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Psychotic symptoms in ambulatory assessment and longitudinal studies: Development of state measures and evaluation of stress-related predictors

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“An important question in psychiatry
shouldn't be ‘what's wrong with you’,
but rather ‘what’s happened to you’.”

(Eleanor Longden)

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Abstract

Vulnerability stress models of psychotic disorders postulate that in predisposed individuals, a stressor triggers hyperarousal and subsequently psychotic symptoms such as paranoia and auditory hallucinations. In line with this, lab studies found that experimentally inducing a stressful condition leads to the emergence of symptoms in patients as well as phenomenologically equivalent psychotic experiences in general population samples. Recent developments in mobile technology furthermore allowed for conducting ambulatory assessment studies, in which the time-order and association between stressors, stress and psychotic experiences and symptoms can be captured in real-time as it appears under real life conditions. The majority of these ambulatory assessment studies focused on clinical samples with acute symptoms and used non-validated assessments to measure symptoms.

The aim of this dissertation project was to develop and validate assessment procedures for psychotic experiences and symptoms such as paranoia and auditory hallucinations that can be applied in clinical and subclinical samples (studies 1-3). A second aim was to utilize the validated measures in longitudinal and ambulatory assessment studies in order to explore the role of stress in etiologically early stages of subclinical psychotic experience formation (studies 4 and 5) as well as the role of coping with stressful situations in symptomatic improvement over the course of therapy (study 6).

The assessment development and validation studies corroborated existing results for the German version of trait-level measure of psychotic symptoms (study 1) and yielded reliable, valid, and change-sensitive state assessments for paranoia (study 2) and hallucination spectrum experiences (i.e., auditory hallucinations and their subclinical precursors, study 3). Despite the fact that full validation in clinical samples is pending, these state assessments constitute valuable tools in future ambulatory assessment studies to ensure psychometric quality. A first general population study on self-reported and physiological stress over the course momentary psychotic experience showed a stress response prior to and during momentary episodes of paranoia, but no consistent findings regarding hallucination spectrum experiences (study 4). A second study found emergence of hallucination spectrum experiences to be predicted by prior social stress due to experiencing social exclusion (study 5). Finally, continuous improvement in coping was found to predict continuous improvement of depression, negative symptoms, and some positive symptoms in patients with psychosis over course of therapy (study 6). In sum, this project contributes to

the understanding of the working mechanism in early etiology and treatment of psychotic disorders that warrants further research on the complete dynamics of stress, resilience and vulnerability factors, and symptoms in subclinical and clinical levels of psychosis. This knowledge could further inform and optimize future prevention and treatment strategies.

Zusammenfassung

Gemäß gängiger Vulnerabilitäts-Stress Modelle für psychotische Störungen kommt es in vorbelasteten Individuen ausgelöst durch bestimmte Stressoren zunächst zu Hyperarousal und schließlich zu psychotischen Symptomen wie Paranoia und auditiven Halluzinationen. Dies bestätigend konnte in Laborexperimenten durch Herstellung von Stressbedingungen nicht nur das Auftreten von Symptomen bei Patienten herbeigeführt werden, sondern auch das Auftreten Symptom-äquivalenter psychotischer Erfahrungen in Normalbevölkerungs-stichproben. Durch Fortschritte in der Mobilfunktechnologie ist es heute zudem möglich, ambulante Assessment Studien durchzuführen, in denen die zeitlichen Abfolgen und Zusammenhänge zwischen Stressoren, Stress und psychotischen Erfahrungen und Symptomen in Echtzeit und unter Alltagsbedingungen erfasst werden können. Der Großteil existierender ambulanter Assessment Studien im Themenfeld Psychosen beschäftigte sich dabei mit Patientengruppen mit florider Symptomatik, wobei zumeist nicht-validierte Erhebungsmethoden verwendet wurden.

Dieses Dissertationsprojekt zielte dementsprechend darauf ab, zunächst Verfahren zur Selbstberichterhebung von psychotischen Erfahrungen und Symptomen wie Paranoia und auditive Halluzinationen zu entwickeln und zu validieren (Studien 1-3). Ein zweites Ziel bestand darin, die zuvor validierten Messinstrumente in longitudinalen und ambulanten Assessment Studien zu nutzen. Zum einen sollte so in Normalbevölkerungsstichproben die Rolle von Stress in frühen Phasen der Entstehung von psychotischen Erfahrungen untersucht werden (Studien 4 und 5). Zum anderen sollte untersucht werden, inwiefern die Verbesserung von Stressbewältigungsfähigkeiten (Coping) die symptomatische Besserung von Patienten mit psychotischen Störungen über den Verlauf einer Psychotherapie erklärt (Studie 6).

In den Entwicklungs- und Validierungsstudien konnten vorhergehende Ergebnisse in der deutschen Version eines Trait-Level Fragebogens über die Lebenszeitprävalenz von Psychosesymptomen bestätigt werden (Studie 1) sowie reliable, valide, und veränderungssensitive State-Fragebögen für Paranoia (Studie 2) und Halluzinationsspektrumserfahrungen (d.h., auditive Halluzinationen und deren subklinische Vorläufer, Studie 3) erstellt werden. Obgleich eine vollständige Validierung in klinischen Stichproben aussteht, können die Fragebögen in zukünftigen ambulanten Assessments zur Sicherung der psychometrischen Qualität eingesetzt werden. Eine erste Studie an einer

Normalbevölkerungsstichprobe ergab, dass selbstberichtete und physiologische Stresslevel vor und während momentaner Paranoia-Episoden anstiegen; für Halluzinationsspektrums-erfahrungen zeigten sich jedoch keine solchen globalen Effekte (Studie 4). In einer zweiten Studie wurde der Beginn von Halluzinationsspektrumserfahrung wiederum mit vorhergehendem sozialem Stress in Form von sozialen Ausschlusserfahrungen in Verbindung gebracht (Studie 5). Schließlich ließ sich die fortgesetzte Verbesserung in Coping-Fähigkeiten mit nachfolgender symptomatischer Besserung von depressiven Symptomen, Negativsymptomen, sowie einzelnen Positivsymptomen über den Therapieverlauf in Verbindung bringen (Studie 6). Zusammengefasst liefert dieses Projekt somit Beiträge zum Verständnis der frühen Entstehungsmechanismen und zum Verständnis der Therapiewirkmechanismen bei psychotischen Störungen, die zu weiteren Studien der vollständigen Dynamik zwischen Stress, Vulnerabilitäts- und Resilienzfaktoren, sowie psychotischen Erfahrungen und Symptomen in subklinischen und klinischen Stadien der Psychose anregen sollten. Das genaue Wissen um diese Dynamiken wiederum hat das Potential, substantielle Informationen für die Optimierung zukünftiger Präventions- und Behandlungsstrategien zu liefern.

1. Background

1.1. Psychotic disorders

With life-time prevalence rates of 1.44% for the group of non-affective psychotic disorders (Perälä et al., 2007) and 0.30% to 0.70% for schizophrenia alone (McGrath, Saha, Chant, & Welham, 2008), psychotic disorders are comparatively rare. Nevertheless, the burden of psychotic disorders is disproportionally high, with a range of personal and financial costs beyond mental health alone (van Os & Kapur, 2009): The risk for all-cause mortality in psychotic disorders is found to be increased two- to threefold across systematic reviews (Bradford & Cunningham, 2016; McGrath et al., 2008); On average, patients with schizophrenia die 12–15 years younger than the general population (van Os & Kapur, 2009). Furthermore, schizophrenia alone is estimated to cause 2.8% of all years lived with disability (Rössler, Salize, van Os, & Riecher-Rössler, 2005). Finally, the economic burden of psychotic disorders is disproportionally high due to a low employment rates of people with psychosis (e.g., 10.24% in a recent population-based estimation Evensen et al., 2016) and high costs for psychiatric hospitalizations and long-term care (e.g., 3% of a regions total health care budget; De Oliveira, Cheng, Rehm, & Kurdyak, 2016). Hence, there is a dire need of a better understanding of the etiological and maintaining mechanisms of psychotic disorders that could inform prevention and treatment of psychotic disorders.

The symptoms of psychotic disorders stem from various psychopathological domains, which can be divided into five main categories (van Os & Kapur, 2009): (1) the positive dimension, (2) the negative dimension, (3) the cognitive dimension (including difficulties in memory, attention, and executive functioning), and affective dysregulation with (4) symptoms of depression, and (5) manic symptoms. The positive dimension includes delusions and hallucinations. Paranoia constitutes the most frequent type of delusions (e.g., 78.7% point-prevalence among patients with delusions; Appelbaum, Robbins, & Roth, 1999), whereas auditory hallucinations are the most common type of hallucinations (64.3%-83.4% point-prevalence among patients with a psychotic disorder; Thomas et al., 2007). The negative dimension encompasses symptoms of reduced motivation and goal-directed behavior, decreased levels of emotional experience and outward emotional expression, diminished speech, and social withdrawal. In consequence, the clinical picture of psychotic disorders is heterogeneous and covers a range of symptoms, whereby this dissertation

focuses mainly on the positive dimension (delusions and hallucinations) and its most common types of symptoms: paranoia and auditory hallucinations.

1.2. The occurrence of positive symptoms: A continuum perspective

The prevalence of paranoia and auditory hallucinations is not only large within patients who experience delusions or hallucinations, respectively. A large percentage of all people with psychotic disorders experience symptoms of paranoia (50%; Freeman, 2007, p. 427) and auditory hallucinations (70%; McCarthy-Jones, 2012). A closer look at their frequency and duration shows considerable variation of how these symptoms present in patients' everyday lives. For example, an interview study (Steel et al., 2007) on delusions and auditory hallucinations found that the majority of patients who experience delusions are preoccupied with them at least once per day (35.5%), followed by two approximately equally large groups who are preoccupied with them at least once per hour (24.6%) or almost continuously (26.3%). Only a minority of patients thinks about their delusions less than daily (at least once per week: 13.2%; less than once per week: 0.4%). For about a third of the patients, respectively, the preoccupation with delusions typically lasts several minutes (31.6%) to at least an hour (33.3%). Another quarter of patients (25.9%) spends hours at a time to think about them, whereas only few are preoccupied for only mere seconds at a time (9.2%). Regarding auditory hallucinations, a comparable distribution was found: most patients experienced hallucinations at least once per day (32.6%), at least once per hour (22.2%) or almost continuously (19.4%). The remaining quarter of patients does not experience auditory hallucinations on a daily basis (at least once per week: 24.3%, less often: 1.4%). Auditory hallucination episodes most often lasted for several minutes (34.7%) or a few seconds (25.0%), with longer hallucinations being less prevalent (at least an hour: 16.0%, several hours: 24.3%). Similar variability is found in the distress and the disruption to life associated with these symptoms (Steel et al., 2007). In sum, the presence of paranoia or auditory hallucination encompasses a phenomenological continuum of symptom severity, ranging from rare, fleeting episodes to continuous, severely disruptive experiences.

For a long time, research on psychosis was limited to clinical samples, in part due to the dichotomous definition of psychosis as a mental disorder that is either present or absent (van Os, Hanssen, Bijl, & Ravelli, 2000). More than in other psychopathological conditions, a mindset inspired by early psychiatric accounts declaring psychotic symptoms to be qualitatively different, abnormal thought processes not accessible by rational interpretation

(Jaspers, 1913) persevered the idea that psychotic experiences do not occur in healthy populations. In recent decades, however, an abundance of studies (for a review, see: van Os, Linscott, Myin-Germeys, Delespaul, & Krabbendam, 2009) provided evidence for a "continuity of psychotic phenomena" (van Os et al., 2000) that extends from clinical samples to the general population. Determining the exact prevalence of these psychotic experiences is difficult due to heterogeneous assessment methods (van Os et al., 2009). Estimates for the combined prevalence of hallucinations and delusions in population samples varies between 2% (25^{th} percentile) to 16% (75^{th} percentile; van Os et al., 2009). When prevalence of these psychotic experiences and the prevalence of psychotic disorders are differentiated, only a fraction of the reported symptoms amount to a clinically relevant phenotype. In other words, the clinical definition of psychosis constitutes a minor section at the upper end of a phenotypic continuum (Johns & van Os, 2001), whereas most of the psychotic experiences reported in general population samples are transitory to varying degrees (van Os et al., 2009).

Regarding paranoia, Freeman and colleagues (2005) proposed a hierarchical model of paranoid thoughts based on data from a large general sample: They found considerable variety in the prevalence of different paranoid thoughts when a frequency-range of at least once a week up to several times per day was considered:

> "30–40% of the respondents had ideas that negative comments were being circulated about them and 10–30% had persecutory thoughts, with thoughts of mild threat (e.g., 'People deliberately try to irritate me') being more common than severe threat (e.g., 'Someone has it in for me'). In contrast, only a small proportion (approximately 5%) of respondents endorsed […] the most improbable [items] (e.g., that there was a conspiracy)." (Freeman et al., 2005, p. 433).

Freeman and colleagues (2005) concluded that the hierarchy of paranoia starts with very common types of social-evaluative concerns including worrys that the world is potentially dangerous. Presence of social evaluative concerns increases the risk for more severe ideas of reference (e.g., people talking about you) to appear. Finally, with increasing subjective significance of the threat, beliefs can transform into increasingly rare mild (e.g., people trying cause irriation), moderate, and ultimately severe threat beliefs (e.g., strangers being dead set on causing grave harm). In conclusion, up to a third of the general population

regularly experiences paranoia similar to clinical levels, with precursors such as social evaluative concerns being even more common.

By comparison, the prevalence of auditory hallucinations in general population samples is somewhat lower, with prevalence ranging from 4% (25th percentile) to 8% (75th percentile; van Os et al., 2009). Moreover, the frequency of hallucinations in the general population is low (Ohayon, 2000): The majority of people who experience hallucinations report them to occur less than once a month (50.6%) or monthly (16.4%), whereas only a minority (6.2%) reports hallucinations to occur several times per week. However, a range of subclinical experiential phenomena or "non-clinical sensory distortions" (Bell, Raballo, & Larøi, 2010, p. 380) have been linked to hallucination proneness and are often assessed alongside auditory hallucinations in dimensional measures for studies on population samples (Bell et al., 2010). Depending on the dimensional measure, these subclinical precursor phenomena include vivid mental imagery (Morrison, Wells, & Nothard, 2002; Waters, Badcock, & Maybery, 2003), intrusive thought (Larøi, Marczewski, & van der Linden, 2004; Larøi & van der Linden, 2005), musical hallucinations (Bell et al., 2010), sleep-related hallucinations (Larøi & van der Linden, 2005; Ohayon, 2000) and a sensitivity to external stimuli experienced as sensory flooding (Bell, Halligan, & Ellis, 2006). In population samples, these subclinical precursors are reported to occur more frequently than clinical level hallucinations (Serper, Dill, Chang, Kot, & Elliot, 2005). Thus, there is a continuum of auditory hallucinations, better referred to as a continuum of *hallucination spectrum experiences,* that includes precursors of varying clinical significance as well as clinical level hallucinations.

Taken together, the existence of these symptom continua allows for an investigation of the vulnerability factors and the immediate stressors that trigger the emergence of psychotic experiences prior to the formation of a clinically relevant psychosis phenotype (Verdoux & van Os, 2002) and independent of potentially biasing factors such as antipsychotic medication. Taken together, studies on participants from the subclinical part of the psychosis continuum hold the potential for a better understanding of the early etiological phases of psychosis.

1.3. Stress and psychosis

Today, multifactorial vulnerability stress models of the etiology of psychotic disorders (Nuechterlein & Dawson, 1984; Zubin & Spring, 1977) converge on the assumption that the vulnerability-level modulates a person's susceptibility to stress and to the emergence of

psychotic symptoms. An individual's vulnerability is determined by the sum of the genetic, neurophysiological, social, environmental, and psychological risk factors that have accumulated in their life (i.e., life time etiological processes).

The emergence of clinical symptoms is potentially triggered by "exogenous and/or endogenous challengers [that] elicit a crisis in all humans" (Zubin & Spring, 1977, p. 103). A central role in this etiological mechanism was attributed to "autonomic reactivity anomalies" (Nuechterlein & Dawson, 1984) that facilitate a hyperreactivity to stressors. In consequence, stressors lead to "transient intermediate states of processing capacity overload, autonomic hyperarousal, and impaired processing of social stimuli before the development of psychotic symptoms" (Nuechterlein & Dawson, 1984, p. 305). Thus, symptom emergence due to these triggers depends on an individual's pre-existing vulnerability level and on whether or not the trigger induces high enough levels of stress and physiological hyperarousal when it occurs (i.e., momentary etiological processes).

In line with these models, ample evidence exists for the notion that the persistent dysregulation of the autonomic nervous system is associated with psychosis. Regarding the parasympathetic nervous system, a recent meta-analysis of 34 studies (Clamor, Lincoln, Thayer, & Koenig, 2016) found that the resting state vagal tone measured via heart rate variability (HRV) is reduced in patients with psychotic disorders, with large effect sizes for all HRV-parameters assessed. Clamor and colleagues (2016) conclude that reduced parasympathetic activity associated with low HRV may constitute an endophenotype for the development of psychotic symptoms, given that reduced HRV is closely associated to reduced levels of self-regulation and adaptability (Thayer & Lane, 2000). Moreover, several studies assessed sympathetic arousal in psychosis via parameters of electrodermal activity. Electrodermal activity is used to assess sympathetic activity due to the skin's predominantly sympathetic cholinergic innervations. These studies found evidence of increased sympathetic activity during acute psychotic disorders (Maina, Barzega, Bellino, Bogetto, & Ravizza, 1995; Ohman, 1981), prior to a first episode (Hazlett, Dawson, Schell, & Nuechterlein, 1997) and prior to a relapse (Dawson, Nuechterlein, & Schell, 1992). Finally, a recent review of studies investigating autonomic stress-parameters in psychosis (Montaquila, Trachik, & Bedwell, 2015) proposed a unifying process model of autonomic dysregulation: According to this model, alterations in parasympathetic activity, as indexed by reduced resting state HRV, constitutes a vulnerability factor that reduces the capacity to

effectively regulate and recover from a stress response. This, in turn, increases symptom severity. Over time, the resulting increased burden of symptoms and continuously diminished self-regulation capacity lead to an observed hyper-responsivity of the sympathetic nervous system that becomes dominant due to a lack of parasympathetic inhibition.

Parallel to these developments of dynamic autonomic dysregulation models, recent revisions of the vulnerability stress models have connected the autonomic hyperreactivity emphasized in early models (Nuechterlein & Dawson, 1984) to hypothetical central self-reinforcing mechanisms. Such mechanisms involve the sensitization of the dopamine system – either directly (Howes & Murray, 2014) or as a secondary result of a dysregulated neuroendocrine stress response (i.e., stress-sensitization; van Winkel, Stefanis, & Myin-Germeys, 2008; Walker & Diforio, 1997). Sensitization is a result of both early factors (e.g., genetic factors, developmental insults, or early traumatic experiences) as well as recent to momentary stressors (e.g., social stressors and dysfunctional cognitive processes; Howes & Murray, 2014; Selten, van der Ven, Rutten, & Cantor-Graae, 2013). Subsequent exposure to stress leads to a dysregulated response that triggers an excessive dopamine release leading to severe psychotic experiences (Howes & Murray, 2014; van Winkel, Stefanis, et al., 2008; Walker & Diforio, 1997).

Finally, revisions of the vulnerability stress model (Howes & Murray, 2014) also emphasized the role of the consequences of psychotic experiences. Severe psychotic experiences, in turn, become stressors in and of themselves that lead to further sensitization and persistence of psychotic symptoms (Howes & Murray, 2014). In consequence, research on the interrelation of stress and psychotic experiences encompasses both the investigation of the role of stress as a trigger as well as the exploration of the stress caused by psychotic experiences that could maintain and exacerbate the symptom severity.

In sum, the role of stress and stressful events in the development of psychotic experiences and constitutes a major part of etiological models of psychosis. Of importance, it is central to the part of all etiological processes that are assumed to happen in momentary time-intervals (see Figure 1). As a result, it allows for an investigation of the etiological factors of psychosis with paradigms that capture the immediate stressor-reaction mechanism. Moreover, from a practical perspective, causal-interventionist approaches to ameliorate symptoms could built on this model an target crucial triggering factors and

processes that occur in daily life. Thus, the role of stress in positive psychotic symptoms is not only relevant in epidemiological and basic clinical research, but also in applied clinical research to optimize intervention strategies.

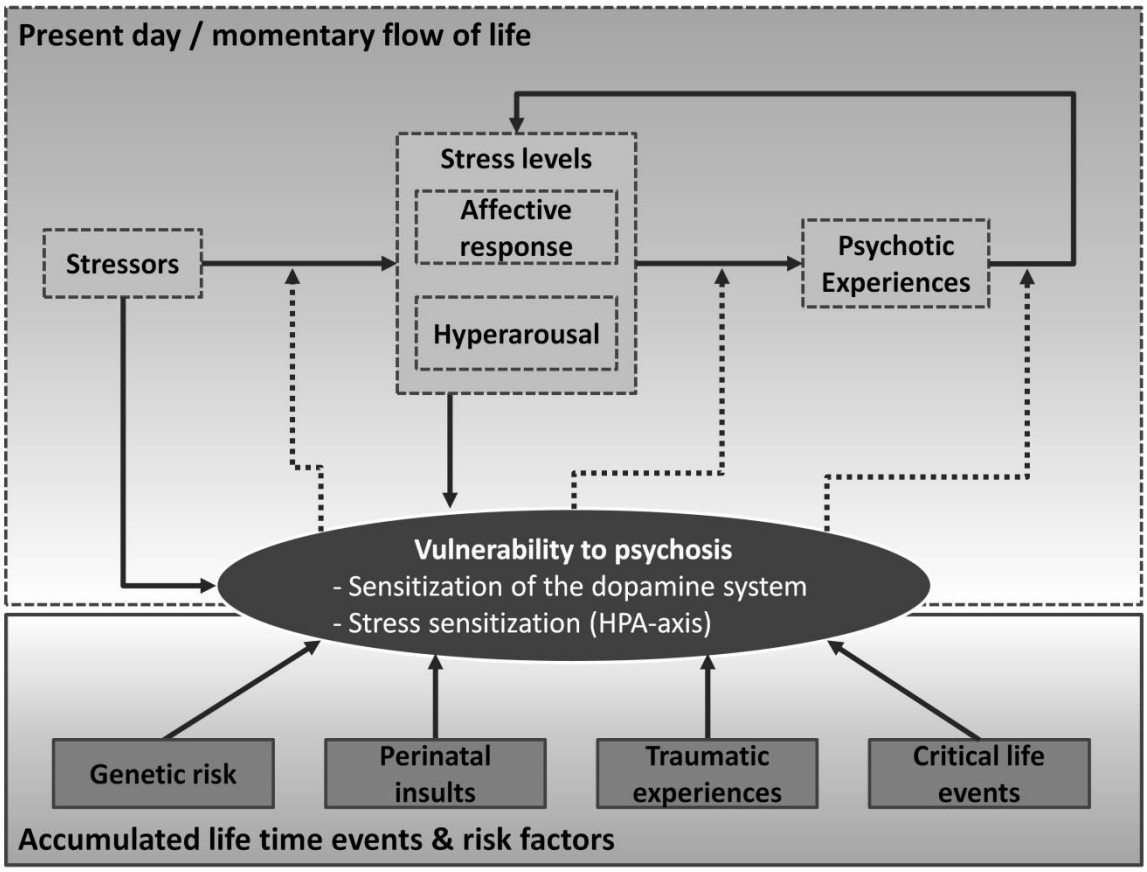

Figure 1. Integrated vulnerability stress model for psychosis. Separated into life-time developmental processes (lower part) consisting of accumulated biological risk factors and environmental events that add to vulnerability and momentary dynamics and interactions (upper part) between stress, vulnerability, and psychotic experiences in the present day flow of life. Arrows indicate a direct effect; dashed arrows indicate a moderating effect.

