychosis: an experience sampling study (*submitted*).

Daemen, M., van Amelsvoort, T., Pijpers, E., Volbragt, N., Postma, M.R., Lindauer, R., Nieman, D., Delespaul, P., Breedvelt, J.J.F., van der Gaag, M., Schruers, K., van den Berg, D., Bockting, C. & Reininghaus, U. Convergent and concurrent validity of explicit, implicit and momentary self-esteem measurement instruments (*in preparation*).

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Other publications

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Scientific communications related to this thesis

- 2021 Oral presentation. 7th Annual Conference of the Society of Ambulatory Assessment (Zurich, Zwitserland, online)
- 2020 Poster presentation. eVoorjaarscongres Nederlandse Vereniging voor Psychiatrie (NVvP) (The Netherlands, online).
- 2020 Oral presentation. Koraal Onderzoekt (The Netherlands, online)
- 2019 Poster presentation. 4th Annual Belgian-Dutch Experience Sampling Method Expert Network Meeting (Tilburg, The Netherlands)
- 2019 Oral presentation. Mondriaan Referaat (Heerlen, The Netherlands)
- 2019 Oral presentation (workshop). Jaarcongres Kinder- & Jeugdpsychiatrie (Bussum, The Netherlands)
- 2019 Oral presentation. 6th Annual Conference of the Society of Ambulatory Assessment (Syracuse, USA)
- 2019 Oral presentation. Brain Awareness Week, MUMC+ (Maastricht, The Netherlands)
- 2018 Oral presentation. 3th Annual Belgian-Dutch Experience Sampling Method Expert Network Meeting (Heerlen, The Netherlands)

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