1.3.1 Stress as a trigger for positive symptoms

The beginnings of research on stress as a symptom trigger date back to findings of increased numbers of retrospectively reported life-events prior to the start of a psychotic disorder (e.g., Lukoff, Snyder, Ventura, & Nuechterlein, 1984). In addition to this, early vulnerability stress models inspired psychophysiological lab studies to test for connections between physiological stress and psychotic symptoms. Over the course of several decades of research, some evidence has indicated that increased severity of positive symptoms in patients as assessed with clinical interviews is associated with physiological hyperarousal,

specifically with reduced resting state HRV (Kim et al., 2004; Valkonen-Korhonen et al., 2003) as well as with an increased heart rate and electrodermal activity during a mildly stressful task (Zahn & Pickar, 2005). Furthermore, early lab studies found the onset of hallucinations over the course of a monitoring session to be associated with increased electrodermal activity (Cooklin, Sturgeon, & Leff, 1983; Levine & Grinspoon, 1971). Thus, there was already early evidence for momentary dynamics between stress levels and psychotic symptoms.

Today, the role of stress as a trigger for psychotic symptoms has been extensively researched with experimental and quasi-experimental lab studies. In these studies, a stressor is presented to participants and increases in momentary levels of psychotic symptoms from pre to post stress-induction are tested for. In many of these studies, the hypothesis that the stress induced by the stressor explains momentary symptom increase is corroborated by showing that an increase in self-reported stress or negative affect following the stressor mediates its effect on increased symptoms. Across the existing studies, patients with psychosis were shown to report higher levels of paranoia when confronted with a stressor. This pertained to noise stressors (Moritz, Burnette, et al., 2011), inducing feelings of social exclusion (Sundag, Ascone, de Matos Marques, Moritz, & Lincoln, 2016) or increased levels of negative affect due to sleep problems (Freeman, Pugh, Vorontsova, & Southgate, 2009). Furthermore, higher levels of paranoia and auditory hallucinations were induced by traversing a busy shopping street versus staying inside (Freeman et al., 2015). In sum, there is considerable evidence for a mechanism of momentary stress triggering psychotic symptoms in patients with psychosis.

Regarding the existence of this mechanism along the continuum of psychosis and in the general population, experimental studies of the effect of stress on psychotic experience severity yielded comparable results. Specifically, an increase in paranoia has been found due to presenting a continuous noise stressor (Lincoln, Peter, Schäfer, & Moritz, 2009), inducing feelings of exclusion (Kesting, Bredenpohl, Klenke, Westermann, & Lincoln, 2013; Westermann, Kesting, & Lincoln, 2012), loneliness (Lamster, Nittel, Rief, Mehl, & Lincoln, 2017) or social status loss (Freeman et al., 2014), and by viewing anxiety-inducing pictures (Lincoln, Lange, Burau, Exner, & Moritz, 2010). Furthermore, induced sleep loss increased paranoia and hallucination severity, which was shown to be substantially mediated by stress levels (Reeve, Emsley, Sheaves, & Freeman, 2018). In sum, experiments and other lab studies point towards the conclusion that the effect of various momentary internal and external

stressors on psychotic symptoms can ubiquitously be found in the subclinical and clinical range of the continuum of psychosis.

With evidence that sufficiently strong stressors in an artificial lab environment increase psychotic experiences in both clinical as well as subclinical group, evidence for the possibility of a stress-based trigger mechanism exists. As a next step, the ecological validity of these findings needs to be verified. The question of which constellations of triggers are the prevalent causes for the emergence of psychotic experiences and symptoms in everyday life becomes a relevant topic in order to understand the etiology of psychosis and subsequently informing prevention efforts.

1.3.2 Stress as a consequence of positive symptoms

Knowledge about the stress associated with psychotic symptoms themselves primarily stems from correlational survey studies and epidemiological research. In clinical samples (Steel et al., 2007), auditory hallucinations are reported to be distressing more than half the time to always by the majority (61.1%) of interviewed patients, with highly (30.6%) or extremely (21.5%) intense distress levels being common. Regarding delusions, a comparable pattern in terms of the amount of distress (more than half the time: 32.5%, always: 36.4%) and the intensity of distress (highly intense: 43.9%, extremely intense: 16.7%) can be found (Steel et al., 2007). Even in these samples, however, more than ten percent feel no distress due to hallucinations (13.2%) or delusions (10.5%) at all. The negative consequences due to psychotic symptoms vary considerably even within the clinical range of the continuum of psychosis.

In contrast, population samples often show lower levels of distress due to their psychotic experiences. Populations prone to psychotic experiences but without need for care have repeatedly been shown to differ from clinical groups in distress level, but not in the frequency of psychotic experiences: For example, participants from certain religious groups and people with psychotic disorders have been shown to endorse a comparable number of delusional beliefs, but only the latter group shows high levels of distress due to these beliefs (Peters, Day, McKenna, & Orbach, 1999). Similarly, symptom distress has repeatedly been shown to differentiate between healthy voice-hearers (reporting frequent experiences of auditory hallucinations in absence of a need for care) and patients with acute psychotic disorders (Cottam et al., 2011; Larøi et al., 2012; Sorrell, Hayward, & Meddings, 2010). Of importance, this variability in distress somewhat contradicts the assumption of

contemporary vulnerability stress models (e.g., Howes & Murray, 2014) that propose an exacerbation of psychosis once severe psychotic symptoms emerge. Providing answers to the question which factors shield healthy populations with psychotic experiences from experiencing symptom-level distress and how they cope with their psychotic experiences can provide crucial information to optimize the treatment for psychosis.

1.4. Longitudinal and ambulatory assessment methods to elucidate the role of stress

In recent years, technological advancement has allowed for the widespread use of ecologically valid research methods in the context of people's natural environment (Trull & Ebner-Priemer, 2013). These ambulatory assessments (or ecological momentary assessments or experience sampling methods) utilize mobile technology to facilitate an automated, structured longitudinal assessment scheme. An application on a smartphone or other mobile devise is set up to cue self-assessments in fixed intervals over the course of the day for a fixed amount of time. In mental health research, sampling schemes usually consist of 1.5 to 2.5 hour sampling intervals over the course of six to seven days (Palmier-Claus et al., 2011). Concerning the research of psychosis, ambulatory assessment studies hold a considerable potential. For example, they allow for a close to real-time assessment of the phenomenology of psychotic experiences and symptoms, including their frequency, duration and related distress (Myin-Germeys et al., 2009) with minimal risk of retrospective biases (Trull & Ebner-Priemer, 2013). In sum, they allow for an investigation of etiological mechanisms and dynamics (Myin-Germeys et al., 2009; Trull & Ebner-Priemer, 2013) of psychotic experiences and symptoms, including the exploration of the association with hypothesized triggers and consequences and their temporal order in daily life.

As for the role of stress, existing ambulatory assessment studies have found evidence for increased sensitization to stress in patients compared to their relatives and healthy controls (Myin-Germeys & van Os, 2007): Across several studies, a higher emotional reactivity to subjective stress due to daily hassles was found. Furthermore this pattern of momentary stress reactivity has been connected to genetic (van Winkel, Henquet, et al., 2008) and psychosocial (Lardinois, Lataster, Mengelers, van Os, & Myin-Germeys, 2011) vulnerability factors. Furthermore, self-reported stress levels have repeatedly been found to co-vary with self-reported symptom severity at the same time-point (Peters et al., 2012; Reininghaus, Kempton, et al., 2016; Udachina, Varese, Myin-Germeys, & Bentall, 2014; Varese, Udachina, Myin-Germeys, Oorschot, & Bentall, 2011) and at following time-point

(Ben-Zeev, Ellington, Swendsen, & Granholm, 2011). Interestingly this time-lagged association between symptom severity and previous stress levels has also been found with physiological stress parameters: A recent study found that momentary autonomic dysregulation in the form of reduced HRV predicted later auditory hallucination severity (Kimhy et al., 2017). Finally, in addition to this symptom severity approach, some studies (Delespaul, deVries, & van Os, 2002; Oorschot et al., 2012; Thewissen et al., 2011) utilized the repeated assessment of symptom severity levels (most commonly of hallucination symptoms) to determine symptom presence and absence for each sampling interval. Subsequently, assessment intervals were categorized into momentary symptom episodes, intervals immediately prior to symptom episodes, or intervals following symptom episodes. These symptom phase studies converge on the finding that symptom phases are characterized by increased self-reported stress. Furthermore, whereas one study found no increase in negative affect prior to auditory hallucination episodes (Oorschot et al., 2012), other studies found that increased stress levels (i.e., negative affect) in intervals immediately prior to symptom episodes (Delespaul et al., 2002). Finally, the intensity of stress at the beginning of symptom episodes was found to predict the overall duration of one symptom episode over consecutive sampling intervals (Thewissen et al., 2011). In sum, the existing ambulatory assessment studies on patients provide evidence for stress-sensitization, a connection between the emergence and intensity of psychotic symptoms and prior stress, and the interrelation between psychotic symptoms and elevated stress levels. Studies with subclinical populations are scarce by comparison, yet they could provide crucial information regarding symptom formation prior to a clinical state.

1.5. Current challenges of ambulatory and longitudinal assessment in psychosis

Although the origins of self-recorded longitudinal diary studies in psychology can be traced back to the late nineteenth century (Wilhelm, Perrez, & Pawlik, 2011), ambulatory assessment in its current form is a relatively young research method. At present, there are several methodological challenges associated with ambulatory assessment. Further refinement of its methods is required to establish psychometric standards. Regarding ambulatory assessment of positive psychotic experiences and symptoms in clinical and general population samples, these challenges pertain to

(1) creating valid state inventories optimized for the repeated, longitudinal assessment of fluctuations in psychotic experiences (Palmier-Claus et al., 2011, 2012),

(2) establishing that these state inventories are feasible for the use in subclinical populations that have not been a focus of ambulatory assessment studies yet, and

(3) fitting sampling schemes to the phenomena assessed in terms of expected frequencies and durations and expected pace of change in order to approximate real-time assessment (Myin-Germeys et al., 2009).

Regarding the challenge of valid ambulatory assessment inventories, it needs to be noted that filling out ambulatory assessment diaries (i.e., the comprehensive list of questionnaires/items presented at the end of each interval) should disrupt normal living conditions as little as possible to avoid reactivity (changes in measured constructs due to the measurement procedures) and low compliance rates (i.e., missing data due to ignored assessment cues). As a rule of thumb, answering an ambulatory assessment diary should take no longer than three minutes (Palmier-Claus et al., 2012). Consequently, ambulatory assessment measures need to be brief, but cover a representative content selection of the assessed variable (Palmier-Claus et al., 2012). Furthermore, internal consistency at the single assessment level, validity, and sensitivity to change between assessments should ideally be pre-established before the start of ambulatory assessment studies (Palmier-Claus et al., 2011, 2012) in order to avoid biased results due to the quality of methods. To date, however, few validated measures exist that have been specifically optimized for ambulatory assessment of general variables (e.g., Wilhelm & Schoebi, 2007) or psychotic symptoms (e.g., Palmier-Claus et al., 2012). Current studies often rely on self-developed one-item measures for each assessed variable (Wilhelm & Schoebi, 2007), which is no doubt the result of the multitude of variables that can meaningfully be assessed in daily life. Nevertheless, it is worthwhile to at least produce thoroughly validated measures for central variables – such as paranoia and hallucinations – that are part of ambulatory assessment diaries in psychosis research across an ever-growing number of studies.

Furthermore, if ambulatory assessment measures are to be used in clinical as well as in subclinical populations, their content should ideally be representative for the typical phenomena experienced across the respective symptom continuum. For paranoia, this could be done in different ways. For example, continuum-wide validity of a state paranoia assessment could be ensured by assessing the core characteristics of this symptom (Freeman, 2007), that is the perceived threat of imminent harm and an perceived intent by others to cause said harm. For auditory hallucinations, it needs noting that only a small

fraction of general population experiences hallucinations on a frequent basis. As has been described above, however, a number of subclinical hallucination spectrum experiences have been identified (Bell et al., 2010) that apparently occur more frequently in the general population (Ohayon, 2000; Serper et al., 2005). In order to successfully assess a continuum of psychotic symptoms, precursor experiences should be implemented into ambulatory assessment procedures for general population samples.

Finally, the one week, 90 minute assessment interval sampling scheme may provide a pragmatic solution to ensure that for each participant, a sufficient number of assessments is recorded (Palmier-Claus et al., 2011). However, recommendations in reviews and practical guides (Conner & Lehman, 2011; Myin-Germeys et al., 2009) emphasize that sampling intervals and assessment time-frames need to be adapted to the variables of interest. Specifically, sampling intervals need to fit the occurrence of the assessed phenomena in everyday life to capture a representative sample at the within-subject level. On the one hand, longer assessment intervals (up to 24 hour intervals and more) over a longer time are conceivable, if the phenomena assessed occur in corresponding patterns (Palmier-Claus et al., 2012). Possible examples are 24 hour intervals for the assessment of sleep parameters (Hennig & Lincoln, 2018), or weeklong assessment intervals to assess therapy-outcomes as a function of therapy sessions held (Lincoln, Jung, Wiesjahn, & Schlier, 2016). On the other hand, high frequency assessments with sampling intervals well below 90 minutes are a theoretical possibility (Myin-Germeys et al., 2009), for example to assess psychotic symptoms more contingent to their median duration and frequency in daily life.

In sum, there is considerable room for improvement of ambulatory assessment methods to optimize research on psychosis and the continuum of psychosis in daily life.

2. Aims of this dissertation

The aim of this dissertation project was to develop valid and reliable instruments that allow for ambulatory assessment of psychotic experiences across the full spectrum of psychosis-continuum in a first part. In a second part, these instruments were utilized to assess the dynamics between stress and psychotic experiences and symptoms. This included research on the association of stress levels and specific stressors with subclinical psychotic experiences and on the dynamic interplay between improvements in the ability to deal with stressful events (coping) and symptomatic improvement in patients receiving therapy.

Regarding the relevance of the first part, the unique requirements for instruments that assess psychotic experiences in ambulatory assessment and along the continuum demonstrate the need for psychometrically sound questionnaires that are specifically developed for this task. Moreover, symptom assessment constitutes a necessary part in all types of ambulatory assessment research domains, including the study of phenomenology, etiological mechanisms and dynamics, and mechanisms of change during treatment (Myin-Germeys et al., 2009). Thus, the relevance and potential gain of providing thoroughly evaluated and validated measures for future research extends far beyond the scope of the subsequent studies in the second part of this dissertation project.

Regarding the relevance of the second part, it needs noting that research on various populations and in different everyday life contexts provides a more complete picture of pathological processes. On the one hand, a focus on the mechanisms of the formation of subclinical psychotic experiences and symptom adds to a more complete picture of whether working mechanisms in everyday life are universal across the continuum of psychosis (as indicated by experimental stress studies) or specific to subclinical or clinical populations. Psychological processes and dynamics that are specific to the formation of psychotic experiences in subclinical populations may inform theories of etiological processes. On the other hand, exploring the mechanisms that explain the reduction or cessation of clinical symptoms in clinical populations receiving treatment can provide evidence for the validity of treatment rationales. All of these findings hold the potential for crucial information regarding the optimization of existing interventions. In sum, the following main questions are investigated in this dissertation project:

1. *Can the continuum of psychotic experiences be validly assessed within ambulatory assessment?* Valid measures for this purpose need to be brief enough to be included in ambulatory assessment diaries that can be answered in a matter of few minutes. At the same time, they need to include a selection of phenomena that is both representative for the respective symptoms and experiences they are supposed to capture. Finally, their quality needs to be ensured in terms of 'classic' psychometric criteria such as reliability and validity, but also in terms of sensitivity to change.

2. Are the interrelations between specific stressors, stress levels, and psychotic experiences in subclinical samples equivalent to the dynamics found in clinical samples? When taking the vulnerability stress models into consideration, two interpretations are

possible regarding the generalization of the evidence from ambulatory assessment studies with clinical populations to the entire continuum of psychosis. On the one hand, the associations between stress and psychotic symptoms could be functionally identical in the general population. In at risk populations and patients, these associations just become more pronounced due to the modulation by increasing levels of vulnerability. On the other hand, it is possible that a threshold minimum vulnerability (or an unusually intense stressor) is necessary for stress to produce these associations. By elucidating the triggering mechanisms in clinical and subclinical populations, the exact etiological mechanisms prior to the exacerbation of clinical symptoms can be determined. This, in turn, can inform causal interventionist prevention strategies as to whether stress itself or specific stressors are an effective target for early prevention of psychosis.

3. Is coping a mechanism of change in state of the art therapy for psychosis? Based on a causal-interventionist approach, the evidence for stress constituting a trigger for subsequent symptoms would dictate that an intervention aimed at improving effective coping with stressful situations reduces symptoms. Cognitive behavior therapy has multiple aims – including the improvement of coping with stress in general and coping with distress due to symptoms (NCCMH, 2014). Thus, improvement in coping is a candidate mechanism of change in cognitive behavior therapy. Evidence for this theoretical process could be shown with longitudinal studies that links change in coping to later change in symptoms over the course of multiple assessments.

3. Part I: Assessment methods

In the first part of this dissertation, self-report assessments for psychotic experiences and symptoms were either validated, modified for state assessment, or newly developed. Study 1 marks the first validation study of the German version of the most commonly used retrospective self-report instrument for psychosis symptoms in population and clinical samples, the Community Assessment of Psychic Experiences (CAPE, Stefanis et al., 2002). In study 2, the widely used Paranoia Checklist was subjected to a revision with the aim of deriving valid state-adapted versions that detect change in momentary paranoia levels. Finally, in study 3, a new questionnaire to assess hallucination spectrum experiences in ambulatory research, the Continuum of Auditory Hallucinations - State Assessment, was developed and validated.

3.1. Study 1. Validation of the German version of the Community Assessment of Psychic Experience (CAPE)

Schlier, B., Jaya, E. S., Moritz, S., & Lincoln, T. M. (2015). The Community Assessment of Psychic Experiences measures nine clusters of psychosis-like experiences: A validation of the German version of the CAPE. *Schizophrenia Research*, *169*, 274–279.

Background. The CAPE is one of the most widely used self-report questionnaires for psychotic symptoms and perhaps the most widely used questionnaire when assessing the continuum of psychosis in the general population. It comprises 42 items describing "clinical symptoms of patients" (Stefanis et al., 2002) and includes the three dimensions positive symptoms, negative symptoms, and symptoms of depression. The questionnaire now exists in a multitude of different languages, including for example Greek (Stefanis et al., 2002), English and French (Brenner et al., 2007), Spanish (Fonseca-Pedrero, Paino, Lemos-Giráldez, & Muñiz, 2012), Italian (Armando et al., 2010), Dutch (Hanssen et al., 2003), Indonesian (Jaya, 2017), and German (van Os, Verdoux, & Hanssen, 1999). Yet despite its repeated use in clinical research the German version of the CAPE has never been validated.

A validation of the German translation of the CAPE has become increasingly necessary, since a review of the psychometric quality analyses of the CAPE by Mark and Toulopoulou (2015) showed that across different language versions, only the original validations study reported good fit of a three-dimensional model (Stefanis et al., 2002). Replication of these results in three other validation studies was not or only partially successful (Brenner et al., 2007; Fonseca-Pedrero et al., 2012; Vleeschouwer et al., 2014). Based on the results of a multitude of studies using exploratory factor analysis, Mark and Toulopoulou (2015) proposed a single symptom factors solution that split the positive symptom dimension into up to five factors (paranoia, hallucinations, bizarre experiences, delusions of grandiosity, and magical thinking) and the negative symptom dimension into three factors (amotivation, social withdrawal, and affective flattening). However, the proposed symptom factors solution has yet to be subjected to confirmatory factor analysis in order to test for increased model fit.

This study aimed to validate the German version of CAPE. We hypothesized that a single symptom factors model with five positive symptom factors, three negative symptom factors and one depression factor yields sufficient goodness of fit in factor analysis and superior goodness of fit compared to the original three-dimensional model. Furthermore,

we hypothesized that all factors show substantial associations with assessments for their respective symptom dimensions (convergent validity), but no association with assessments for the other two symptom dimensions (discriminant validity).

Methods. Data from eight community (*n* = 934) and three patient samples (*n* = 112) were combined (*N* = 1046) and re-analyzed for this study. The competing original three dimension model (Stefanis et al., 2002) and the recently proposed multiple single symptom factors model (Mark & Toulopoulou, 2016) were tested for goodness of fit in the full sample and in the community subsample, using confirmatory factor analysis (CFA). The fit-indices utilized were the comparative fit index (CFI, with *CFI* > 0.90 indicating sufficient fit and *CFI* > 0.95 indicating good fit), the root mean square error of approximation (RMSEA, with *RMSEA* < 0.10 indicating sufficient fit and an *RMSEA* < 0.05-0.06 indicating good fit), and the standardized root mean square residual (SRMR, with *SRMR* < 0.08 indicating good fit). The convergent and discriminant validity was assessed with correlation analysis of subsamples that were assessed with a clinical interview for positive and negative symptoms (i.e., the Positive and Negative Syndrome Scale, PANSS; Kay, Fiszbein, & Opler, 1987) or self-report questionnaires for positive symptoms (i.e., the Paranoia Checklist, Freeman et al., 2005), for depression (i.e., the Beck Depression Inventory, BDI; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961; Hautzinger, Keller, & Kühner, 2009; and the German version of the Center for Epidemiologic Studies Depression Scale, CES-D; Martin Hautzinger, 2012; Radloff, 1977) and for a crucial affective component of negative symptoms (i.e., the Temporal Experience of Pleasure Scale – Anticipatory pleasure, TEPS-Ant; Gard, Gard, Kring, & John, 2006). Partial correlations controlling for the remaining CAPE-factors were calculated.

Main results. In the full sample, the three-dimensional model showed good fit according to two indices (*RMSEA* = 0.054, *SRMR* = 0.067), but the *CFI* = 0.639 was below the threshold for sufficient fit. Similarly, the single symptom factors model showed good fit (*RMSEA* = 0.041, *SRMR* = 0.062), but not according to all indices (*CFI* = 0.791). Similar results were found when only the community subsample was analyzed (three-dimensional model: *CFI* = 0.664, *RMSEA* = 0.054, *SRMR* = 0.066; single symptom factors model: *CFI* = 0.810, *RMSEA* = 0.041, *SRMR* = 0.061). Exploratory analysis showed that due to low overall intercorrelations between items, the null model in CFA yielded an RMSEA below 0.158 (full sample: $RMSEA_{null}$ = 0.088, community sample: $RMSEA_{null}$ = 0.091), which limits the possible range for the CFI to CFI_{max} < 0.90 (Kenny, 2014).

Criterion validation of the three dimensional model yielded significant partial correlations of the positive symptom dimension and all assessments for positive symptoms (PANSS-positive symptoms score: n = 33, $r_{partial}$ = 0.51, p < 0.001, Paranoia Checklist: n = 207, $r_{partial}$ = 0.28, p < 0.001) as well as a smaller correlation with one criterion for negative symptoms (TEPS-Ant: n = 222, $r_{partial}$ = -0.14, p < 0.050). The CAPE depression dimension showed convergent validity with both depression assessments (BDI: n = 222, $r_{partial}$ = 0.49, p < 0.001, CES-D: n = 207, $r_{partial}$ = 0.34, p < 0.001), but also a substantial correlation with the Paranoia Checklist (n = 207, $r_{partial}$ = 0.28, p < 0.001). Finally, the negative symptom dimension was only significantly correlated with one of two convergent validity criteria (TEPS-Ant: n = 222, $r_{partial}$ = 0.23, p < 0.001) and showed a larger correlation with the BDI than with TEPS-Ant (n = 222, $r_{partial}$ = 0.27, p < 0.001).

The results of the criterion validation of the positive symptom factors of the single symptom factors model yielded convergent validity for paranoia in one criterion (Paranoia Checklist: n = 207, $r_{partial}$ = 0.35, p < 0.001) with no other significant partial correlation. No significant partial correlations were found for any of the other positive symptom factors. Among the symptom factors from the negative dimensions, significant associations between one convergent validity criterion, the TEPS-Ant, and social withdrawal (n = 222, $r_{partial}$ = 0.16, p < 0.050) as well as affective flattening ($r_{partial}$ = 0.28, p < 0.001) were found. The negative symptom factor amotivation, in contrast, was only significantly associated with a discriminant validity criterion (BDI: n = 222, $r_{partial}$ = 0.23, p < 0.001).

Discussion. Contrary to our hypothesis, the single symptom factors model for the CAPE did not show a substantially better model fit than the three-dimensional model. Both models showed an inconsistent pattern of two indices indicating good fit and one index indicating insufficient fit. Furthermore, in line with previous findings (Stefanis et al., 2002), the positive symptom dimension showed sufficient convergent and discriminant validity, whereas the negative symptom and depression dimensions showed limited discriminant validity.

The reason for the inconsistent results regarding model fit may be inherent to the CAPE's premise of assessing clinical-level symptoms (i.e., using items that describe symptoms as they are typically experienced by patients) in subclinical samples. Epidemiological research on the prevalence of psychosis symptoms in the general population frequently describe a pattern of single fleeting psychotic symptoms prevalent in a large percentage of the population, in contrast to only a small percentage of the population

experiencing multiple symptoms frequently (Freeman et al., 2005; Johns & van Os, 2001). Possibly, future assessments for population samples need to include subclinical precursors of psychotic symptoms as well as symptoms at the clinical level to achieve sufficient psychometric quality.

In the meantime, and provided we assume that the inconsistent result pertaining to the CFI is due to the aforementioned characteristics of the CAPE item-list, the German CAPE in both the three-dimensional and single symptom scoring form can be considered valid in terms of factor structure. Nevertheless, because of a slightly better model fit and the possibility to disentangle the effect of the various symptoms subsumed into the dimensions, the results of this study may be regarded as an invitation to carefully double-check the results of any future research involving the CAPE with the single symptom model scoring.

3.2. Study 2. Development of a change-sensitive state Paranoia Checklist

Schlier, B., Moritz, S., & Lincoln, T. M. (2016). Measuring fluctuations in paranoia: Validity and psychometric properties of brief state versions of the Paranoia Checklist. *Psychiatry Research, 241*, 323–332.

Background. The vast majority of paranoia questionnaire are retrospective assessments of the past one week or the life-time prevalence of paranoia (Fenigstein & Vanable, 1992; Freeman et al., 2005; Peters et al., 1999; Stefanis et al., 2002). State measures specifically designed to capture momentary levels of paranoia for repeated assessment are scarce and are – at best – validated in the context of their first application in a specific study (Bodner & Mikulincer, 1998; Ellett, Allen-Crooks, Stevens, Wildschut, & Chadwick, 2013; Freeman et al., 2007). As a result, studies with repeated measurement either rely on one item measures of state-paranoia (as described above) or on modified versions of thoroughly validated trait-like paranoia questionnaires with a state-adapted answer format (e.g., to a self-rating of the extent to which each item applies to oneself “at the moment” (Lincoln, Hartmann, Köther, & Moritz, 2015). The convergent validity and internal consistency of an original questionnaire has been shown to extend to state adapted versions (Lincoln, Hohenhaus, & Hartmann, 2012; Lincoln et al., 2009). However, an item-selection originally intended for retrospective assessment in weeklong intervals may comprise items that are non-sensitive to momentary fluctuations (Palmier-Claus et al., 2012), which leads to an underestimation of true changes in state paranoia. A possible way to uphold the psychometric quality of a source questionnaire and simultaneously guarantee the suitability of the corresponding state-

adaptation is to select a subset of change-sensitive items from the questionnaire for a revised state assessment. Specifically, such a state assessment should only include items that show a sufficient amount of pre to post (PP) change due to pre-established paradigms that either increase or decrease state paranoia levels. Furthermore, these changes should sufficiently differ from PP changes in a neutral control condition (PP control or PPC effect).

In this study, we aimed to derive valid and change sensitive state versions from the widely used Paranoia Checklist (Freeman et al., 2005) for the use in ambulatory assessment and experimental research. In step 1, candidate item selections were derived based on their PP and PPC effect sizes across various studies. In step 2, the model fit and increase in PP change in comparison to the original 18-item scale were tested for all versions. Finally, in step 3, the sufficiently brief versions were tested for their amount of within-subject variation in a pilot diary study with daily assessments. Concurrently, convergent and discriminant validity of the derived versions were assessed based on the data collected in step 1 and 2.

Methods. For step 1, data from 13 existing studies (total N = 860, including n = 288 patients with psychosis and n = 489 participants from community samples) using the state adapted Paranoia Checklist to measure a PP or PPC effect was subjected to item-wise random effects meta-analyses. The average PP and PPC effect of each item were ranked based on a preconceived rating scheme (see Appendix B). Based on the rankings, item selections for sufficiently brief versions for ambulatory assessment were derived, as well as a long version for experimental studies that is devoid of items insensitive to change.

In step 2, a large holdout-sample (N = 1893) from an online study on a population sample (Moritz, Göritz, et al., 2014) was used to subject all item-selections to CFA and determine goodness of fit based on the RMSEA and the CFI. Furthermore, Cohen's d for PP effects was calculated for the full scale and all item selections. The increase in PP effect size of each selection in comparison to the full scale, Δd, was calculated to evaluate whether the item selections yield improved sensitivity to change.

In step 3, a new longitudinal online study was conducted in which a small sample of psychology students (N = 32, 78.1% female) answered the brief versions of the Paranoia Checklist once per day for one week. Random-intercept multilevel regression models of assessments nested in participants were calculated. The relative amount of within-subject variance in these calculated models served as an indicator for the amount of fluctuation in state paranoia captured by the brief versions.

For convergent and discriminant validity correlation tests with self-report questionnaires for paranoia and social anxiety from the existing studies (steps 1and 2) were conducted.

Main results. The item selection based on meta-analyses (step 1) yielded a three-item and a five-item brief version of the items with the highest-ranking PP and/or PPC effect sizes. Furthermore, exclusion of those items showing average PP and/or PPC effects close to or below d = 0 yielded a 13-item version. Subsequent CFA (step 2) yielded sufficient to good model fit according to all indices for the brief versions (three-item version: *RMSEA* = 0.064, *CFI* = 0.98; five-item version: *RMSEA* = 0.089, *CFI* = 0.96). For the 13-item version, RMSEA indicated sufficient fit (*RMSEA* = 0.081), whereas the CFI (*CFI* = 0.86) was below the threshold but still higher than the CFI for the 18-item version (*CFI* = 0.73). Compared to the PP effect size for the full scale, the PP effect sizes were increased by 10% with the 13-item version (Δd = 0.02) and by 60% in the three-item and five-item versions ($0.11 \leq \Delta d \leq 0.12$). The longitudinal diary study (step 3) showed that state paranoia scores substantially varied within subjects even at the subclinical level with 26.5% (three-item version) and 31.7% (five-item version) of total variation in paranoia scores due to within-subject variation. Finally, all tests for convergent validity were significant and all versions yielded patterns of a higher correlation with other paranoia questionnaires ($0.472 \leq r \leq 0.545$) than with a social anxiety questionnaires ($0.417 \leq r \leq 0.459$)

Discussion. The analyses produced two versions of a brief state Paranoia Checklist that are sufficiently short to be included in ambulatory assessment studies, as well as one 13-item state Paranoia Checklist. Due to the fact that the item selection was based on multiple studies encompassing samples from the full continuum of paranoia and diverse paradigms to increase or decrease state paranoia, we can assume that the change-sensitivity is not limited to specific settings or study types. Regarding the content of the item selections, it needs noting that even the briefest version of the scale (three items) retains a direct assessment of the two defining characteristic of paranoia (Freeman, 2007): the fear or anticipation of harm ("I need to be on my guard against others") intentionally directed at the individual by a perpetrator ("people are trying to make me upset"). In line with this, even the brief versions show a higher correlation with other paranoia assessments (i.e., convergent validity) than with social anxiety (i.e., discriminant validity), despite the fact that social anxiety and

paranoia have repeatedly been shown to overlap considerably (Freeman et al., 2008; Gilbert, Boxall, Cheung, & Irons, 2005; Lysaker et al., 2010; Taylor & Stopa, 2013).

In sum, all analyses indicate that these revised versions equal the original Paranoia Checklist in psychometric quality, while simultaneously showing sensitivity to change. Future studies can use the state versions of the Paranoia Checklist to ensure valid results in experimental, longitudinal, and ambulatory assessment research.

3.3. Study 3. Development of a change-sensitive state measure for hallucination spectrum experiences

Schlier, B., Hennig, T., & Lincoln, T. M. (2017). Measuring fluctuations across the Continuum of Auditory Hallucinations. Development and validation of a state inventory. *Psychiatry Research, 253*, 325–332.

Background. In many aspects, the current status of momentary assessment of auditory hallucinatory experiences mirrors the previously described status regarding the momentary assessment of paranoia: Established self-report questionnaires were developed for retrospective assessment (Larøi et al., 2004; Launay & Slade, 1981; Morrison et al., 2002; Steel, Hemsley, & Jones, 1996) and thoroughly validated state questionnaires do not exist. Perhaps due to the experiential nature of hallucinations and the resulting face-validity of simply inquiring a person whether they "have heard […] things others could not" (Barrantes-Vidal, Chun, Myin-Germeys, & Kwapil, 2013), ambulatory assessment in psychosis almost exclusively utilizes one-item assessments for auditory hallucinations. In contrast to this assessment practice, the continuum of hallucination spectrum experiences encompasses a large variety of qualitatively different precursor experiences, including early precursors such as vivid mental imagery (Waters et al., 2012), and later precursors such as intrusive thoughts (Waters et al., 2003) or sensitivity to auditory stimuli (Bell et al., 2010). Thus, only a fraction of the range of hallucination spectrum experiences is captured in current state-assessments. However, typical items in existing "trait-like" hallucination spectrum experience questionnaires often pertain to experiences specific to a certain context or content (e.g., mistakenly hearing one's phone ring; Morrison et al., 2002). Consequently, they are of limited use in ambulatory assessment, where context and content vary considerably and the duration of individual assessments needs to be brief. Longitudinal research on the continuum of auditory hallucinations needs assessment methods that tap into the full

spectrum of subclinical and clinical hallucination spectrum experiences with few items describing experiences that theoretically apply in any everyday-life situation.

In this study, we aimed to develop a state self-report questionnaire, the Continuum of Auditory Hallucinations - State Assessment (CAHSA), that captures auditory hallucinations as well as the most common subclinical precursors (i.e., vivid mental imagery, intrusive thoughts, and perceptual sensitivity; Bell et al., 2010). First, an item list was selected based the items' within-subject variation in longitudinal assessment (step 1) and subjected to factorial and criterion validation (step 2). Next, sensitivity to change in population samples with and without a history of self-reported positive symptoms was analyzed in a second longitudinal study (step 3). Finally, the internal structure of auditory hallucinations and the three precursors along the continuum of hallucination spectrum experiences was explored cross-sectionally and longitudinally (steps 2 and 3).

Methods. In step 1, a set of items that were generated on the basis of existing trait measures of hallucinatory experiences (Grant et al., 2013; Larøi et al., 2004; Launay & Slade, 1981; Morrison et al., 2002; Steel et al., 1996; Stefanis et al., 2002). All items suitable for self-assessment unspecific to a certain context were added to state item lists for vivid imagination, intrusive thoughts, perceptual sensitivity, and auditory hallucinations. In a first pilot online study, these items were answered by a population sample once (N = 84, 60.7% female, age: M = 25.49, SD = 5.51) or once per day for seven consecutive days (subsample: n = 24, 60.0% female, age: M = 24.92, SD = 5.48). Items with low item-scale correlation and/or low within-subject variation in a random intercept multilevel regression of daily assessments nested in participants were excluded from the final item list.

In a second online study (step 2), a large population sample (N = 534, 67.6% female, age: M = 21.31, SD = 1.73) answered the final CAHSA item list as well as the CAPE (Stefanis et al., 2002). Model fit of a four factor solution was tested with CFA and criterion validity was assessed with correlation tests between of CAHSA-scores with CAPE positive symptom scores (convergent validity), as well as CAPE depression and negative symptom scores (discriminant validity). Moreover, interrelation of the four factors assessed by the CAHSA was explored using network analysis of the partial correlations of the factor scores.

In step 3, sensitivity to change of the CAHSA was tested in two population samples with low (n = 43, 64.3% female, age: M = 21.35, SD = 1.51) and high levels (n = 42, 62.8% female, age: M = 21.35, SD = 1.38) of lifetime-experiences of positive symptoms. Group

allocation was determined by a screening assessment with the CAPE (Stefanis et al., 2002). With the pooled data from the validation study (study 1), the 25% and 75% quantile of the CAPE positive symptom score were determined and served as cut-off for the low levels and high levels of positive symptoms group, respectively. Participants recruited into one of the samples were invited to the Universität Hamburg for the baseline assessment and answered the CAHSA online once per day for 14 consecutive days via smartphone or computer. Daily variation in hallucination spectrum experiences were explored with analyses of the within-subject variation similar to the analysis strategy in study 2, step 3. Finally, the analysis of the interrelation of CAHSA factors was continued with time-lagged multilevel-regression models for each CAHSA-factor predicted by all four factors from the previous time-point.

Main results. The selection of items based on item-scale correlation and within-subject variation (step 1) yielded a nine-item list, consisting of two items for vivid imagination, intrusive thought, and perceptual sensitivity, respectively, as well as three items for auditory hallucinations. CFA of the nine-item questionnaire (step 2) yielded good model fit according to all indices tested (*CFI* = 0.988, *RMSEA* = 0.029, *SRMR* = 0.025). This remained unchanged when a second-order global factor was added to the model (*CFI* = 0.959, *RMSEA* = 0.050, *SRMR* = 0.050). All factor scores and subscales showed larger correlations with the CAPE positive symptom score than with the negative symptom or depression score. In both the low levels and high levels of positive symptoms group (step 3), a substantial amount of within-subject variation was found for the CAHSA total score (50.1% and 38.5%, respectively) and for all four subscales (44.4% to 67.0% and 33.3% to 57.2%).

Network analysis based on the partial correlations of the factors (step 2) and time-lagged multilevel-regression (step 3) yielded a consistent pattern of associations between the precursor-factors and auditory hallucinations (see Figure 2). As can be seen, this pattern consisted of associations between vivid imagination and concurrent/later perceptual sensitivity and intrusive thought, an interrelation of perceptual sensitivity and intrusive thought, and correlations of intrusive thought and perceptual sensitivity with concurrent/later hallucinations.

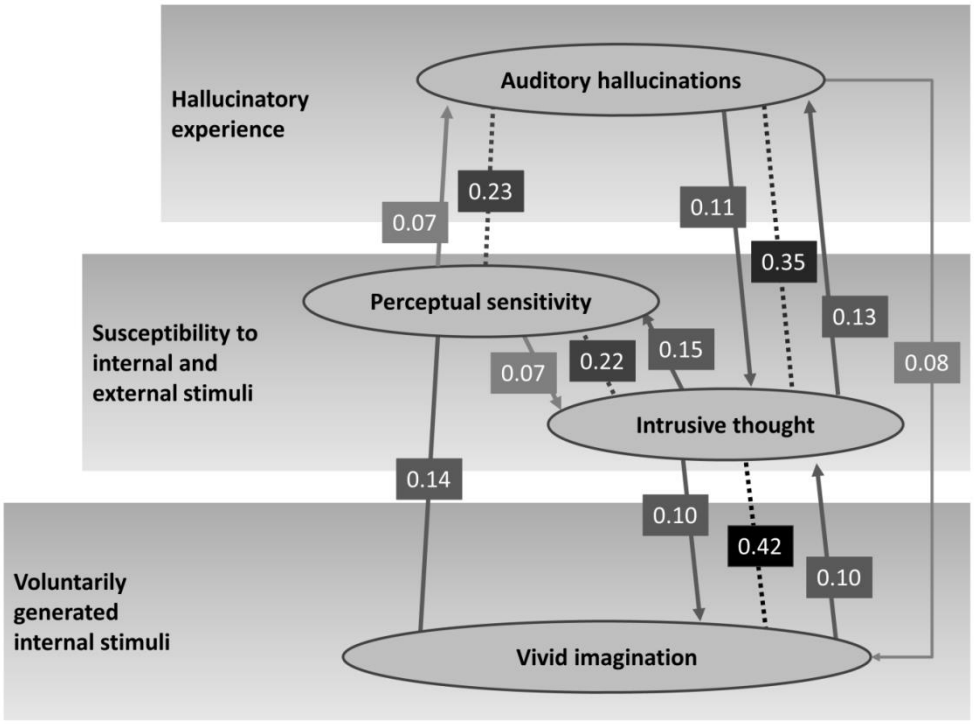

Figure 2. Results of the network model (dashed lines) and time-lagged multilevel regressions (arrows). Significant partial correlations and z-standardized regression coefficients are shown. Darker colored lines mark larger coefficients.

Discussion. Development and validation of the nine-item CAHSA yielded consistent results in terms of factor structure, criterion validity, and sensitivity to change. Moreover, the CAHSA includes subclinical hallucination precursors that have not been assessed together in one questionnaire before (Bell et al., 2010). The results from cross-sectional and longitudinal analysis of the association between these factors provides empirical support for process models of the etiology of hallucinations (e.g., Waters et al., 2012). As can be seen in Figure 2, voluntarily generated vivid internal stimuli are at the lower, subclinical end and auditory hallucinations at the upper end of the continuum of hallucination spectrum experiences. This is in line with a long-term process model from vivid mental imagery over intrusiveness of thought processes to actual hallucinations that has been described in an integrated model of hallucinations (Waters et al., 2012). Interestingly, these associations between subclinical and clinical hallucination spectrum experiences are not only found over a long time of symptom development as implicated in this etiological model, but were also consistently found within the time-frame of mere days in this study. Thus, this validation process also produces some evidence for interconnected state fluctuations in hallucination spectrum

experiences that need to be explored in further etiological and ambulatory assessment research.

It needs noting that for the entire scale development process, only community samples were recruited. This does not necessarily limit the use of the CAHSA to subclinical samples. The source questionnaires for the CAHSA item list have been shown to produce equal factor structures in clinical and population samples (e.g., the Launay Slade Hallucination Scale, Serper, Dill, Chang, Kot, & Elliot, 2005). Nevertheless, future research is warranted to further validate of the CAHSA in clinical samples. At the moment, the CAHSA constitutes a brief state measure of hallucination-like experiences and auditory hallucinations without restrictions to a specific context or content of the assessed experiences.

4. Part II: Longitudinal and ambulatory assessment studies on stress and psychotic symptoms

In the second part of this dissertation, the previously developed self-report assessments are utilized in three studies that assess the mechanisms and dynamics of the relationship between stress and psychotic experiences and symptoms across the continuum of psychosis. The studies focus on subclinical samples to elucidate the mechanisms of the formation of psychotic experiences and on patients with psychosis over the course of therapy to explore the mechanism of symptom reduction.

In study 4, the symptom phase approach is transferred to an ambulatory assessment of subclinical paranoia and hallucination spectrum experiences to test for alterations in self-reported and physiological stress parameters over the course of momentary psychotic experiences. In study 5, the time-order and association between social stressors and hallucination spectrum experiences in a subclinical sample is tested. Finally, in study 6, it is tested whether improvement in coping with internal and external stressors constitutes a mechanism of change that explains the continuous symptomatic improvement over the course of cognitive behavioral therapy.

4.1. Study 4. Changes in self-reported and physiological stress over the course of momentary psychotic experiences

Schlier, B., Krkovic, K., Clamor, A., & Lincoln, T. M. (submitted for publication). Autonomic arousal during psychosis spectrum experiences: results from a high resolution ambulatory assessment study over the course of symptom on- and offset.

Background. As has been described before, some ambulatory assessment studies (e.g., Delespaul, deVries, & van Os, 2002) utilized the near real-time assessment of symptom levels to infer discrete momentary symptom episodes. This approach allows to evaluate the role of momentary stress levels as a predictor and/or consequence of positive psychotic experiences and symptoms. Specifically, alterations in stress levels immediately before, during, and immediately after the emergence of momentary symptom episodes in everyday life can be assessed. Assessing stress levels over the course of momentary symptom episodes can provide crucial information, not only in terms of the role of stress as a causal or maintaining factor (e.g., Howes & Murray, 2014), but also in terms of corroborating psychological models (Myin-Germeys et al., 2009). For example, declining stress levels from immediately prior to immediately after a momentary paranoia episode could be interpreted as evidence for the theory that paranoia constitutes a dysfunctional self-regulation strategy that is initially used because it provides a short term amelioration of a stressful state (Clamor & Krkovic, 2018; Lincoln, Stahnke, & Moritz, 2014).

In order to ensure an unbiased assessment of stress over the duration of momentary symptom episodes, the methodological opportunities and limitations derived from previous symptom phase and ambulatory assessment studies need to be considered: Previous studies utilized standard 90 minute assessment intervals (Delespaul et al., 2002; Oorschot et al., 2012; Thewissen et al., 2011). This interval length does not match a median duration of momentary symptom episode, which is well below one hour (Steel et al., 2007). In consequence, the majority of symptom episodes derived from 90 minute interval ambulatory assessment is not captured according to their real-time duration. Furthermore, previous definitions of what constitutes the “presence of a symptom” in terms of the self-rated symptom level in an ambulatory assessment measure using Likert scales have been somewhat arbitrary. Most studies used the mid-point of said Likert scales as the threshold for the absence vs. presence (Oorschot et al., 2012; Thewissen et al., 2011). To date, no study provided a theoretical or methodological explanation, why symptoms, such as

auditory hallucinations, are considered to be definitely present when the item “I hear voices” (Oorschot et al., 2012) is self-rated with a “4” on scale from “1 = not at all” to “7 = very”, but not when it is rated with a “3”. Finally, recent ambulatory assessment studies have successfully included an ambulatory sensor assessment of physiological stress parameters, consisting of monitoring of the heart rate to assess the HRV (Cella et al., 2018; Kimhy et al., 2017) and of the electrodermal activity to assess the skin conductance level (SCL, Cella et al., 2017). To date, however, no study has connected the symptom phase approach with sensor monitoring to provide a multifaceted perspective of the stress reaction to momentary symptom episodes, including assessment of the stress levels prior to and following a momentary symptom episode.

The aim of study 4 was to utilize the questionnaires developed in studies 2 and 3 to establish the presence of psychotic experiences in a psychometrically reliable and valid way. Furthermore, we aimed to map the self-reported and physiological stress levels over the course of paranoia and hallucination spectrum experience episodes. We expected to find increases in self-reported stress and SCL and a decrease in HRV preceding the onset of momentary episodes and during momentary episodes. Furthermore, we explored whether alterations in self-reported stress, SCL and HRV persisted prior to and immediately after momentary episodes.

Methods. Participants with elevated levels of positive symptoms (*n* = 67 out of a screened sample of *N* = 292) were included in this study (71.6% female, age: *M* = 23.01, *SD* = 4.63). Similar to study 3, step 3, a screening assessment with the CAPE (Stefanis et al., 2002) preceded inclusion in the study. Participants were included, when their CAPE positive symptom score exceeded the median level of the large pooled data sample from study 1.

For the duration of one day (from 9am to 22pm), participants reported their current stress levels, current levels of paranoia, and to what extent they had hallucination spectrum experiences in 20 minute intervals using a Motorola Moto G smartphone with a pre-installed movisensXS EMA application (movisens GmbH). For all items, participants answered whether they applied to them on 11 point Likert scales (0 = ”not at all”; 10 = ”very much”). Self-reported stress was assessed with a four-item state stress assessment used in experimental stress-induction studies (e.g., Lincoln, Köther, Hartmann, Kempkensteffen, & Moritz, 2015). Paranoia was assessed with the three-item brief state Paranoia Checklist developed and validated in study 2. Hallucination spectrum experiences were assessed with an abbreviated

version of the CAHSA developed in study 3. The items of each CAHSA factor were summarized in one item. For example the three CAHSA items for auditory hallucinations were summarized into “I have heard something others could not hear (e.g., random noise sounding like someone mumbling or hearing a voice in my head)”. Internal consistency at the within-subject level was acceptable for self-reported stress (α = 0.73) and paranoia (α = 0.62), but low for hallucination spectrum experiences (α = 0.51).

For the duration of the ambulatory assessment, heart rate and SCL were measured continuously with two 62.3 x 38.6 x 11.5 mm ambulatory sensors, the Movisens ecgMove and the Movisens edaMove (Movisens GmbH). The edaMove was attached to the non-dominant arm with a wristband and SCL was monitored with a 32 Hz sample rate using two reusable non-polarizing sintered Ag/AgCl-edaMove-electrodes attached to the inner wrist. The ecgMove was attached to the left side of the chest with two disposable, self-adhesive Ag/AgCl-electrodes (Ambu® BlueSensor VL). The range-corrected SCL was calculated for each participant. For HRV, we calculated the root mean square of successive normal-to-normal interval differences (RMSSD), a frequently used parameter reflecting parasympathetic activity (Laborde, Mosley, & Thayer, 2017). Physiological parameters were calculated and corrected for artefacts using the DataAnalyzer (Movisens GmbH) and averaged for each 20 minute interval.

Using the within-subject reliability, a reliable change index (RCI; Jacobson & Truax, 1991) was calculated for the Paranoia Checklist (*RCI* = 1.51) and the CAHSA mean scores (*RCI* = 2.33), respectively. For each interval the presence of paranoia and hallucination spectrum experiences was determined based on whether the respective score was reliably different from the lower end of the range (mean score = 0, all respective items indicated to “not at all” apply at the respective assessment). Assessment intervals were then categorized into event phases for paranoia and hallucination spectrum experiences, respectively. Based on the presence or absence of the respective symptom at a given interval and their neighboring intervals, the interval was classified as (1) “no event”, (2) “pre-onset”, (3) “event”, (4) “pre-offset”, or (5) “post offset” phase (for an example, see Figure 3). Six random slope, fixed intercept multilevel regressions of assessments nested in participants were calculated. Paranoia phases or hallucination spectrum experience phases were the independent variable and one of the stress parameters (self-report, SCL, and RMSSD) the dependent variable.

Stress levels at all event phases (2-5) were contrasted with stress levels at respective no-event phase. All significance tests were Bonferroni-Holm corrected.

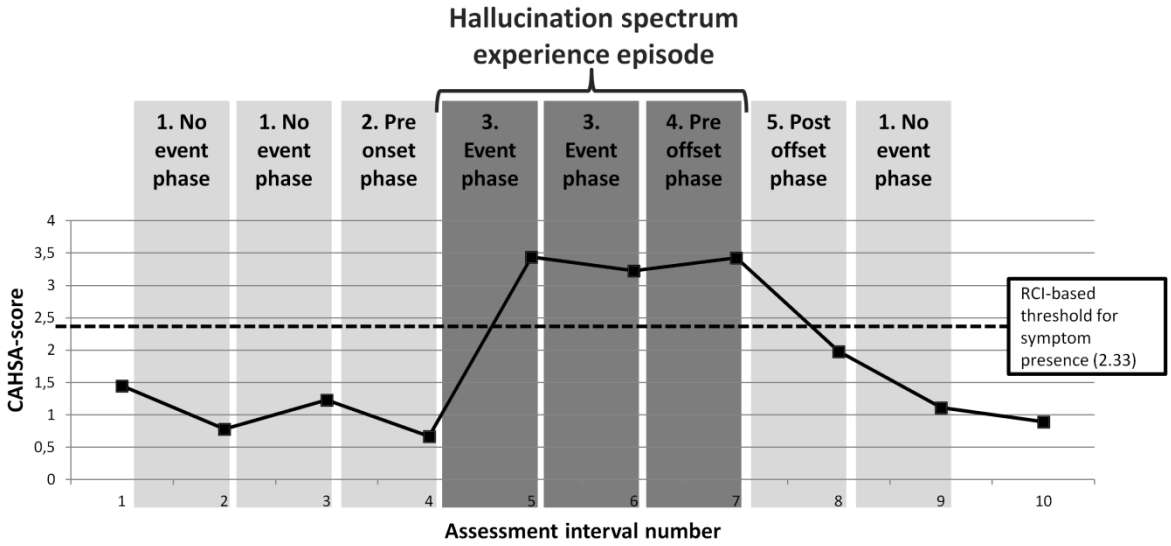

Figure 3. Example of the phase allocation process for hallucination spectrum experiences based on the CAHSA scores of a participant (black line). Hallucination spectrum experiences are present in intervals with a CAHSA score above the RCI (dashed line). Based on symptom presence in a given interval, the prior interval and the following interval, it is categorized in one of the five hallucination spectrum experience event phases.

Main results. Over the course of paranoia phases, stress levels diverged from no event phases in all three stress parameters and were u-shaped over the course of the successive phases (see Figure 4): At pre-onset phases self-reported stress levels increased (b = 0.850, T = 5.15, p_{corr} < 0.001) and RMSSD decreased (b = -10.008, T = -4.85, p_{corr} < 0.001). At event-phases as well as pre-offset phases increased self-reported stress (event phases: b = 1.561, T = 10.71, p_{corr} < 0.001, pre-offset phases: b = 1.425, T = 9.16, p_{corr} < 0.001), increased SCL (event phases: b = 0.129, T = 5.26, p_{corr} < 0.001, pre-offset phases: b = 0.133, T = 4.87, p_{corr} < 0.001), and decreased RMSSD (event phases: b = -6.879, T = -3.60, p_{corr} = 0.009, pre-offset phases: b = -9.526, T = -4.81, p_{corr} < 0.001) were found. Finally, for post-offset phases, stress parameters no longer significantly differenced from no event phases.

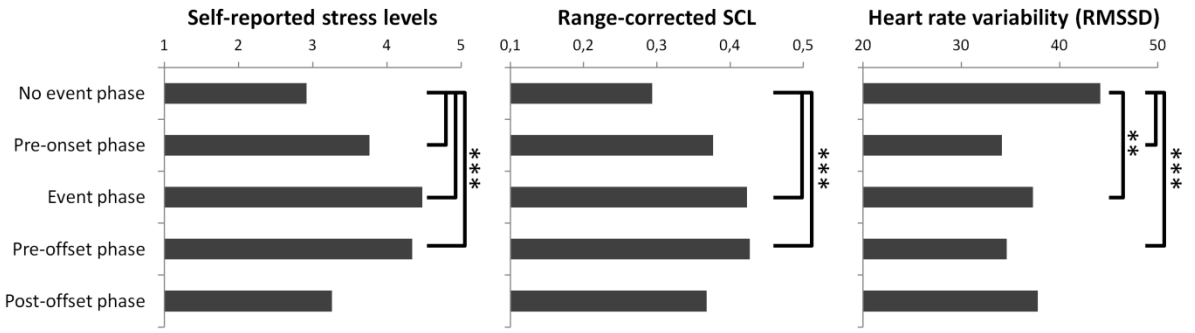

Figure 4. Results of the multilevel models of paranoia phase predicting stress levels in self-report, range-corrected SCL, and RMSSD. *** = $p_{corr} < 0.001$, ** = $p_{corr} < 0.01$

Regarding hallucination spectrum experiences, none of the stress parameters differed from no event phases at pre-onset, event, pre-offset, or post-offset phases. Exploratory analysis of the different types of hallucination spectrum experiences (using event phases defined by symptom presence in all intervals with the item score >0; Delespaul et al., 2002) yielded diverging patterns of significant results: No significant effects were found for vivid imagination. For intrusive thoughts, decreases in RMSSD were found at event phases (b = -6.102, T = -3.61, p_{corr} = 0.015) and pre-offset phases (b = -7.239, T = -4.02, p_{corr} = 0.003). For perceptual sensitivity SCL was increased at pre-onset phases (b = 0.094, T = 4.02, p_{corr} = 0.003), whereas both self-reported stress and SCL were increased at event phases (self-report: b = 0.600, T = 4.20, p_{corr} = 0.001; SCL: b = 0.088, T = 3.96, p_{corr} = 0.004) and pre-offset phases (self-report: b = 0.576, T = 3.90, p_{corr} = 0.004; SCL: b = 0.089, T = 3.60, p_{corr} = 0.016). Finally, self-reported stress levels were increased during auditory hallucination event phases (b = 0.920, T = 4.22, p_{corr} = 0.001) and pre-offset phases (b = 0.812, T = 4.18, p_{corr} = 0.001).

Discussion. In line with our hypotheses and with a previous ambulatory assessment study (Thewissen et al., 2011), self-reported stress levels were increased prior to and during paranoia episodes. Furthermore, this pattern was found not only for self-reported stress but also for the parasympathetic physiological reaction (RMSSD), whereas sympathetic alterations (SCL) were only found during the paranoia episodes. This temporal pattern mirrors theoretical accounts that a preexisting reduction of parasympathetic activity leads to a dominant state of sympathetic arousal over the course of psychotic states (Montaquila et al., 2015). Finally, no stress parameter differed significantly from no event phases to post event phases, which is in line with the notion that paranoia can be understood as a

dysfunctional cognitive coping style that ends a stress-eliciting state in the short term (Bentall et al., 1994; Maher, 1988) at the cost of ever increasing the level of persecutory ideation, which ultimately leads to the persistence of the symptoms.

Contrary to our hypotheses, we found no alteration in any stress parameter over the course of hallucination spectrum experiences. The fact that in subclinical populations, hallucinations have repeatedly been found to be unrelated to distress (Larøi et al., 2012) constitutes a potential explanation for this pattern. However, some limitations of the hallucination spectrum experience assessment need to be considered. The internal consistency of the modified brief CAHSA was low. Furthermore, exploratory item-based analysis of hallucination spectrum experiences yielded diverging patterns for the different types of experiences: For intrusive thoughts, perceptual sensitivity and hallucinations, significant findings in different stress parameters were found in event and post offset phases. Potentially, hallucination spectrum experiences at the lower end of the continuum (i.e., vivid imagination) are unrelated to distress, whereas experiencing phenomena closer to the upper (thus potentially clinical) end of the continuum (i.e., intrusive thought, perceptual sensitivity, and hallucinations) is associated with increased stress levels. However, these speculations need to be tested in future studies that utilize a more detailed assessment of hallucination spectrum experiences and more diverse (i.e., subclinical, at risk, and clinical) samples.

In sum, this study adds to the existing research on symptom phases by offering an alternative way to define symptom episodes, showing the feasibility of a sampling scheme that approximates the average duration of momentary symptom episodes more closely, and providing initial evidence for the convergence of self-reported and physiological stress parameters. This opens up the possibilities of varying sampling schemes in other samples as well to match the assessed phenomena and of supplementing or even replacing self-report stress assessment with physiological parameters to reduce the potential of reactivity effects and make ambulatory assessment procedures less distracting or taxing for participants.

4.2. Study 5. Social exclusion as a stressor contributing to the emergence of hallucination spectrum experiences

Schlier, B., Winkler, K., Jaya, E. S., & Lincoln, T. M. (2018). Fluctuations in Hallucination Spectrum Experiences Co-vary with Social Defeat but not with Social Deafferentation. A 3-Week Daily Assessment Study. *Cognitive Therapy and Research, 42*, 92-102.

Background. Following the finding that hallucination spectrum experiences are generally less consistently associated with preceding stress levels than paranoia in a subclinical population, we started to explore whether specific social stressors, emphasized by etiological models for psychosis (Hoffman, 2007, 2008; Selten & Cantor-Graae, 2005; Selten et al., 2013) predict emerging hallucination spectrum experiences more consistently and thus constitute triggers for these experiences in everyday life.

To this end, two competing models of the causal role of social factors were compared: The *social deafferentation hypothesis* (Hoffman, 2007, 2008) proposes that an objective lack of social contact can trigger a process in which the source for spurious neural information in brain regions associated with social cognition is misidentified as external social stimuli. This process manifests in self-generated 'phantom' experiences including "complex, emotionally compelling hallucinations" (Hoffman, 2007), comparable to the phantom limb sensation following lack of neural input after losing a limb. In contrast, the *social defeat hypothesis* (Selten & Cantor-Graae, 2005; Selten et al., 2013) postulates that only negatively appraised experiences of social exclusion constitute a social risk factor for psychosis. As has been shown in large epidemiological and population studies (Jaya & Lincoln, 2016; Stilo et al., 2013; Valmaggia et al., 2015; van Nierop et al., 2014), indicators of social exclusion from a majority group that bear a risk to be interpreted as defeating (e.g., growing up in an urban environment, migrant status, childhood trauma, low intelligence, and drug abuse; Selten et al., 2013) are associated with increased levels of psychotic symptoms. According to the social defeat hypothesis, experiences of social defeat gradually sensitize the mesolimbic dopamine system for negatively valent social stimuli, until an excess dopamine response to social defeat suffices to trigger psychosis symptoms. In sum both hypotheses emphasize the role of a form social isolation factor, but according to the social deafferentation hypothesis isolation needs to take the form of objective deprivation of social contact, whereas the social defeat hypothesis proposes the crucial factor to be the appraisal of exclusion and defeat irrespective of the objective amount of contact.

In this study, we tested whether the day to day fluctuations in social deafferentation and social defeat levels constitute potential triggers for episodes of auditory hallucinations and of their subclinical precursors in a community sample. We hypothesized that social deafferentation and social defeat co-vary with and precede the presence of hallucination spectrum experiences in daily life, whereas social deafferentation and social defeat are not predicted by preceding hallucination spectrum experiences. Finally, we tested whether these associations are specific to stress associated with social deafferentation or defeat and no mere by-product of general negative mood. We hypothesized that the associations between social factors and hallucination spectrum experiences remain stable when general mood levels are controlled for.

Methods. In a three week longitudinal online-study, a community sample (*N* = 75) recruited on social media and among university students provided one daily self-assessment of current hallucination spectrum experiences, of two indicators of current social deafferentation and social defeat, respectively, and current mood levels. Hallucination spectrum experiences were assessed with the nine-item CAHSA developed and validated in study 3. Social deafferentation was assessed with the two-item indicator “time spent alone” and the one-item indicator “amount of social interactions”, both of which were based on modified items from the environment and functioning section of the computerized Ecological Momentary Assessment Questionnaire (EMAc; Granholm, Loh, & Swendsen, 2007). The two indicators for social defeat included the EMAc-based two-item indicator “amount of unpleasant social interactions” and social exclusion, measured with the three-item group fit subscale of the Social Comparison Scale (Allan & Gilbert, 1995). Current mood levels were assessed with the six-item Multidimensional Mood Questionnaire (MDMQ; Wilhelm & Schoebi, 2007). CAHSA global and factor scores we dichotomized into “experiences not present” (i.e., score = 0) and “experiences present” (i.e., score > 0, similar to previously-used liberal classification system, Delespaul, deVries, & van Os, 2002) for each daily assessment. We calculated random intercept, random slope logistic multilevel regression models of the CAHSA global score and factor scores, predicted by one of the social deafferentation or social defeat indicators at the same day, respectively. For time-lagged associations, the respective social deafferentation/defeat indicators from the previous day were entered as predictors in another set of logistic multilevel regression models. Finally, reverse time-lagged effects of

dichotomized CAHSA scores predicting social deafferentation and social defeat indicators at the following day were tested using linear multilevel regression models.

Main results. The multilevel models for the hallucination spectrum experience global score yielded no significant effect of the social deafferentation predictor variables. Among the social defeat predictor variables, higher levels of social exclusion were significantly associated with the presence of hallucination spectrum experiences at the same day (*OR* = 1.270, *Z* = 2.10, *p* = 0.036) and at the following day (*OR* = 1.461, *Z* = 2.37, *p* = 0.018). These associations remained stable when mood (i.e. the MDMQ-scores) was controlled for (cross-sectional model: *OR* = 1.244, *Z* = 2.75, *p* = 0.006; time-lagged model: *OR* = 1.200, *Z* = 2.14, *p* = 0.032). No significant reverse time-lagged effect was found.

When individual CAHSA subscales were analyzed, the cross-sectional effect of social exclusion was found for the factors vivid imagination (*OR* = 1.175, *Z* = 2.28, *p* = 0.023), intrusive thoughts (*OR* = 1.242, *Z* = 2.70, *p* = 0.007), and perceptual sensitivity (*OR* = 1.272, *Z* = 2.44, *p* = 0.014). Furthermore, time-lagged prediction by social exclusion was significant for the presence of vivid imagination (*OR* = 1.215, *Z* = 2.46, *p* = 0.014) and intrusive thoughts (*OR* = 1.272, *Z* = 2.44, *p* = 0.015) at the following day. Finally, among the reverse prediction models, vivid imagination significantly predicted lower levels of social exclusion at the following day (*b* = 0.312, *T* = 3.09, *p* = 0.002).

Discussion. Contrary to our hypothesis, no associations were found between social deafferentation indicators and hallucination spectrum experiences, possibly indicating that this social risk factor plays no role in the emergence of these experiences at a subclinical level. It has to be noted though that large parts of the empirical evidence for the social deafferentation hypothesis consists of isolation experiments that induce extreme sensory deprivation (e.g., Schulman, Richlin, & Weinstein, 1967). It is likely that these levels of isolation are rarely achieved in the daily lives of the general population. Given that high risk groups and people with psychosis show increased levels of social withdrawal and more often report isolated living conditions (Kwapil, 1998; van Os, Driessen, Gunther, & Delespaul, 2000), we cannot exclude that social deafferentation becomes a trigger for hallucination spectrum experiences at a prodromal or acute psychotic phase.

In line with our hypothesis, we found that social exclusion, an indicator of social defeat, co-varies with and predicts some types of hallucination spectrum experiences. The fact that these associations pertained to subclinical experiences only may be due to the

sample type, which was not pre-selected for attenuated symptoms, leading to insufficient prevalence of auditory hallucinations (see Appendix E, supplements section). Nevertheless, our results are in line with a growing body of evidence, in which experimental induction of a feeling of exclusion increases positive psychotic symptoms in patients (Gradin et al., 2012), people at risk for psychosis (Lincoln, Sundag, Schlier, & Karow, 2018), and population samples (Kesting et al., 2013; Stewart et al., 2017; Westermann et al., 2012). Moreover, the influence of social exclusion on hallucination spectrum experiences remained stable when overall mood levels for a given day were controlled, indicating that social exclusion is more than just one stressor among a large group of stress-related triggers for hallucination spectrum experiences. Finally, the interpretation that a specific social trigger instigates hallucination spectrum experiences is in line with the comparatively low stress reaction we found over the course of hallucination spectrum experience phases in study 4.

In sum, social defeat in the form of momentary social exclusion constitutes a trigger for hallucination spectrum experiences in healthy individuals. Future research needs to investigate the effect of social exclusion versus global stress levels across different psychotic symptoms and in different samples along the continuum of psychosis and to narrow down the sampling interval duration to a length that fits real-time assessment of social activity and of psychotic symptoms more closely.

4.3. Study 6. Coping with stressful experiences as a mechanism of change in cognitive behavioral therapy

Schlier, B., Ludwig, L., Wiesjahn, M., Jung, E., & Lincoln, T. M. (submitted for publication). Fostering coping as a mechanism of symptom change in cognitive behavioural therapy for psychosis.

Background. Based on the results that stress triggers psychotic symptoms, the aim of the final study was to examine the role of effective coping with stressful situations in symptomatic improvement. Improving effective coping has always been a target in cognitive behavioral therapy for psychosis (CBTp). Early conceptualizations of CBTp were focused on improving patients' coping strategies for the distress due to psychotic symptoms (Tarrier et al., 1993). Over the recent decades, this focus has been expanded to include coping with distress in general, with distress caused by symptoms, and with those stressors identified in individualized cognitive therapy to be triggering symptoms (NCCMH, 2014).

Previous research has integrated a longitudinal multilevel assessment scheme into research of state of the art cognitive behavioral therapy to track the symptomatic improvement as a function of the progressing therapy (Lincoln et al., 2016), specific therapy content (Schneider, Cludius, Lutz, Moritz, & Rubel, 2018) or fluctuations in therapeutic alliance (Rubel, Zilcha-Mano, Feils-Klaus, & Lutz, 2018). Based on this approach, it is possible to link the amelioration of symptoms to improvement in a potential mechanism of change, such as more effective coping with stress. Specifically, the association and time-order of changes in symptoms and mechanisms of change can be tracked.

Following this approach, we tested whether the association between therapy progress (i.e. the number of therapy sessions a patient had received at a given week) and symptomatic improvement in various positive and negative symptoms is mediated by preceding change in effective coping with a range of stressors, including daily hassles, symptoms, and negative emotions. We hypothesized (1) that coping mediates the association between therapy progress and time-lagged improvement in positive and negative symptoms. Furthermore, we hypothesized (2) that in line with a cause-effect relationship between coping and symptoms, there is no reverse mediation with preceding symptomatic improvement mediating the effect of therapy progress on time-lagged improvement in coping.

Methods. Data from a longitudinal CBTp trial with weekly self-assessments of coping and symptoms (Lincoln et al., 2016) was analyzed for this study. Patients with psychosis (n = 57, 40.3% female, age: M = 14.05, SD = 3,71) received 45 sessions of manual-based (Lincoln, 2014), state of the art, individualized CBTp at a German outpatient clinic. Following each session, coping was assessed with three items selected from an established therapy outcome questionnaire, the CHoice of Outcome In Cbt for psychosEs (CHOICE; Greenwood et al., 2010), that assesses successful coping with stressors in everyday life (daily hassles), with psychotic symptoms, and with negative emotions. Furthermore, psychotic symptoms were assessed with the suspiciousness-item of the nine-item Symptom Checklist (Klaghofer & Brähler, 2001) and an individualized selection of the ten items for the most prevalent positive symptoms, negative symptoms, and/or symptoms of depression, based on a baseline assessment with the German version of the CAPE validated in study 1. One multilevel structural equation model was calculated to test for within-subject mediation of therapy session number (independent variable) via coping (mediator, pathway a) on

suspiciousness, positive symptoms, negative symptoms and depression one week later (dependent variables 1-4, pathways $b_{1\text{-}4}$). To test for directionality, a reverse mediation model with symptoms (mediators 1-4, pathways $a_{rev,1\text{-}4}$) predicting later change in coping (dependent variable, pathways $b_{rev,1\text{-}4}$) was tested (reverse indirect effects $ab_{rev,1\text{-}4}$). For all pathways and indirect effects, the unconflated, within-subject effects were calculated.

Main results. The mediation was significant for suspiciousness (*a* = -0.026, *SE* = 0.006, *Z* = 4.15, *p* < 0.001; b_1 = -0.049, *SE* = 0.021, *Z* = -2.29, *p* = 0.022; *indirect effect* ab_1 = -0.001, *SE* < 0.001, *Z* = -2.87, *p* = 0.004), CAPE negative symptoms (b_3 = -0.201, *SE* = 0.061, *Z* = -3.29, *p* < 0.001; *indirect effect* ab_3 = -0.005, *SE* = 0.002, *Z* = -3.00, *p* = 0.003), and CAPE depression (b_4 = -0.190, *SE* = 0.058, *Z* = -3.30, *p* < 0.001; *indirect effect* ab_4 = -0.005, *SE* = 0.002, *Z* = -2.65, *p* = 0.008), but not for CAPE positive symptoms. Reverse mediation was found for CAPE negative symptoms ($a_{rev,3}$ = -0.037, *SE* = 0.009, *Z* = -4.21, *p* < 0.001; $b_{rev,3}$ = -0.090, *SE* = 0.032, *Z* = -2.85, *p* = 0.004; *reverse indirect effect* $ab_{rev,3}$ = 0.009, *SE* = 0.005, *Z* = -1.99, *p* = 0.014) and CAPE depression ($a_{rev,4}$ = -0.021, *SE* = 0.008, *Z* = -2.47, *p* = 0.013; $b_{rev,4}$ = -0.156, *SE* = 0.029, *Z* = -5.43, *p* < 0.001; *reverse indirect effect* $ab_{rev,4}$ = 0.009, *SE* = 0.005, *Z* = -1.99, *p* = 0.029).

An exploratory analysis of single symptoms according to the alternative CAPE factor structure tested in study 1, yielded some evidence for mediation without corresponding reverse mediation for the positive symptoms hallucinations (*a* = 0.026, *SE* = 0.006, *Z* = 4.07, *p* < 0.001; b_1 = -0.349, *SE* = 0.205, *Z* = -1.70, *p* = 0.089; *indirect effect ab* = -0.009, *SE* = 0.005, *Z* = -1.99, *p* = 0.046) and bizarre experiences *(a* = 0.026, *SE* = 0.006, *Z* = 4.09, *p* < 0.001; b_1 = -0.207, *SE* < 0.108, *Z* = -1.91, *p* = 0.056; *indirect effect ab* = -0.005, *SE* = 0.002, *Z* = -2.48, *p* = 0.013), whereas a significant direct effect without mediation via coping was found for the CAPE based paranoia scores (*direct effect* = -0.021, *SE* = 0.008, *Z* = 2.95 *p* = 0.003).

Discussion. In line with our hypotheses, we found significant mediation effects for some positive symptoms (i.e., suspiciousness, hallucinations, and bizarre experiences), negative symptoms, and depression. Furthermore, for suspiciousness, hallucinations, and bizarre experiences, no reverse mediation was found, indicating a uni-directional path from progress in therapy via more effective coping to improvement in some positive symptoms. The difference in results for the outcomes suspiciousness and paranoia is puzzling. Both outcomes tap into persecutory beliefs. In both outcomes, we found improvement over the course of therapy. Yet, only the improvement in suspiciousness is mediated by preceding improvement in coping. What seems to be an in inconsistency, however, could be the result

of the difference in assessment. Every participant answered the same item for suspiciousness, whereas participants only answered those paranoia items that were ranked as one of the ten most frequent and distressing items in the CAPE baseline assessment. Consequently, the individualized paranoia assessment consists of a pre-selected subgroup of the most severe persecutory beliefs in our sample. Perhaps, these severe paranoia symptoms are not susceptible to change via improved coping alone. Instead improvement may be the result of other mechanisms of change such as changes in dysfunctional beliefs and negative self-schemata (Kuipers et al., 2006) or in cognitive processing (Moritz, Veckenstedt, Randjbar, Vitzthum, & Woodward, 2011; Moritz, Andreou, et al., 2014). Uni-directionality of all significant results for positive symptoms corroborated the theory that effective coping leads to symptomatic reduction via eliminating stress-related symptom triggers or via de-sensitization to stress (Peters et al., 2012; Reininghaus, Depp, & Myin-Germeys, 2016) and subsequent elimination of the cognitive and emotional impact of stressors . For negative symptoms and depression, however, there is no clear answer to the question of directionality. Possibly, the loss of interpersonal resources due to social withdrawal (Evert, Harvey, Trauer, & Herrman, 2003), the reduction of goal-directed behavior aimed at a positive outcome due to amotivation (Schlier, Engel, Fladung, Fritzsche, & Lincoln, 2017), and/or depression-related loss of reinforcement (Lewinsohn, 1974) hamper effective coping. Loss of coping resources in turn further exacerbates negative symptoms and symptoms of depression, leading to a vicious cycle. However, in terms of therapy, this interrelation could indicate that improvement in either negative symptoms or coping with a targeted intervention has a chance to spread to the other outcomes.

In sum, we found some evidence that coping with demanding, stressful situations constitutes a mechanism of symptomatic change in CBTp. Future studies are needed to further investigate this finding in order to optimize CBTp. Specifically, session-wise longitudinal approaches are required to compare the separate effect and combined effect of different potential mechanisms of change and as a tool for dismantling research to connect changes in mediators (e.g., coping) and therapy outcomes (e.g., symptomatic improvement) to specific interventions and thus evaluate their efficacy over the course of therapy.

5. General discussion

This dissertation project aimed at developing and validating assessment methods to allow for longitudinal and ambulatory assessment along the continuum of psychosis.

Furthermore, these methods were to be implemented in longitudinal research to explore the role of stress in the formation of psychotic experiences prior to a pathological state as well as to explore the role of coping with stress as a mechanism of symptomatic improvement. Based on the results of the studies outlined before, these general research questions will now be discussed.

5.1. Trait and state assessment of psychotic experiences and symptoms

Regarding the CAPE, the results of this project are mixed: The validation of the CAPE yielded equivalent results for the original and new single symptom based factor structure. However, a pattern of one diverging finding prevailed and may be rooted in an upper limit of model fit inherent to the assessed phenomena: Psychotic symptoms are half-normally distributed in the general population (van Os et al., 2009) with a large positive skew (i.e., many people experiencing no or few symptoms and few people experiencing many symptoms). Thus, the success of any attempts to further increase the factorial validity of existing trait measure with common methods may be limited. At the present moment, validity of the CAPE can be assumed under the premise of an artificial limit to comparative model fit indices, and the use of this scale as a general estimate of life-time psychotic experiences can continue. Nevertheless, the popularity of the CAPE warrants further efforts to revise its content in order to increase validity.

In contrast to the mixed result regarding the CAPE, the validation of state assessments for paranoia and hallucination spectrum experiences in continuum samples was successful in all steps of the validation procedure. For paranoia, this was accomplished with a set of core items that are part of the “mild threat” midlevel category of the hierarchy of paranoia (Freeman et al., 2005). As described before, these mild threat beliefs share core features with clinical levels of paranoia (Freeman, 2007). Moreover, as mild threat beliefs are by definition unspecific, vague feelings of impeding harm by a third party (Freeman et al., 2005), it is possible that they constitute the state component of paranoia. In contrast, severe, more complex interpretations (e.g., conspiracy theories or theories about the long-term plans of the allegedly persecuting parties) may constitute a stable component of paranoia. Using another distinction (Moritz, van Quaquebeke, & Lincoln, 2012), one could hypothesize that suspiciousness constitutes the fluctuating state aspect, whereas persecutory beliefs are the trait aspect of paranoia. To corroborate this hypothesis, however, further testing of the structure of persecutory beliefs in general is needed. In the

meantime, the state Paranoia Checklists constitutes a viable, thoroughly validated tool for future research.

Regarding the state assessment of hallucination spectrum experiences, a broad spectrum of subclinical precursor experiences as well as auditory hallucinations proved to be feasible in longitudinal and ambulatory assessment. As has been described before (see Figure 2, p. 29), the pattern of direct and indirect pathways between these precursors and clinical-level auditory hallucinations equaled the phenomenological pathway described by etiological models for hallucinations (Waters et al., 2012). According to these models, external input or internal conditions can cause a "hyperactivation in functional networks involving the auditory cortex that generates aberrant auditory signals" (Waters et al., 2012, p. 688). Furthermore "specific forms of auditory signals […] may be more likely to be converted into [auditory hallucinations]" (Waters et al., 2012, p. 688), which also "account[s] for some of the verbal phenomenological properties of the [auditory hallucinations]" (Waters et al., 2012, p. 689). Possibly, susceptibility to hyperactivation by external input presents itself as a sensitization to auditory stimuli (i.e., perceptual sensitivity), whereas internal conditions of hyperactivation present themselves in the form of particularly vivid mental imagery (i.e., vivid imagination). In the sequence of processes "such information fails to be suppressed by faulty intentional inhibition mechanisms and becomes functionally autonomous" (Waters et al., 2012, p. 689). At first, this may present itself in the form of intrusiveness and a reduced sense of control of one's thoughts, which would be in line with the central role of intrusive thoughts in the hierarchical model that was found in study 3. Over time, however, as experiences intensify and/or beliefs about their uncontrollability are re-affirmed (Waters et al., 2012), they are gradually perceived as a genuine external stimulus (i.e., an auditory hallucination). Prior to this project, some cross-sectional evidence for the interrelation between single precursors and hallucinations existed (e.g., intrusive thoughts and voice-hearing; Morrison & Baker, 2000). Yet, the validation of the CAHSA included the first analysis of the interrelation and time-order of the full range of these phenomena in everyday life. Thus, the developed questionnaire not only allows for the assessment of the phenomenology of hallucination spectrum experiences, but also for the interplay between subclinical and clinical-level experiences.

In sum, the developed and validated state assessments can be used in future studies to ensure psychometric quality of ambulatory assessment and other repeated measure

designs. In fact, the state assessments have already been implemented in a multitude of studies, including ambulatory assessment studies in both general population (Hennig, Schlier, & Lincoln, in prep.) and patient samples (Krkovic, Clamor, Schlier, & Lincoln, submitted; Ludwig, Krkovic, Mehl, & Lincoln, in prep.) as well as experimental and quasi-experimental lab studies with repeated assessment in subclinical (Clamor, Koenig, Thayer, & Lincoln, 2016; Clamor & Krkovic, 2018; Gollwitzer, Wilczynska, & Jaya, 2018; Lincoln et al., 2018) and clinical samples (Cowles & Hogg, 2018). This may be interpreted as an indicator for the relevance and timeliness of these development and validation studies.

5.1.1. Implications for future studies using the validated state assessments

The results of the scale development and validation procedures so far open up several new possibilities for data analysis of ambulatory assessment studies. Specifically, these possibilities include the application of RCI based methods in different types of studies and the test for moderators (i.e., vulnerability or resilience factors) for the interrelation between subclinical and clinical hallucination spectrum experiences.

Based on the success of the multi item state instruments developed and validated in studies 2 and 3, RCI based statistical approaches as used in study 4 become a possibility for ambulatory assessment. The usefulness of this approach is not just limited to determining “reliable presence” of symptoms. The RCI can also become another method of determining reliable differences between two assessments. Thus with the assessment of hypothesized change (or lack of change), predictors of reliable reduction in momentary psychotic experiences can be connected to predictors using logistic multilevel regression in a way comparable to the strategy for data-analysis in study 5. Furthermore, the brief state Paranoia Checklist and the CAHSA could be used as feasible tools for ecological momentary interventions. In ecological momentary interventions, participants are provided with automated self-help strategies to ameliorate symptoms based on the results of continuous self-assessment (Heron & Smyth, 2010). The RCI-based thresholds for the brief state Paranoia-Checklist and the CAHSA could be used to optimize the automated presentation of interventions contingent on symptom emergence or sudden increases in symptoms (i.e., only a reliable difference between successive assessments cues a self-help intervention).

In addition to these possibilities for data-analysis based on reliable mean scores, the development of a brief assessment of a range of phenomena along the continuum of hallucination spectrum experiences provided new opportunities for etiological studies on

hallucination formation. Since time-lagged associations between subclinical precursors (e.g., vivid mental imagery and intrusive thoughts) and between precursors and clinical level hallucinations were found over brief periods of one day, the question of what modulates transition from precursor to more “severe” precursors to hallucinations can be investigated in everyday life within brief time periods. Based on these findings, ambulatory assessment using the CAHSA can explore, whether trait-level vulnerability factors govern the transition from one type of hallucination spectrum experience to another as has been proposed by various etiological theories. For example, neuro-cognitively rooted self-monitoring deficits (Frith, 2000) or beliefs about uncontrollability of thought processes (Morrison & Baker, 2000) predispose people to experiencing thoughts as intrusive or even alien, increasing the risk for experiencing internally generated stimuli as hallucinations. With the CAHSA, ambulatory assessment studies can investigate whether baseline levels in these vulnerability factors are a moderator of the time-lagged association between vivid imagination and intrusive thoughts or intrusive thoughts and hallucinations. Thus, the developed scales not only ensure psychometric quality but also extend the scope of possible avenues for researching the dynamics of symptom formation.

5.1.2. Future directions for optimization

Beyond the implications for utilization of the scales as they are, the results of the validation procedures have implications for the optimization of assessment methods when further improvement of the scales is aimed at.

With the assessment of momentary frequency/presence of paranoia and hallucination spectrum experiences in place, it becomes possible to add further dimensions to the assessments to the respective experiences, including for example distress or conviction for paranoia (Lincoln, 2007; Peters, Joseph, & Garety, 1999). In a diary study about the effect of self-compassion meditation on paranoia, this option was explored for the brief state Paranoia Checklist: For each item answered with more than the lower end of the score range, participants were asked how distressed they felt because of experiencing the phenomenon described in the item (Schlier, Ascone, & Lincoln, submitted). Regarding hallucination spectrum experiences, similar additions are likely to provide further insight into the phenomenology of subclinical experiences. Possible additional dimensions that have been used in trait measures include symptom distress, perceived control about the experiences, and disruption to other activities (Siddi et al., 2018).

Finally, several approaches are possible for the further improvement of trait and state assessment of psychotic experience frequency. Three strategies are conceivable and can be described based on the assumed core problem regarding the trait level assessment with the CAPE: First, it may be feasible to treat item scores of the CAPE in its existing form as non-parametric and try to validate the CAPE with non-parametric estimation methods. Second, the answer form may be optimized to allow for item scores with a normal distribution. At the moment, the standard four-point answer form includes the options "0 – never", "1 – sometimes", "2 – often", and "3 – nearly always" to quantify the frequency with which one previously experienced the described phenomena. Possibly, the skewness of item scores could be reduced by including a larger number for intermediary options with fixed frequencies such as "once or twice in my life", "once a month", and "once per week" instead of few extreme categories. The third and last possible option for improving trait assessment is to revise the CAPE and its items to include subclinical precursors of the symptoms assessed. Based on what we know about the distribution of milder forms and precursors of psychotic symptoms in the general population (Serper et al., 2005; van Os et al., 2009) and based on the results of this approach when developing the CAHSA (study 3), this option will most likely change the distribution of item scores, increase their variance, and change the pattern of item intercorrelations. However, this approach would also constitute a deviation of the original goal of assessing psychotic experience of equivalent phenomenology to the core symptoms of psychotic disorders (Stefanis et al., 2002). Thus, the preferable option for further improvement of trait assessments depends on whether the focus in terms of content should remain limited to the clinical-level symptoms. This decision, in turn, needs to be informed by etiological research on the continuity and hierarchy of subclinical and clinical experiences. To date, such research, however, mainly exists for the most common symptoms such as paranoia (Freeman et al., 2005) and hallucinations (Aleman, Nieuwenstein, Böcker, & De Haan, 2001; Larøi et al., 2004; Serper et al., 2005; Waters et al., 2003).

5.2. The roles of stressors, stress levels, and coping with stress

5.2.1. Stressors and stress levels prior to and during psychotic experiences

Taken together, the ambulatory assessment studies in subclinical populations showed that for paranoia, increased self-reported stress levels as well as physiological hyperarousal in general precede symptom emergence. For auditory hallucinations and their subclinical precursors, this association may be limited to specific social stressors such as present

experiences of social defeat. The findings converge on the fact that in the general population, stress caused due to taxing situations in daily life triggers psychotic experiences in healthy people.

Thus, on a large scale, the pathway from stress to psychotic symptoms found in several previous ambulatory assessment studies with patients extends to the full continuum of psychosis. This leads to the follow-up question of what (vulnerability-)mechanisms amplify the impact of stress and increase subclinical experiences to psychotic symptoms and how these mechanisms interact over time. Contemporary vulnerability stress theories feature a central mechanism by which continuous sensitization of the central nervous system over time leads to a hyperactivation of the dopamine system either directly (Howes & Murray, 2014) or as a by-product of general stress-sensitization (Selten et al., 2013; Walker & Diforio, 1997). Due to the fact that we did find a pattern increased stress levels prior to paranoia, but not prior to hallucination spectrum experiences in study 4, one could even speculate that the sensitization mechanisms diverge for different symptoms, with a stress-sensitization mechanism driving the emergence of early paranoid experiences and a mechanism related to dopamine hyperrelease driving the emergence of hallucination spectrum experiences. Taking into account the results of study 5, this latter mechanism could even be driven by a specific type of social stress indicative of experiencing social defeat. Of importance, this hypothesis of different sensitization processes would not be contradicted by findings of a broad range of triggers for all symptoms in patients (e.g., hyperarousal triggering hallucinations; Kimhy et al., 2017), since cross-sensitization over time is to be expected following repeated exposure to relevant stressors (Howes & Murray, 2014). Consequently, a clear picture of the etiological processes that start and underlie sensitization processes may best be found with further stressor studies using subclinical samples, in which the relevant neural systems have not yet been cross-sensitized to more atypical types of stressful events.

Another interesting finding is that paranoia and hallucination spectrum experiences differ in terms of hyperarousal and stress during the respective experience. In subclinical samples, hallucination spectrum experiences are not universally accompanied by stress and hyperarousal, whereas paranoid thoughts seem to universally coincide with stress. This is in line with an etiological model of experiential abnormalities (such as hallucination spectrum experiences) being an earlier part of the formation of clinical level symptoms (Howes & Murray, 2014). The model states that distress due to symptoms is not a product of the

abnormal experience itself, but of the delusional interpretation of the experience that makes the experience more distressful. Further corroboration of this theory with ambulatory assessment data, however, requires an analysis of the time order of hallucination spectrum experiences, paranoia, and stress levels.

Finally, in subclinical populations, self-reported stress and physiological hyperarousal seem to return to baseline following the end of momentary psychotic experiences. Possibly, this constitutes a key difference between patients with psychotic disorders and healthy people with transient psychotic experiences. As has been described before, survey studies indicate that symptom distress levels differentiate between a pathological state and a state of general functioning with no need for care (Cottam et al., 2011; Lincoln, 2007; Sorrell et al., 2010; Yung et al., 2006). Furthermore, a laboratory study monitoring the vagal stress-response during and following a stressful activity found that reduced HRV-levels persisted for a longer time after the end of the stressful activity in patients with psychosis, but not in healthy controls (Castro et al., 2008). In a comparable pattern, sensitization processes could over time extend the period needed to recover from the stress of momentary psychotic experiences, which leads to prolonged hyperarousal and increased distress due to psychotic experiences.

5.2.2. Coping with stress as a mechanism of change

Improvement in functional coping with stressful events was found to precede symptomatic improvement in patients. This is in line with a logical deduction from the core etiological mechanisms proposed in vulnerability stress models: If symptoms are triggered by stress, successful down-regulation of stress may counteract the formation of symptoms. It needs noting, though, that this pattern was not found for paranoia when an individualized assessment of the most severe symptoms of each patient was analyzed. In other words, the improvement in a symptom that has been shown to be triggered by stress (e.g., study 4) could not be sufficiently explained by successful removal of the triggering mechanism. Possibly, severe and persisting delusions require an improvement in different factors that play a specific role in the persistence of symptoms and are also addressed in CBTp, hence the direct effect of CBTp on this symptom. An example for a candidate mechanism would be the reduction of reasoning biases that otherwise reduce the influence of information that disconfirms a delusional belief held with high levels of conviction (Moritz, Veckenstedt, et al., 2011; Moritz, Andreou, et al., 2014; Morrison et al., 2014; Schneider et al., 2018).

Intriguingly, there was a connection between improvement in coping and reduced suspiciousness that was assessed with the same item in all patients. Continuing on the aforementioned interpretation, this would mean that across all levels of starting severity, there is an average effect of improving coping. Therefore, reducing the impact of stress due to prior symptoms or external and internal stressors ameliorates later positive symptoms, but only to a limited degree at severe levels of some positive symptoms.

A noteworthy result out of the main focus of this dissertation project is the significant connection between preceding negative symptoms and depression and later coping – and vice versa. The lack of a clear time-order does not permit for a conclusion of what is cause and effect in these associations. Yet, the fact that other symptom dimensions such as negative symptoms show a complex interrelation with mechanism of change for ameliorate positive symptoms may in part explain why negative symptoms have been found to predict poor outcomes of therapy (Kukla, Davis, & Lysaker, 2014; Thomas, Rossell, Farhall, Shawyer, & Castle, 2011) and other psychosocial interventions (Erickson, Jaafari, & Lysaker, 2011). In sum, these findings warrant the inclusion of other symptom dimensions when studying the dynamics that explain changes in one symptom domain over time.

5.2.3. Clinical implications

If we assume that the distress due to psychotic experiences is a risk factor for progression into a clinical state (Hayward, 2003; Lincoln, 2007), then the most relevant type of subclinical psychotic experience is paranoia, followed by some types of hallucination spectrum experiences such as intrusive thought and perceptual anomalies. This is in line with previous cross-sectional findings on psychotic experiences, which consistently showed the highest distress levels among psychotic experiences in paranoia (Armando et al., 2010; Yung et al., 2006). In consequence, the severity of these experiences (in terms of frequency and distress) could be a feasible criterion when selecting candidates for prevention programs as well as when measuring the outcome or monitoring the success of preventive efforts.

As for the content of prevention programs, the fact that hyperarousal and specific external stressors play a significant role in subclinical symptom formation suggests that programs to decrease stress levels or improve the ability to cope with stressors are feasible options. In particular, improving functional emotion regulation could be a feasible strategy, since recent studies found emotion regulation to modulate the association between stress and psychotic experiences (Krkovic, Krink, & Lincoln, 2018) as well as between social

stressors and psychotic experiences (Gollwitzer et al., 2018) in population samples. The aforementioned association between improvements in suspiciousness and prior increase in general coping, which includes coping with negative emotions, may be viewed as additional evidence for the efficacy of such a program on the highly prevalent mild threat beliefs in subclinical populations. Finally, if psychosis prevention programs target coping with stress or specific stressors, they do not need to be labeled as a program for “psychosis” to convey their content. This could be a further benefit, since potential negative effects due to the stigma that is attached to the psychosis label is avoided (Rüsch et al., 2013).

Finally, for the optimization of an individualized treatment of positive symptoms in clinical groups, the evidence suggests that the severity of negative symptoms and depression needs to be accounted for when aiming to increase coping. Possibly, a more extensive intervention at a slower pace can compensate for the potentially interfering effects of these symptoms. Regarding the group of positive psychotic symptoms, the findings provide further evidence for the feasibility of symptom specific interventions. Specifically, the results indicate that improving coping has an effect on suspiciousness and experiential symptoms (i.e., bizarre experiences and hallucinations), but not on more severe paranoid delusions or other delusion types. To this end, there is a range of established general coping programs for symptoms (Tarrier et al., 1993) as well as recent symptom specific therapies tailor-made for increasing coping resources to deal auditory hallucinations (Hayward, Jones, Bogen-Johnston, Thomas, & Strauss, 2017; Leff, Williams, Huckvale, Arbuthnot, & Leff, 2014) that can be implemented when treating the aforementioned symptoms.

5.2.4. Future directions

Based on the initial results reported in studies 4 to 6, a reasonable next step would be to expand the focus of the assessments to capture the full process hypothesized in the underlying model. Regarding subclinical ambulatory assessment, this means capturing the dynamic change from stressor to (self-report/physiological) stress reaction to the emergence of psychotic experiences in daily life. Regarding longitudinal therapy studies, improvement in mechanisms of change could be tied to specific modules or interventions. With this approach, the most effective treatment option can be found with similar mediation models as in study 6. Finally, by integrating ambulatory assessment into therapy studies, future research could capture how the change in the associations between symptoms and stress in

brief-interval assessments is modulated by improvements in mechanisms of change such as coping.

On another note, future ambulatory assessment of subclinical groups aimed at exploring the dynamic processes of symptom formation needs to investigate the role of vulnerability factors and how they modulate the impact of stressors on hyperarousal and/or the impact of hyperarousal on psychotic experiences (see Figure 1). Some studies have shown that specific vulnerability factors (e.g., traumatic experiences; Krkovic, Schlier, & Lincoln, 2018) amplify the association between the affective stress-response and subsequent symptoms. Future studies are warranted to extend on these results and close the gap between distal vulnerability factors to proximal mechanisms of sensitization and changes in everyday life.

One particular opportunity to advance the research on vulnerability factors may be rooted in the cross-sensitization mechanism described in one contemporary vulnerability stress model: The proposed mechanism that "exposure to one challenge leads to an elevated subsequent […] response to a different challenge" (Howes & Murray, 2014, p. 1680) could be investigated in ambulatory assessment and related longitudinal studies. Repeated short term exposure to a hypothetically central stressor could be captured over the course of an ambulatory assessment period. Short-term changes in vulnerability could then be analyzed by testing for moderator effects of repeated exposure on the response to stress (e.g., stress triggering increasingly severe psychotic experiences or symptoms as a function repeated exposure). Such an approach would supplement the existing perspective of vulnerability as a pre-existing biological condition (e.g., in from of a genetic vulnerability) or as a long-term result of critical life events (e.g. childhood trauma, growing up in an urban environment or as a second-generation migrant). Specifically, it would allow for a direct test of the presumed central sensitization mechanisms in existing models (e.g., Howes & Murray, 2014) on a phenomenological level. Possibly, future studies with general population samples (with low baseline vulnerability) or at risk groups (with medium baseline vulnerability) could map such sensitization process in everyday life.

Finally, as physiological parameters and self-reported stress levels showed similar changes prior to and during symptom episodes in a narrow time-frame, the option of replacing self-report based assessments for the stress-related triggers of symptoms with physiological monitoring should be tested. Potentially, an ambulatory intervention using

sensor data to provide self-help strategies in stressful situations is less taxing and more acceptable for the users and consequently increases the overall efficacy of a program.

5.3. Limitations

Some general limitations need to be noted regarding both the assessment procedures and over study designs. First, the validated instruments (studies 1 to 3) were construed and validated with the aim of assessing psychotic experiences and symptoms in both clinical and subclinical population. Clinical samples, however, made up a small fraction of the overall samples that were used to validate the assessment methods. For the CAPE (study 1) that is basically a clinical self-report assessment modified for the use in population samples (Stefanis et al., 2002), increased validity may be justifiably assumed for clinical samples. Regarding the state Paranoia Checklists, the change-sensitivity based item selection included clinical samples, so the item selection likely works in clinical and general population samples. Nevertheless, a formal test of the amount of fluctuation in the brief state Paranoia Checklist scores in ambulatory assessment studies with patients with psychotic disorders is warranted. The CAHSA, in contrast, was developed entirely with data from subclinical samples. The assumption that it is applicable to clinical sample is based on previous research with trait-level self-report questionnaires that found similar factor structures of subclinical and clinical hallucination spectrum experiences in patients with psychotic disorders and healthy comparison groups (e.g., Serper et al., 2005). At the present time, a test of whether this equivalence in factor structure extends to sufficient frequency and fluctuation in everyday life is still pending.

With respect to the longitudinal studies 4 to 6, the problem of multiple testing needs to be noted. The problem that multiple statistical tests are at risk of producing falsely positive, significant results can be averted by accounting for alpha error accumulation with a correction of all p-values. On a theoretical level, this procedure is preferable in any research, in which the significance of a test has roughly the same consequence for answering the research questions. In study 4, this was athe case, since all tests served the purpose of detecting a presumed state of altered stress levels over the course of symptom episodes. In studies 5 and 6 however, a pattern of findings in line with the respective research hypothesis (i.e., a uni-directional temporal association between preceding predictor-/mediator-levels and later symptom-levels) consists of significant test results (for the time-lagged associations) and non-significant results (for the reverse time-lagged associations).

Consequently, correcting for alpha error accumulation would lead to a test of the research question that is more conservative for the first half and more liberal for the second half of statistical tests. Due to the lack of previous, comparable data on both research questions, we decided for no alpha-error correction in both study 5 and study 6. Consequently, both the time-lagged and the reverse time-lagged associations were subjected to uncorrected "liberal" testing. It has to be noted though that the methodological rigor of future studies can and should be optimized. To this end, future studies can use the initial results from this dissertation project to estimate the expected effect sizes for comparable studies a priori, to optimize test power, and thereby minimize the probability of both alpha- and beta-errors.

Finally, the ambulatory assessment studies 4 and 5 aimed to test association between symptoms and stress/stressors that were pre-established in clinical samples for their applicability to psychotic experiences in subclinical samples. Under ideal conditions, such a test for the universality of an effect would directly compare different groups along the continuum of psychosis, such as the general population, at risk groups, and patients. Without such a direct comparison, generalization of any new finding (or lack thereof) in subclinical populations to patients is purely hypothetical and in need of verification in replication studies with more diverse samples.

5.4. Conclusion

In this dissertation project, self-report measures were developed and validated that broadened the range of possibilities in ambulatory assessment. These measures can be used to ensure a psychometric quality in ambulatory assessment studies of psychosis and allow for alternative ways of data-analysis in subclinical, at-risk, and clinical samples. Application of these methods in subclinical samples showed that physiological hyperarousal, self-reported stress, and social stressors play a role in triggering psychotic experiences, attesting to the potential importance of these early stressor for etiological models and prevention programs. In patients with psychotic disorders, the connection between treatment-progress and symptomatic improvement was shown to be explained by improvement in coping with stressful internal and external factors. Thus, indirectly reducing symptoms by targeting the triggering stressors and stress levels constitutes a possible way even when the phenomena have reached clinical symptom levels. Based on these findings, further research is warranted to explore the working mechanisms of symptom-formation and successful treatment of symptoms in both clinical and subclinical populations. A better understanding of the working

mechanisms along the continuum of psychosis holds the potential to significantly improve future prevention, treatment, and relapse-prevention programs and ultimately alleviate the impact psychotic disorders have on those affected by them.

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Appendix A: Study 1

Schlier, B., Jaya, E. S., Moritz, S., & Lincoln, T. M. (2015). The Community Assessment of Psychic Experiences measures nine clusters of psychosis-like experiences: A validation of the German version of the CAPE. *Schizophrenia Research*, *169*, 274–279.

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The Community Assessment of Psychic Experiences measures nine clusters of psychosis-like experiences: A validation of the German version of the CAPE

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ABSTRACT

Aim: This study examined the factorial and criterion validity of the Community Assessment of Psychic Experiences (CAPE). We compared the validity of the original three-dimensional model and a recently proposed multidimensional model, in which positive symptoms are subdivided into the subfactors hallucinations, bizarre experiences, paranoia, grandiosity and magical thinking and negative symptoms are subdivided into social withdrawal, affective flattening and avolition.
Methods: Eleven community ($n = 934$) and three patient samples ($n = 112$) were combined and the proposed models were tested using confirmatory factor analysis. Criterion validity was calculated based on self-report measures for depression and paranoia as well as observer-based ratings for positive and negative symptoms.
Results: The multidimensional model showed better relative quality (AIC, BIC) than the original three-dimensional model of the CAPE, but both models showed acceptable absolute model-fit (RMSEA, SRMR). The criterion validity was good for the positive symptom scales and negative symptom subfactors social withdrawal and affective flattening.
Conclusion: Factorial validity was found for the three-dimensional and multidimensional model for the CAPE. The multidimensional model, however, shows better comparative fit and promising results in regard to criterion validity. Thus, we recommend a hierarchical multidimensional structure of positive and negative symptoms for future use of the CAPE.

1. Introduction

Over the last decades, studies on community samples have found that a considerable part of the general population report psychosis-like experiences (Rössler et al., 2007; Stefanis et al., 2002; Tien, 1991; Yung et al., 2006). Increasing evidence supports a continuum hypothesis of psychosis, with clinical psychosis on the one end, complete absence of psychotic experiences on the opposite end, and non-clinical psychosis-like experiences in between.

The Community Assessment of Psychic Experiences (CAPE) has served as an essential assessment tool in many of the studies investigating the continuum hypothesis of psychosis (e.g., Stip and Letourneau, 2009; van Os et al., 2009). The CAPE is a self-report questionnaire that measures the lifetime prevalence of psychosis-like experiences in the general population. The CAPE consists of 42 items based on "clinical symptoms of patients" (Stefanis et al., 2002, p. 354) that assess three dimensions: positive symptoms, negative symptoms, and depression. The questionnaire has been used in genetic research (e.g., Stefanis et al., 2007), experimental research (e.g., Lincoln et al., 2010a), and studies that aim to elucidate the risk factors of schizophrenia, such as child abuse (e.g., DeRosse et al., 2014) or cannabis use (e.g., Schubart et al., 2011).

Despite the CAPE's wide application, the validity of its original factor structure has not always been replicated. A recent review (Mark and Toulopoulou, 2015) showed that out of four confirmatory factor analyses, only one reported good fit of a three-dimensional model (Stefanis et al., 2002), while three other studies were inconclusive (Brenner et al., 2007; Fonseca-Pedrero et al., 2012; Vleeschouwer et al., 2014). As a potential alternative, Mark and Toulopoulou (2015) reported nine exploratory factor analyses (EFA) of the positive symptom dimension and two EFA of the negative symptom dimension. These analyses consistently found that both dimensions can be split into smaller symptom subfactors (e.g. delusions, hallucinations, and bizarre experiences).

A multidimensional factor structure for the CAPE based on specific symptoms rather than broader syndromes fits in with recent theoretical models that tie specific etiological factors to different symptoms of psychosis (Bentall et al., 2014). It is likely that different psychosis-like

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experiences share these unique causes and that the prevalence of each one of them is relatively independent of the prevalence of the others. The continuing attempts to validate the CAPE by searching for a more intricate factor structure than the original three-dimensional model reflects this changed understanding. It also mirrors the validation of clinical assessment tools for psychosis. For example, the widely used Positive and Negative Syndrome Scale (PANSS, Kay et al., 1987), which was also originally conceptualized as three-dimensional, has since been found to consist of five or more factors (Emsley et al., 2003; van der Gaag et al., 2006). As of today, however, no CFA-study exists that tested a multidimensional model for the full CAPE, with both the positive and negative symptom dimension divided into first-order factors (Mark and Toulopoulou, 2015).

This study aims to compare the three-dimensional model of the CAPE with a multidimensional model that divides positive and negative symptoms into first-order subfactors. Additionally, we aim to rule out an alternative explanation that may have produced the unsatisfactory findings on the three-dimensional factor structure in previous studies: Many of the CAPE items assess psychosis symptoms of about the same severity as usually reported by patients with psychosis (Stefanis et al., 2002). In validation studies, however, the CAPE has been used on different populations, including groups at risk for psychosis (e.g., Mossaheb et al., 2012), but predominantly in community samples. In these samples a considerable part of the continuum of psychosis (i.e., patients with psychosis) is possibly not included, resulting in an incomplete distribution of the symptoms, with the upper end being "cut off". The resulting reduced variation could have biased the results of previous factor analyses. Thus, in the present study we included both community samples and patients with clinical psychosis in the analyses and compared the results with and without the patient subsample. Finally, we tested the convergent and discriminant validity of the factors of the three-dimensional and multidimensional model.

2. Methods

2.1. Participants

The sample consisted of participants pooled from different studies conducted by our research group. There were 1046 participants, of which 112 participants were diagnosed with a psychotic disorder (Jung et al., unpublished data; Lincoln et al., 2014a, 2014b) and 934 participants were from samples without a diagnosis of psychosis (Hartmann et al., 2013; Lincoln et al., 2014a, 2014b, 2014c; Lincoln et al., 2012, Lincoln et al., 2010a, Lincoln et al., 2009; Roggenbuck, 2012; Schlier, 2012). The demographic characteristics of the participants are summarized in Table 1. Due to the multiple data sources, not all participants were screened for mental disorders. However, all of the samples (except for 30 participants with depression who were recruited as a control sample) were drawn from the general population (i.e. community samples) or university students. A more detailed description of the sample characteristics of each of the thirteen original studies is added as a supplement (Suppl. 1).

All participants in the original studies gave informed consent for their participation and the respective studies were carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki).

2.2. Measures

2.2.1. Community Assessment of Psychic Experiences (CAPE)

All studies used the German translation of the CAPE by Domen (http://www.cape42.homestead.com/index.html). The CAPE was administered in paper-and-pencil ($n = 462$) or in an online format ($n = 574$). Participants indicated the lifetime prevalence of each of the 42 psychosis-like experiences on a four point Likert-scale ranging from 0 = "never" to 3 = "nearly always".

2.2.2. Additional symptom measures

To test the convergent and discriminant validity of the original positive, negative and depressive symptom dimensions and the subfactors obtained in the novel multidimensional model, we used several measures of psychotic symptoms and depression.

The PANSS is a structured clinical interview that consists of 30-item with 7-point rating scales (Kay et al., 1987). We used the positive symptom scale (7 items) and negative symptom scale (7 items), for which good reliability ($.73 \leq \alpha \leq .83$) and convergent and discriminant validity have been reported (Kay et al., 1987).

The Paranoia Checklist is an 18-item self-report scale that measures paranoid thoughts (Freeman et al., 2005). For its German translation, high reliability ($\alpha = .86$) and criterion validity have been shown (Lincoln et al., 2010b).

The Beck Depression Inventory (BDI-II) is a self-report scale that consists of 21-items rated on 4-point scales (Beck et al., 1961). The German translation shows good to excellent reliability ($.84 \leq \alpha \leq .94$) and high correlations to other depression measures (Hautzinger et al., 2006).

The German version of the Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977; Hautzinger, 2012) has 15 items with 4-point rating scales that assess depressive symptoms during the past

Table 1
Demographic and psychopathological characteristics.

	Participants with psychosis ($n = 112$)	Participants from community sample ($n = 934$)	Total sample ($n = 1046$)
Age in years	42.6 ($SD = 12.9$)	26.1 ($SD = 9.0$)	27.8 ($SD = 10.7$)
Gender			
Male	58.1%	31.7%	34.4%
Female	41.9%	68.3%	65.6%
Education level			
Secondary school (10 years of school)	31.1%	5.2%	7.7%
College entrance diploma (Abitur; 12–13 years of school)	47.6%	92.4%	87.9%
Psychotic disorders			
Schizophrenia	75.9%	0%	8.1%
Schizoaffective disorder	16.1%	0%	1.7%
Brief psychotic disorder	2.7%	0%	0.3%
Delusion disorder	3.6%	0%	0.4%
Affective disorder with psychotic symptoms	1.8%	0%	0.2%
Years since first diagnosis ($n = 64$)	13.9 ($SD = 12.1$)		
CAPE sum scores			
Positive symptoms	14.5 ($SD = 11.6$)	8.2 ($SD = 5.2$)	8.8 ($SD = 6.5$)
Negative symptoms	14.4 ($SD = 7.7$)	12.9 ($SD = 5.5$)	13.0 ($SD = 5.8$)
Depression	8.7 ($SD = 5.3$)	7.3 ($SD = 3.2$)	7.5 ($SD = 3.5$)

week. The internal consistency is good (.88 ≤ α ≤ .95) and convergent validity has been shown multiple times (Hautzinger, 2012).

The 10-item anticipatory pleasure subscale of the Temporal Experience of Pleasure Scale (TEPS-Ant, Gard et al., 2006) measures the pleasure experienced in anticipation of future positive activities (e.g., "I look forward to a lot of things in my life."). The subscale shows high internal consistency ($\alpha = .74$) and test-retest reliability ($r = .80$). Negative symptoms, particularly anhedonia, have repeatedly been linked to a deficit in anticipatory pleasure (e.g., Chan et al., 2010; Gard et al., 2007).

The validation measures were administered to patient (PANSS) and community subsamples (Paranoia Checklist, BDI-II, CES-D, TEPS-Ant). The corresponding sample sizes are shown in Table 3.

2.3. Statistical analyses

All analyses were performed in R (version 3.1.1). We utilized the package lavaan (version 0.5-17; Rosseel, 2012) for the factor analyses.

2.3.1. Establishing a multidimensional model

The multidimensional model consisted of positive and negative symptom dimensions with their respective first-order factors and an independent first-order factor of depression (see Table 2).

Subfactors of positive symptoms were based on the nine EFA-studies (Armando et al., 2012; Armando et al., 2010; Barragan et al., 2011; Stefanis et al., 2004; Therman et al., 2014; Wigman et al., 2011; Yung et al., 2009; Yung et al., 2006; Ziermans, 2013) that were reviewed and summarized by Mark and Toulopoulou (2015). For each item, we identified the factor it was allocated to most frequently in these studies (see Suppl. 2 for details). As there were only two EFA studies of the negative symptom dimension (Barragan et al., 2011; Ziermans, 2013), we added a theory-driven item allocation schema: We sorted all items of the CAPE negative symptom dimension to the subfactors social withdrawal, affective flattening and avolition. These constitute the negative symptom categories assessed by self-report in state-of-the-art diagnostic instruments (Horan et al., 2011) and were found in both EFA studies. One author (B.S.) allocated the items to these subfactors and another author (E.J.) rated the allocation of each item. If there was disagreement on a specific item allocation, both authors discussed the specific item and located it based on a consensus. The final allocation of the negative symptom items was then based on the most common placement across the three models.

Table 2
Item allocation based on most common solutions in previous exploratory analyses.

Item	Subfactor allocation	% studies with this allocation
Positive symptoms dimension		
5. Message on TV/magazines especially for you	Biz. exp.	47%
17. Electrical devices can influence the way you think	Biz. exp.	78%
24. Thought withdrawal	Biz. exp.	78%
26. Thoughts in your head are not your own	Biz. exp.	78%
28. Thoughts so vivid that other people may hear them	Biz. exp.	78%
30. Thoughts echoed	Biz. exp.	78%
31. Feeling under the control of some force or power	Biz. exp.	78%
33. Hearing voices	Hallucinations	78%
34. Hearing voices talk to each other	Hallucinations	78%
41. Capgras	Hallucinations	57%
42. Seeing things other people cannot see	Hallucinations	86%
2. People drop hints/say things with a double meaning	Paranoia	100%
6. People are not what they seem to be	Paranoia	100%
7. Feeling persecuted	Paranoia	100%
10. Conspiracy against you	Paranoia	100%
22. People look at you oddly	Paranoia	100%
11. Feeling destined to be someone important	Grandiosity	67%
13. Being a very special or unusual person	Grandiosity	67%
15. Believing in telepathical communication	Mag. think.	71%
20.Believing in witchcraft/voodoo/the occult	Mag. think.	71%
Negative symptoms dimension		
3. Not very animated person	Soc. withd.	100%
4. Not much of a talker	Soc. withd.	100%
16. No interest to be with others	Soc. withd.	67%
29. Lacking spontaneity	Soc. withd.	67%
8. Experiencing no/few emotions	Aff. flatten.	100%
27. Emotions lack intensity	Aff. flatten.	100%
32. Blunted emotions	Aff. flatten.	100%
18. Lack of motivation to do things	Avolition	100%
21. Lack of energy	Avolition	100%
23. Empty mind	Avolition	67%
25. Spending days doing nothing	Avolition	100%
35. Neglect of appearance/personal hygiene	Avolition	100%
36. Never getting things done	Avolition	100%
37. Lack of hobbies/interests	Avolition	100%

Note. Biz. exp. = bizarre experiences; Mag. think. = magical thinking; Soc. withd. = social withdrawal; Aff. flatten. = affective flattening.

2.3.2. Model comparison

To compare the three-dimensional and multidimensional model we used Satorra–Bentler corrected maximum likelihood CFA. Both models were tested on the whole sample and the community sample separately in order to explore potential differences due to sample type.

We computed the comparative fit index (CFI, good model-fit >0.95), the root mean square error of approximation (RMSEA, good model-fit <0.06), and the standardized root mean square residual (SRMR, good model-fit <0.08) to explore the absolute goodness of fit. Moreover, we compared the relative goodness of fit of the competing models with the Akaike information criterion (AIC) and the Bayesian Information criterion (BIC), where smaller values indicate a better fit.

2.3.3. Convergent and discriminant validity

In order to compensate for the intercorrelation of psychosis symptoms, we tested convergent and discriminant validity by calculating partial correlations of each CAPE-factor with a criterion while controlling for all other factors of the respective model. We used external criteria for positive symptoms (PANSS-Positive, Paranoia Checklist), depression (BDI-II, CES-D) and negative symptoms (PANSS-Negative, TEPS-Ant). For validity of the positive symptom factor(s), for example, we expected the largest partial correlation for the PANSS-positive scale and the Paranoia Checklist and low partial correlations for all other scales.

3. Results

3.1. Model comparison

The fit indices for both models in both types of samples are presented in Table 3. As can be seen, RMSEA and SRMR reached the respective threshold values for acceptable fit in all models, whereas the CFI was below 0.95 for all models. AIC and BIC were lower for the multidimensional compared to the three-dimensional model for both types of samples.

3.1.1. Post hoc analysis of the negative symptoms dimension

The multidimensional factor solution of the negative symptoms dimension was based on only two EFA from previous studies (Barragan et al., 2011; Ziermans, 2013). As a result, the subfactors of the negative symptom dimension might have been specified in a suboptimal fashion. We thus explored alternative solutions for this dimension post-hoc. We split the CAPE negative items into five pre-established negative symptom categories (Horan et al., 2011): avolition (items 18, 21, 23, 35, 36), alogia (item 4), anhedonia (i.e., experience of pleasure: items 8, 37), blunted affect (items 27, 32) and social withdrawal (items 3, 16, 29). A five factor model based on these categories and a four factor solution that combined social withdrawal and alogia into one factor could not be fitted to the data since it resulted in negative variance estimates. A two factor solution reminiscent of the clinical assessment interview

Table 3
Fit indices of all proposed models, calculated on basis of the full sample and the community sample only.

Model	Satorra–Bentler χ^2			Absolute goodness of fit			Comparative fit		
	χ^2_1	df	p	RMSEA (90%CI)	CFI	SRMR	AIC_1	BIC_1	Factor loadings
Full sample ($n = 1046$)									
Three-dimensional model	3303	816	<0.001	0.054 (0.053–0.056)	0.639	0.067	71,507	72,145	0.352–0.694
Multidimensional model	2246	808	<0.001	0.041 (0.040–0.043)	0.791	0.062	69,960	70,637	0.402–0.803
Community sample ($n = 934$)									
Three-dimensional model	3170	816	<0.001	0.054 (0.053–0.056)	0.664	0.066	57,920	58,543	0.349–0.681
Multidimensional model	2081	808	<0.001	0.041 (0.039–0.043)	0.810	0.061	56,630	57,292	0.335–0.846

Note: 1 = rounded to the next integer.

for negative symptoms (CAINS, Horan et al., 2011) with the factors "motivation and pleasure" (I. avolition, anhedonia, and social withdrawal) and "expressivity" (II. blunted affect and alogia) and a three factor model (I. avolition, II. anhedonia, III. social withdrawal/alogia/blunted affect) yielded no better fit than the original multidimensional model (all *AIC* > 69,959, all *BIC* > 70,636).

3.1.2. Post hoc analysis of inconsistent model-fit indices

The CFI implies insufficient fit of the models while RMSEA and SRMR indicate good fit. Kenny (2014) pointed out that the CFI is negatively biased in cases in which the correlations between items are generally low and the RMSEA of the proposed model is good (i.e., RMSEA < 0.05). This is because when correlations are low, the baseline model of a factor analysis (i.e., the model in which all items are supposed to be uncorrelated) shows a comparatively good fit. The CFI, however, compares the fit of a tested model against the fit of this baseline model. Kenny (2014) calculated that when a baseline model shows a fit of RMSEA <0.158, a tested model with good fit (RMSEA = 0.05) is bound to have a CFI below 0.90. Thus, the comparative fit shown with the CFI is no valid indicator in these cases. In our analyses, calculation of baseline model RMSEA yielded RMSEA = 0.088 for the whole sample and RMSEA = 0.091 for the community subsample. Thus, the CFI value in this study needs to be interpreted with caution and it seems reasonable to base the conclusions on the RMSEA and SRMR rather than on the CFI.

3.2. Convergent and discriminant validity

In the three-dimensional model (see Table 4), the positive symptom scale showed the largest partial correlation with the positive symptom criteria (PANSS positive and PCL). The depression scale predicted CES-D-scores, but both depression and negative symptom scales showed partial correlations with BDI-scores. The PANSS-negative scale was not significantly predicted by any of the dimensions.

In the multidimensional factor structure (see Table 4) only the subfactor paranoia showed a partial correlation with the Paranoia Checklist scores. Hallucinations, grandiosity and paranoia showed the strongest partial correlations with the PANSS positive symptom scores on a descriptive level. The BDI covaried with the depression factor and the subfactor avolition. The TEPS-Ant showed a higher correlation with the subfactors affective flattening and social withdrawal than with any positive/depression symptom factor, but this was not the case for the subfactor avolition.

4. Discussion

In this study, we compared a three-dimensional and multidimensional factor model of the German version of the CAPE and the convergent and discriminant validity of the factors.

Table 4
Cronbach's alpha and validity coefficients for all CAPE factors.

CAPE model CAPE factor	Cronbach's alpha	Partial correlation controlling for all other CAPE factors of the respective model					
		Positive symptoms		Depression		Negative symptoms	
		PANSS-positive ($n = 33$)	Paranoia checklist ($n = 207$)	BDI ($n = 222$)	CES-D ($n = 207$)	PANSS-negative ($n = 33$)	TEPS-Ant ($n = 222$)
Three dimensional model							
Positive symptoms	0.88	0.51*** **	0.28***	−0.02	−0.09	0.20	−0.14*
Depression symptoms	0.81	−0.07	0.28***	0.49***	0.34***	−0.27	0.02
Negative symptoms	0.85	0.02	0.09	0.27***	0.08	0.26	0.23***
Multidimensional model							
Positive symptoms							
Bizarre experiences	0.79	−0.03	0.06	−0.02	−0.01	−0.25	−0.11
Hallucinations	0.73	0.29	0.05	0.08	−0.04	0.16	0.04
Paranoia	0.70	0.32	0.35***	0.13	0.1	0.08	0.03
Grandiosity	–	0.24	−0.11	−0.08	0.03	−0.11	0.01
Magical thinking	–	0.09	−0.01	−0.11	−0.1	0.21	−0.14*
Depression	0.81	−0.16	0.14	0.39***	0.27***	−0.30	0.08
Negative symptoms							
Social withdrawal	0.65	0.16	0.02	0.13*	−0.01	0.16	0.16*
Affective flattening	0.83	−0.12	0.1	0.02	−0.18	0.03	0.28***
Avolition	0.79	−0.01	−0.05	0.23***	0.17*	0.25	0.11

Note: PANSS-Positive = Positive Symptom Scale of the Positive and Negative Syndrome Scale. BDI = Beck's Depression Inventory. CES-D = Center for Epidemiologic Studies Depression Scale. PANSS-Negative = Negative Symptom Scale of the Positive and Negative Syndrome Scale. TEPS-Ant = Anticipatory pleasure subscale Temporal Experience of Pleasure Scale, reverse scored so that high values indicate low anticipatory pleasure.

*** $p < 0.001$.
** $p < 0.01$.
* $p < 0.05$.

4.1. Factorial validity

On the one hand, we found sufficient fit of the originally proposed three-dimensional model (positive symptom, negative symptom and depression factor, Stefanis et al., 2002). Two fit-indices (RMSEA and SRMR) indicate good fit, while a third inconsistent result (CFI) may be the result a negative bias due to the data structure. Overall, this supports the dimensional structure of the CAPE that has most frequently been used in research.

However, a multidimensional model that divides both the positive and negative factor into subfactors had a better fit than the original model. Despite the fact that a three-dimensional negative symptom model was only derived from two previous EFA (Barragan et al., 2011; Ziermans, 2013) rather than nine as in the case of the positive symptom model, it showed better fit than any alternative, theory-derived model we tested. Thus, our study is the first confirmatory factor analysis that supports a symptom-based hierarchical factor structure of the full CAPE as suggested by Mark and Toulopoulou (2015).

Factorial validity remained the same when the subsample of participants with psychosis was excluded from the analysis. Thus, we can assume that irregularities in the factor structure found in previous studies (e.g., Brenner et al., 2007) are probably not caused by restricted variability of the item scores in community samples.

4.2. Convergent and discriminant validity

In part, our study confirms good criterion validity of the original three-dimensional model (Stefanis et al., 2002). The positive symptom dimension showed good convergent and discriminant validity. The negative symptom dimension lacked a significant association with the PANSS negative scale and was also associated with one of the depression measures. Thus, the validity of the negative symptom dimension is questionable.

Within the multidimensional model, convergent validity was shown for the paranoia subfactor. While no positive symptom subfactor had a significant partial correlation with the PANSS positive scale, the paranoia, hallucination and grandiosity subfactor correlated with the PANSS positive scale with a medium strength, respectively. The lack of criterion-validity for the negative symptom dimension pertains to the subfactor avolition, whereas social withdrawal and affective flattening show convergent validity with one criterion and overall good discriminant validity.

4.3. Discussion of the findings on model fit

In support of the positive symptom dimension of the three-dimensional factor structure, we found sufficient fit and good convergent and discriminant validity. This justifies further use of the CAPE positive scale as global self-report measure of psychotic symptoms.

Based on our data, however, a multidimensional model has the better fit. From a practical point of view, the use of subfactors emphasizes to what extent specific symptoms are represented in the CAPE. A sum-score of all positive symptoms, by contrast, inherently over-represents paranoia (5 items) and bizarre experiences (7 items) because of the relatively higher number of items that focus on these facets. From a theoretical point of view, symptom-specific subfactors reflect the nature of psychotic experiences in the population better than a general non-specific dimensions. First, the frequency of subclinical psychotic symptoms in the general population varies. For example, mind control thoughts (22.6% in 20 year olds) are more common than hearing voices (3.2% in 20 year olds) in healthy people (Rössler et al., 2007). Second, psychotic experiences have been shown to differ in their respective etiology (Bentall et al., 2014) and consequences in terms of distress (Yung et al., 2006). Thus, a multidimensional model of the CAPE is more appropriate from both a theory-driven and data-driven point of view.

Criterion validity, however, has yet to be further established for all symptom subfactors. Particularly, criterion validation of the negative dimension and its subfactor avolition yielded some inconsistencies. Although Stefanis et al. (2002) have previously shown convergent and discriminant validity for the negative dimension, it needs noting that the coefficients they reported were but a fraction of the coefficients reported for positive symptoms, indicating far better validity of the latter. Future research needs to further investigate the validity of the negative symptom dimension by exploring the correlation with both the established measures for negative symptom assessment (e.g., the SANS, Andreasen, 1989) and the recently developed measures that mirror the specific negative symptom factors of the CAPE (e.g., the CAINS, Horan et al., 2011).

5. Limitations

Two limitations need noting. First, the participants were rather highly educated and young. Results may thus be restricted to this type of population. Second, due to the patchwork nature of our sample, criterion validation is limited to a few scales, resulting in incomplete criterion validation for the multidimensional model.

6. Conclusion

To conclude, we found sufficient evidence to legitimate the use of the three-dimensional model of the CAPE. However, due to better comparative fit and due to the overrepresentation of items revolving around certain symptoms, we recommend a hierarchical–multidimensional model of the CAPE. Nevertheless, it may be favorable in the long run to revise the CAPE and create a questionnaire with both factorial and criterion validity. Such a revision should aim to include an equal amount of items for each core symptom in the positive and negative dimension. Moreover, a comprehensive assessment may need additional items to capture reduced expressivity (i.e., alogia and blunted affective expression; Horan et al., 2011). A theoretically guided refinement process in accordance with these principles may help to further elucidate the structure of psychotic experiences in the general population.

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Contributors

Björn Schlier designed the study and managed the integration of the source data. Björn Schlier and Edo Jaya undertook the statistical analyses. Edo Jaya wrote the first draft of the manuscript. Tania Lincoln managed the literature searches and was involved in designing the study. All authors contributed to and have approved the final manuscript.

Conflict of interest

Björn Schlier, Edo Jaya, Steffen Moritz, and Tania Lincoln declare that they have no conflicts of interest.

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Appendix A. Supplementary data

Supplementary tables.

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Appendix B: Study 2

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Measuring fluctuations in paranoia: Validity and psychometric properties of brief state versions of the Paranoia Checklist

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ABSTRACT

Research increasingly assesses momentary changes in paranoia in order to elucidate causal mechanisms. Observed or manipulated changes in postulated causal factors should result in fluctuations in state paranoid ideation. Previous studies often employed a state-adapted Paranoia Checklist (Freeman et al., 2005) to measure state paranoia. This study examined whether the Paranoia Checklist or subsets of its items are appropriate for this purpose.

Thirteen studies (N=860) were subjected to meta-analyses of each Paranoia Checklist item. We selected items based on (1) whether they showed pre-to-post change in the expected direction and (2) whether this effect was larger in experimental vs. control conditions. All resulting item selections were cross-validated on a hold-out sample (n=1893). Finally, we explored how much variation in paranoia was captured by the state-adapted version in a brief ambulatory assessment study (N=32).

A thirteen item *State Paranoia Checklist* as well as a five item and a three item *Brief State Paranoia Checklist* were extracted. Cross validation revealed better model fit and increased sensitivity to change. Multilevel analysis indicated 25-30% of the variance in the *Brief State Paranoia Checklists* to be due to intra-individual daily fluctuations in paranoia.

Our analyses produced reliable and valid revised scales. Increases in change sensitivity indicate that future assessment of state paranoia in experimental and ambulatory assessment studies can be optimized by using the revised scales.

1. Introduction

In their seminal work on the contribution of genetic and environmental causes of psychosis Van Os et al. (2010) emphasize the importance to pinpoint stressors and other environmental factors that contribute to the formation of psychotic symptoms. Since then, there has been a shift of research paradigms in favor of experimental studies that manipulate stressors in order to identify the causal mechanisms of psychotic symptoms such as paranoia (Garety and Freeman, 2013). In these studies, paranoid ideation is measured as a fluctuating state rather than as a stable symptom (Ben-Zeev et al., 2011; Kesting et al., 2013; Hartley et al., 2014).

However, most of the established self-report questionnaires capture trait levels of paranoid ideation (Fenigstein and Vanable, 1992; Peters et al., 1999; Stefanis et al., 2002; Freeman et al., 2005). So far, state paranoia has often been assessed by adapting trait paranoia scales (e.g., Thewissen et al., 2008; Lincoln et al., 2009). Others have applied self-construed scales (Bodner and Mikulincer, 1998; Ellett et al., 2013), which were then used by other researchers (Ellett and Chadwick, 2007; Kingston and Ellett, 2014; Flower et al., 2015). Finally, Freeman et al. (2007) developed a State Social Paranoia Scale and demonstrated its convergent validity, test-retest reliability and internal consistency.

In our research, we have used a state-adapted version of the Paranoia Checklist (Freeman et al., 2005), in which the presence of each paranoid thought is rated on Likert scales according to the extent to which it applies "at the moment" (e.g., Lincoln et al., 2014a).

Good reliability and validity have been demonstrated for the Paranoia Checklist (Freeman et al., 2005) and its state-adapted version (Lincoln et al., 2009, 2012), indicating equal psychometric quality when compared to generic state paranoia scales (Freeman et al., 2007; Ellett et al., 2013). However, the state-adapted Paranoia Checklist has never been formally validated. Specifically, the sensitivity to change across different settings and in response to stressors and interventions, which is a critical component required

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to ensure valid assessment of state paranoia, has never been formally tested. In fact, neither the state-adapted Paranoia Checklist nor generic state paranoia scales have been formally validated in this way. Instead, currently used state paranoia scales have been developed ad hoc for a given experiment. Using such a scale for another experiment, however, bears some risk because the assumption that a state paranoia scale measures fluctuations in paranoia in different settings is based on successful detection of change in only one specific experiment. Undisputedly, it is a reasonable decision to use a scale that has been field-tested once before. However, now that there is an abundance of research on state paranoia using the Paranoia Checklist, it is possible to evaluate whether this scale is a valid measure for state paranoia – in terms of change-sensitivity – across different experimental settings and in different samples (e.g., population vs. patient samples).

For the Paranoia Checklist, such a validation is all the more warranted, given that it was originally developed to measure the prevalence of paranoid thoughts over long periods of time (with anchor points ranging from "rarely" over "once a month" to "at least once a day"). The Paranoia Checklist may comprise items that are non-sensitive to momentary fluctuations. If that is the case, true changes in state paranoia might be underestimated by a state-adapted Paranoia Checklist unless only a subset of change sensitive items is used.

Thus, we aimed to derive and validate a state-adapted Paranoia Checklist from its original item pool. We combined factor analysis with a meta-analytic approach and integrated data from thirteen studies, in which the state-adapted version of the Paranoia Checklist was used to assess changes in paranoid thoughts before and after an active/experimental or control intervention. Sensitivity to change was evaluated on single item basis, along the two criteria Lambert and colleagues (Lambert et al., 1996; Vermeersch et al., 2000) established for a clinical assessment scale: an item changes in the theoretically proposed direction following an intervention (criterion 1) and the change measured on an item is greater in individuals treated by an evidently effective intervention than in untreated individuals or individuals treated with a control intervention (criterion 2).

In a first step (item selection), we assessed both criteria for each item of the Paranoia Checklist using meta-analyses. Based on these results, we aimed to exclude all items that lacked sensitivity to change. Furthermore, we aimed to create a brief state Paranoia Checklist including items with the highest sensitivity to change. This version was derived for use in experimental or experience sampling research which requires parsimonious assessment. In a second step (scale validation), psychometric properties of these item selections were tested on a large hold-out sample. Moreover, a subset of studies from the item selection procedure was used to compare criterion validity of the abbreviated scales with the 18 item version. In a final step (ambulatory assessment pilot test), we collected new data in an ambulatory assessment study to test how much intra-individual variation is captured by the brief version.

2. Item selection

2.1. Methods

2.1.1. Source material and participants

Data for the analyses were derived from thirteen previous studies of the authors that used the state-adapted Paranoia Checklist in a repeated measure design. All of these studies included either a form of anxiety or stress induction assumed to increase paranoia or an intervention aimed at decreasing paranoia as well as measurement of state paranoia with the Paranoia Checklist prior to and after the induction/intervention. No further eligibility or quality criteria were imposed on the source material, since this study compared relative item effect sizes rather than trying to determine "true" effect sizes of a given variable. An exploratory literature search on PsycInfo (full text search for "Paranoia Checklist" and "state") yielded no further candidate studies. Data for this study were derived from the full datasets of these thirteen studies, which allowed for calculation of group means and standard deviations for each single item within each study.

An overview of the included studies with a total of 860 participants (of which $n=288$ were patients with psychosis), who completed the Paranoia Checklist in online ($n=279$) or laboratory studies ($n=581$), is shown in Table 1. The included studies were comprised of seven non-controlled pre-to-post designs (Lincoln et al., 2009, 2014a, 2014b; Moritz et al., 2011, 2014a, 2014b; Jung, 2012; Hartmann et al., 2013) and six pre-to-post-control designs (Lincoln et al., 2012; Roggenbuck, 2012; Kesting et al., 2013; Ascone, 2014; Moritz et al., 2015a, 2015b) consisting of an active intervention/experimental induction and a control condition. Only two clinical subsamples from a large correlational panel study ($N=1966$, Moritz et al., 2014a) were included because its full sample size exceeded the combined size of all other studies. This remaining sample ($n=1893$) served as a hold-out sample for scale validation.

2.1.2. Materials: Paranoia Checklist

The Paranoia Checklist comprises of 18 items, which include statements that range from tapping into mild persecutory ideas (e.g., "There might be negative comments being circulated about me") to more severe paranoid ideations (e.g., "There is a possibility of a conspiracy against me."). In its state-adapted version, participants indicate to what extent each item applies to them "at the moment". Participants provide their answers on Likert scales ranging from "not at all" to "very much". The majority of the studies used all 18 items of the Paranoia Checklist and a five point Likert scale as answer form. Three studies (Lincoln et al., 2012; Roggenbuck, 2012; Ascone, 2014) excluded one item from the scale based on low variance in participant responses ("I can detect coded messages about me in the press/TV/radio"), while a fourth study only used 5 items, which were assumed to be the most change sensitive (Hartmann et al., 2013). Furthermore, three studies changed the answer format to an eleven point Likert scale (Lincoln et al., 2012; Hartmann et al., 2013; Ascone, 2014).

2.1.3. Analyses

Item selection is based on the sensitivity to change over a variety of settings. In order to analyze the integrated sensitivity to change of each item, we conducted separate meta-analyses for all 18 items. We calculated standardized effect sizes based on item gain scores, gain score standard deviations and correlation of pre- and post-test item scores in each sample. All effect sizes were calculated in such a way that positive effect sizes indicated an effect in the expected direction. Effect sizes were integrated with random effects meta-analyses. To determine whether an item i fulfills criterion 1 (i.e., changes in the theoretically proposed direction following an intervention), we calculated the average effect size of pre-to-post (PP) change for each experimental and control sample (see formula 1), resulting in 28 samples for this comparison. To determine whether an item fulfills criterion 2 (i.e., higher change in an experimental group E compared to a control group C), meta-analyses of the pre-to-post-control (PPC) effect sizes were conducted. For the six PPC interventions included in these analyses, the effect sizes were based on mean gain scores and gain scores standard deviations of the treatment and control group (see formula 2, Lipsey and Wilson, 2000).

Table 1
Overview of the included studies and samples.

	N	Group	Study description	Pre-to-post	Pre-post-control
Ascone (2014)	20	Participants with psychosis (EXP)	Compassion imagination (EXP) vs.	Pre-to-post-treatment	PPC effect between EXP and CON
	18	Participants with psychosis (CON)	distraction condition (CON)	Pre-to-post-treatment	
Hartmann et al. (2013)	60	Population	Self-discrepancies: Neutral (CON) vs. ideal-self vs. self-other (EXP)	CON to EXP	–
Jung (2012)	50	Population	Neutral (CON) vs. stressful everyday-life situation (EXP)	CON to EXP	–
Kesting et al. (2013)	42	Population (EXP)	social exclusion via feedback (EXP) vs. neutral feedback (CON)	Pre-to-post-feedback	PPC effect between EXP and CON
	40	Population (CON)		Pre-to-post-feedback	
Lincoln et al. (2014a, 2014b)	35	Participants with psychosis	Neutral condition (CON), noise stressor and social stressor (EXP)	CON to EXP	–
	30	Participants with depression		CON to EXP	
	26	Relatives of people with psychosis		CON to EXP	
	29	Participants with attenuated symptoms		CON to EXP	
	27	Population		CON to EXP	
Lincoln et al. (2012)	36	Population (EXP)	Compassion imagination (EXP) vs.	Pre-to-post-treatment	PPC effect between EXP and CON
	35	Population (CON)	distraction (CON)	Pre-to-post-treatment	
Lincoln et al. (2009)	64	Population	Neutral condition (CON) vs. noise stressor (EXP)	CON to EXP	–
Moritz et al. (2011)	20	Participants with psychosis	Neutral condition (CON) vs. noise stressor (EXP)	CON to EXP	–
	15	Population		CON to EXP	
Moritz et al. (2015a)	27	Participants with psychosis (EXP)	Mindfulness online-training (EXP) vs. muscle-relaxation (CON)	Pre-to-post-treatment	PPC-effect between EXP and CON
	34	Participants with psychosis (CON)		Pre-to-post-treatment	
Moritz et al. (2015b)	29	Participants with psychosis (EXP)	Metacognitive training (EXP) vs. waitlist (CON)	Pre-to-post-treatment	PPC effect between EXP and CON
	35	Participants with psychosis (CON)		Pre-to-post-treatment	
Moritz et al. (2014a)[a]	41	Participants with psychosis	Paranoia reduction by snowy picture task with pre and post measurement	Baseline to reduction	–
	31	Participants with OCD		Baseline to reduction	
Moritz et al. (2014b)	29	Participants with psychosis	Virtual reality task with pre and post measurement	Baseline to reduction	–
	31	Population		Baseline to reduction	
Roggenbuck (2012)	29	Population (EXP)	1 Session compassion training (EXP) vs. distraction condition (CON)	Pre-to-post-treatment	PPC effect between EXP and CON
	31	Population (CON)		Pre-to-post-treatment	

Note: a = hold out sample for cross validation was derived from this study (n = 1893). Population = Healthy Population Sample, EXP = experimental or treatment condition, CON = Control Condition.

$$d_{i,pp} = \frac{M_{i,diff}}{SD_{within}} = \frac{M_{i,post} - M_{i,pre}}{SD_{within}},\ withSD_{within} = \frac{SD_{diff}}{\sqrt{2(1-r)}} \quad (1)$$

$$d_{i,ppc} = \frac{M_{i,diff,E}}{SD_{within,E}} - \frac{M_{i,diff,C}}{SD_{within,C}} \quad (2)$$

Data was analyzed using R 3.2.0 (R Core Team, 2014). For the meta-analysis, the package metafor 1.9–7 (Viechtbauer, 2015) was used.

Items were selected based on the average PP effect size and the average PPC effect size. Results from the 18 meta-analyses of PP and PPC effects of each item, respectively, were compared with each other. Each item was classified with two numerical indicators of its change sensitivity, one based on the PP meta-analysis and one based on the PPC meta-analysis of the item. Indicators ranged from not acceptable (−1; i.e., average effect < 0 by descriptive value), to neutral (0), acceptable (1), good (2), and excellent (3). For the indicators from neutral to excellent, effect size ranges were determined post-hoc based on the overall range of the results. Items were excluded from a state sensitive Paranoia Checklist if the sum score of both indicators fell below three. Items with an indicator sum score of at least 4 (i.e., at least acceptable quality in one and excellent quality in the other indicator of change sensitivity) were included in a novel brief state Paranoia Checklist to be validated.

Finally, possible moderator effects of answer format (5 point vs. 11 point Likert scale) and sample type (psychosis vs. population) were tested. The former analyses served as an indicator as to how the resulting brief scales should be presented. With the latter analyses we tested whether different scales may need to be used for different populations.

2.2. Results

2.2.1. Meta-analyses

PP effect sizes ranged from $d = -0.01$ to $d = 0.18$ (see Fig. 1), while PPC effect sizes ranged from $d = -0.06$ to $d = 0.26$ (see Fig. 2). Nine of the meta-analyses of the PP effect sizes reached significance (items 3, 5, and 15, all $d > 0.1$, all $p < 0.01$; items 1, 4, 7, 8, 9, and 12, $d > 0.05$, all $p < 0.05$). Among the meta-analyses of the PPC effect sizes, only item 5 showed an average effect significantly different from 0 ($d = 0.26$, $z = 3.04$, $p = 0.002$).

2.2.2. Item classification

For the PP comparisons, items were classified as showing excellent quality (Index = 3) if their average effect size was $d \geq 0.1$ and if they were significantly different from 0 ($p < 0.05$), good quality (Index = 2) if their average effect size was $d \geq 0.05$ and differed significantly from 0 ($p \leq 0.05$), acceptable quality (Index = 1) if they showed an average, yet insignificant effect of $d \geq 0.05$, and neutral (Index = 0) when they showed an average effect between $d \leq 0.05$ and $d \geq 0.00$ (see Fig. 1).

Given the low number of samples ($k = 6$) for the PPC comparisons, we did not factor significance into the item selection. Items were classified as showing excellent quality (Index = 3) when their average effect size was $d \geq 0.2$, good quality (Index = 2) when their average effect size was $d \geq 0.1$, acceptable quality (Index = 1) when their average effect size was $d \geq 0.$ 05, and neutral (Index = 0), when their average effect size was between $d < 0.05$ and $d \geq 0.00$ (see Fig. 2).

2.2.3. Item selection

Five items failed to show a sum of quality indicators of three or more, indicating low change sensitivity in either PP or PPC comparisons or both (items 10, 11, 13, 16, 17). The remaining thirteen items were included in the revised State Paranoia Checklist.

Five items showed a sum of quality indicators of four or more, indicating at least a combination of neutral sensitivity in one comparison and excellent sensitivity in the other. These items (1, 5, 7, 15, and 18) formed the five item version of the Brief State Paranoia Checklist. Furthermore, three items (1, 5, and 7) showed good quality in both indicators. Thus, we decided to select the items 1, 5, and 7 for an optimized Brief State Paranoia Checklist.

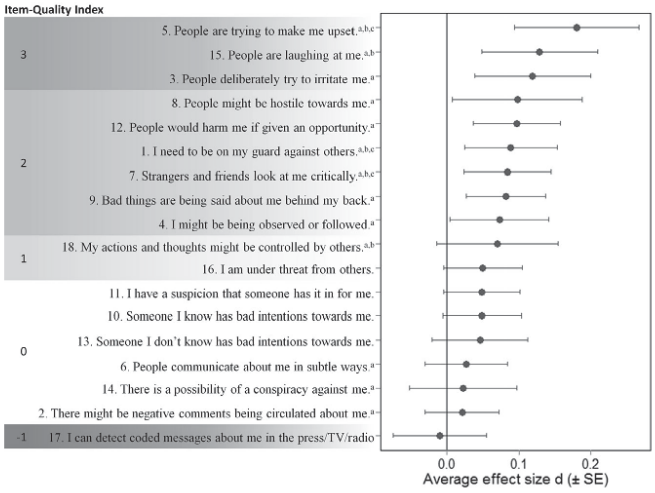

Fig. 1. Average effect sizes of pre-to-post comparisons for all items. Items are grouped into those with excellent quality (Index = 3, $d \geq 0.1$, $p \leq 0.05$), good quality (Index = 2, $d \geq 0.05$, $p \leq 0.05$), acceptable quality (Index = 1, $d \geq 0.05$), neutral items (Index = 0, $0.05 < d \leq 0.00$), and low quality (Index = −1, $d < 0.00$). a = item is included in the revised state Paranoia Checklist; b = item is included in the five item Brief Paranoia Checklist; c = item is included in the three item Brief Paranoia Checklist.

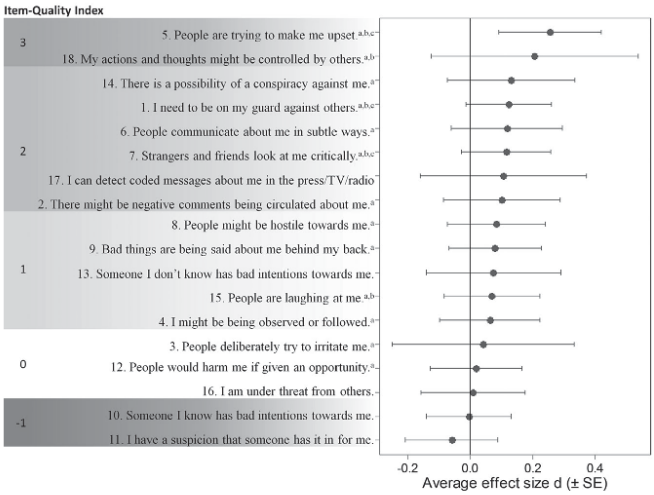

Fig. 2. Average effect sizes of pre-post-control (PPC) comparisons for all items. Items are grouped in items with excellent quality (Index = 3, $d \geq 0.2$), items with good quality (Index = 2, $d \geq 0.1$), items with acceptable quality (Index = 1, $d \geq 0.05$), neutral items (Index = 0, $0.05 < d \leq 0.00$), and items with low quality (Index = −1, $d < 0.00$). a = item is included in the revised state Paranoia Checklist; b = item is included in the five item Brief Paranoia Checklist; c = item is included in the three item Brief Paranoia Checklist.

2.2.4. Moderator effects of answer format

PP effect sizes of items 1, 7, 8, 9 and 12 were significantly larger (all $p < 0.05$) with an 11 point Likert scale when compared to a 5 point Likert scale (Differences in effect size: $0.135 \leq d_{11\text{-}point\text{-}5\text{-}point} \leq 0.337$). For PPC effect sizes, there were no significant differences.

2.2.5. Moderator effects of sample type

Sample type was a significant moderator for the PP effect size of items 1 ($d_{population} = 0.164$, $d_{psychosis} = 0.043$, $z = -2.02$, $p = 0.043$), 5 ($d_{population} = 0.256$, $d_{psychosis} = 0.068$, $z = -2.25$, $p = 0.025$) and 4 ($d_{population} = 0.148$, $d_{psychosis} = 0.068$, $z = -2.25$, $p = 0.025$), with less change in psychosis compared to population samples. While there were no significant differences in the PPC samples, PPC effect sizes were larger in the psychosis samples by descriptive values for the items 1, 7, 15, and 18 ($0.029 \leq d_{psychosis\text{-}population} \leq 0.127$). Item 5 showed a smaller PPC effect size in the psychosis ($d_{psychosis} = 0.198$) compared to the population sample ($d_{population} = 0.293$), but still showed the second highest PPC effect size in the psychosis samples (highest PPC effect size, item 18: $d_{psychosis} = 0.231$).

3. Scale validation

In a second step, the item characteristics, internal consistencies, unidimensionality, and criterion validity of the previously derived 13 item, 5 item, and 3 item version were tested in order to validate the subscales and compare goodness of fit to the original 18 item version of the state-adapted Paranoia Checklist.

3.1. Methods

We used the previously described hold-out subsample ($n = 1893$) from the large panel study (Moritz et al., 2014a) to estimate item characteristics and to test the unidimensionality of the revised as well as the brief state Paranoia Checklists with confirmatory factor analysis (CFA). CFA was performed based on Satorra-Bentler corrected Maximum Likelihood estimation (MLM), when non-normality of item-distributions was within acceptable parameters (skew below an absolute value of 3 and kurtosis below an absolute value of 8; Kline, 1998). In case of non-normal item-distributions beyond these parameters, item scores were treated as non-parametric data and CFA was conducted based on robust Diagonally Weighted Least Squares (DWLS) estimation. All CFA were calculated with the R package lavaan 0.5–18 (Rosseel, 2012). Additionally, an increase in the detected change compared to the original scale was tested by comparing pre-to-post effect sizes of the different 18, 13, 5, and 3 item version.

To assess convergent validity, we compared the correlation of the 18, 13, 5, and 3 item Paranoia Checklist with various measures of paranoid ideation that were used in 8 of the studies we used for the item selection procedure. Similarly, discriminant validity with social anxiety was tested based on 4 of these studies. Discriminant validity was analyzed, since the brief versions retained an increased percentage of items that asked about social-evaluative concerns (e.g., "People are laughing at me"), which may reduce discriminant validity in comparison to the 18 item Paranoia Checklist. Correlations of the individual samples were integrated using random effects meta-analyses (for details on the samples and measures used for validation, see Supplement 1).

3.2. Results

3.2.1. Item-characteristics

Means, standard deviations, skew, kurtosis, and item-scale correlations of all items are summarized in Table 2. As can be seen, all items of the 3 item and 5 item versions showed skew below 3 and kurtosis below 8. Among the items of the thirteen item version, however, two items showed skew and kurtosis above the threshold values. On average, excluded items exhibited more skewness and kurtosis than the included items. Item scale correlations were large ($r_{it} > 0.50$) for all items in all versions.

3.2.2. Internal consistency

Internal consistency was calculated with the baseline data from

Table 2
Item properties based on the cross-validation sample ($n=1893$).

	M[a]	SD	Skew	Kurtosis	Item-scale correlation		
					13 Items	5 items	3 items
3 item Version							
1. On my guard against others	1.58	0.88	1.65	2.44	0.74	0.62	0.55
5. People try to make me upset	1.72	0.87	1.26	1.42	0.63	0.591	0.55
7. Strangers/friends look critically	2.05	1.02	0.78	-0.04	0.67	0.67	0.57
5 Item Version addendum							
15. People laugh at me	1.81	0.96	1.20	1.00	0.73	0.71	
18. Actions/thoughts are controlled	1.35	0.73	2.35	5.56	0.60	0.53	
13 Item version addendum							
2. Negative comments	1.73	0.98	1.44	1.48	0.78		
3. People try to irritate me	1.52	0.86	1.81	2.97	0.78		
4. Being observed/followed	1.21	0.57	3.21	11.60	0.62		
6. Communication in subtle ways	1.58	0.84	1.53	2.05	0.77		
8. People might be hostile	1.75	0.95	1.26	1.09	0.75		
9. Bad things said behind my back	1.87	1.03	1.20	0.88	0.79		
12. People would harm me	1.69	0.94	1.43	1.52	0.76		
14. Conspiracy against me	1.22	0.61	3.31	12.31	0.63		
Excluded items							
10. Bad intentions (known person)	1.69	0.99	1.52	1.73			
11. Someone has it in for me	1.34	0.76	2.56	6.67			
13. Bad intentions (unknown person)	1.33	0.69	2.50	6.95			
16. Under threat from others	1.18	0.57	3.87	16.90			
17. Coded messages	1.10	0.42	4.93	27.18			

[a] Possible item range was 1–5.

the large panel study ($n=1966$; Moritz et al., 2014a). For the original 18 item version and the 13 item version, Cronbachs alpha was excellent (18 item version: $\alpha=0.95$; 13 item version: $\alpha=0.94$), while the 3 item and 5 item versions showed lower but nevertheless acceptable to good internal consistencies (5 item version: $\alpha=0.83$; 3 item version: $\alpha=0.74$).

3.2.3. Unidimensionality

Two items in the 13 item version showed considerable deviation from normality indicating DWLS to be the appropriate approach to CFA. No such violations were found for the 5 item and 3 item versions. In order to explore whether the CFA results based on parametric and non-parametric estimation yield diverging results, we performed both parametric and non-parametric CFA for all scale versions.

Results of the CFA are shown in Table 3. The 3 and 5 item version showed acceptable (RMSEA < 0.10) to good (CFI > 0.95) model fit based on parametric estimation. The 13 item version showed better model fit than the 18 item version, but only RMSEA was below the threshold indicating acceptable fit. CFA based on DWLS increased the CFI of all scale versions (all CFI > 0.95), but for the 5 item version the RMSEA fell above the threshold indicating insufficient fit.

3.2.4. Increase in change sensitivity

Increase in change sensitivity of the revised scales was tested based on PP effect sizes of the snowy picture task, which has been shown to reduce paranoid ideation (i.e. a brief task, in which participants need to decide whether each of a series of granulated pictures, in which it is difficult to identify an object, actually contain an object. The task requires participants to grade their degree of confidence, a feature which has been shown to ameliorate delusional ideas; Moritz et al., 2014a). With the original 18 item version, the PP effect size was $d=0.17$ ($t(1882)=18.9$, $p<0.001$). For the 13 item revised version, this effect increased by 10% to $d=0.19$ ($t(1886)=21.5$, $p<0.001$), while it increased by about 60% with the 5 item brief version ($d=0.28$; $t(1891)=22.5$, $p<0.001$) and the 3 item version ($d=0.27$; $t(1886)=19.6$, $p<0.001$).

Table 3
Confirmatory factor analysis of the one for the Paranoia Checklist, based on the hold out sample ($n=1893$).

	Estimation	Chi^2	df	p	CFI	RMSEA [90%-CI]	Loadings	Cronbachs α
18 items	MLM	1985	135	< 0.001	0.73	0.085 [0.082–0.086]	0.46–0.81	0.95
	DWLS	2309	135	< 0.001	0.97	0.092 [0.089–0.096]	0.71–0.92	
13 items	MLM	870	65	< 0.001	0.86	0.081 [0.078–0.084]	0.62–0.81	0.94
	DWLS	1244	65	< 0.001	0.97	0.098 [0.093–0.103]	0.72–0.88	
5 items	MLM	80	5	< 0.001	0.95	0.089 [0.077–0.103]	0.56–0.82	0.83
	DWLS	120	5	< 0.001	0.99	0.110 [0.094–0.128]	0.71–0.87	
3 items[a]	MLM	17	2	< 0.001	0.98	0.064 [0.042–0.088]	0.64–0.71	0.74
	DWLS	3	2	0.261	1.00	0.013 [0.000–0.050]	0.76	

Note: MLM = Satorra-Bentler corrected maximum likelihood estimation; DWLS = robust diagonally weighted least squares estimation.

[a] In order to make estimation of fit indices possible, factor loadings in the three-item version were constraint to be equal.

Table 4
Results from the meta-analyses of convergent (paranoid ideation) and discriminant validation (social anxiety) samples by Paranoia Checklist version.

Paranoia Checklist version	Validation measures	Samples	*N* (patients; population)	*r*	*Fisher Z*	*SE*	*Z*	*p*
18 Items	Paranoia	10	611 (189; 422)	0.538	0.602	0.053	11.411	< 0.001
	Social Anxiety	6	282 (162; 120)	0.450	0.485	0.081	5.982	< 0.001
13 Items	Paranoia	10	611 (189; 422)	0.545	0.611	0.057	10.732	< 0.001
	Social Anxiety	6	282 (162; 120)	0.459	0.496	0.086	5.771	< 0.001
5 Items	Paranoia	10	611 (189; 422)	0.494	0.541	0.060	9.061	< 0.001
	Social Anxiety	6	282 (162; 120)	0.449	0.483	0.084	5.766	< 0.001
3 Items	Paranoia	10	611 (189; 422)	0.472	0.512	0.055	9.355	< 0.001
	Social Anxiety	6	282 (162; 120)	0.417	0.444	0.089	4.995	< 0.001

3.2.5. Convergent and discriminant validity

The average effect size of the correlations between the different versions of the state Paranoia Checklist and trait paranoia as well as social anxiety are shown in Table 4. As can be seen, all versions of the Paranoia Checklist showed comparable effect sizes, with a medium to large mean correlation ($0.472 \leq r \leq 0.545$) with trait measures of paranoia and a medium mean correlation ($0.417 \leq r \leq 0.459$) with social anxiety. There were no significant moderator effects of sample type (population vs. psychosis sample).

4. Ambulatory assessment pilot test

The brief Paranoia Checklist versions were derived based on sensitivity to change in order to provide a validated measure for paranoid ideations in ambulatory assessment studies. However, item selection was based on experimental repeated measure studies. Thus, we tested whether the brief Paranoia Checklist captures daily variation of paranoid ideation (i.e., intra-individual variation) in an ambulatory assessment study.

Furthermore, previous research proposed negative emotional states to be a trigger for paranoid ideations (e.g., Freeman et al., 2002). Building on these results, we explored the association of negative and positive emotions and state paranoia in order to test convergent and discriminant validity.

4.1. Methods

4.1.1. Procedure and materials

As part of an unpublished study (Voss, 2015), university students who reported having experienced psychosis-like events at least sometimes in their life filled out daily questionnaires for seven consecutive days via an online survey platform.

Participants were screened with the Positive Symptoms subscale of the Community Assessment of Psychic Experiences (CAPE, Stefanis et al., 2002), in which lifetime experience of 20 positive symptoms is rated from 0="never" to 3="nearly always". In order to be included, they had to report having experienced at least one positive symptom at least sometimes in their live (indicated by a CAPE positive symptoms sum score equal or above 1).

Upon inclusion, participants received an e-mail for seven consecutive days, which contained a weblink to an online survey and instructions to fill out this questionnaire by the end of the day. The daily questionnaires included a brief 5 item questionnaire, in which participants reported their experience of five emotions (anxiety, anger, depression, shame, joy; Stemmler et al., 2001). Emotional states were assessed by presenting four adjectives describing each state (e.g., "frightened, timid, afraid, scared" for anxiety), respectively, and asking participants how much these items applied to them over the last day (ranging from 0="not applicable" to 10="completely applicable"). Following this, participants were presented with the 5 item Paranoia Checklist and were asked to indicate how much each of the items applied to them during the past day. As an answer format, the previously used eleven point Likert scale format (1–11, see Section 2.1.2.) was chosen. For every item rated with 2 or more, participants were asked to indicate the distress associated with the experience on a Likert scale ranging from 1="none" to 11="very much" (similar to the original Paranoia Checklist, Freeman et al., 2005).

4.1.2. Sample

Thirty-two psychology students (78% female, mean age: 26.6 years) were included in the study. Participants' CAPE positive symptoms score was 10.2 on average (range: 2–31). Three participants reported a diagnosis of depression in their past, while a fourth reported diagnoses of depression, social anxiety disorder and ADHD. Data on daily assessment was completed for 93.3% of all measurement points. Participants were compensated with partial course credit.

4.1.3. Strategy for data analysis

We calculated multilevel regression models with measurement points (level 1) nested in participants (level 2). In order to explore the amount of change in paranoid ideation captured by the brief versions of the Paranoia Checklist, random intercept models were calculated for the 3 item brief version and the 5 item brief version. Based on these models, intra-individual and between participant variance were calculated.

In order to explore convergent validity, we calculated one random-intercept model of paranoid ideation with CAPE paranoia scores (Schlier et al., 2015) as level 2 predictor and four random intercept, random slope models of paranoid ideation by reported anxiety, anger, depression and shame on the same day, respectively. Similarly, joy was entered as predictor to test discriminant validity. All models were calculated for the 3 and 5 item versions and for frequency- and distress-scores.

4.2. Results

Baseline scores of paranoia measured with the CAPE were a significant predictor of prevalence of paranoid ideation (3 item version: $b=1.14$, $t(32)=4.13$, $p<0.001$; 5 item version: $b=1.82$, $t(32)=4.15$, $p<0.001$) and distress (3 item version: $b=1.04$, $t(32)=3.63$, $p<0.001$; 5 item version: $b=1.70$, $t(32)=3.52$, $p=0.001$).

Results of the random-intercept, random slope models are summarized in Table 5. As can be seen, 26% and 31% of the variance in the 5 item and 3 item version frequency scores were associated to daily within subject variation, while within subject variance for the distress scales were 31% and 40%, respectively. Interestingly, internal consistency at day one exceeded the estimates from the validation sample (5 item version: $\alpha=0.88$; 3 item

Table 5
Results of multilevel-analyses of daily measurements of paranoia nested in participants (n=32).

Dependent variable	Random intercept models variance in percent (absolute)		Random intercept, random slope models, slope-estimates of independent variables B; t value				
	Within subjects	Between subjects	Anxiety	Anger	Depression	Shame	Joy
Paranoia frequency							
3 item version	26.5% (17.69)	73.5% (48.97)	0.62** (3.76)	0.72*** (4.10)	0.56*** (4.08)	0.98*** (4.07)	−0.27 (−1.65)
5 item version	31.7% (8.79)	68.3% (18.95)	0.84** (3.77)	1.00*** (3.80)	0.82*** (4.15)	1.32** (3.69)	-0.39 (−1.56)
Paranoia distress							
3 item version	40.1% (12.40)	59.9% (18.52)	0.66* (2.73)	0.60** (3.34)	0.41** (3.14)	1.11** (3.41)	−0.15 (−0.94)
5 item version	31.0% (24.07)	69.0% (52.57)	0.89* (2.81)	0.97** (3.76)	0.67** (3. 56)	1.58** (3.25)	−0.35 (−1.68)

Note: Significance based on Kenward-Roger approximation of degress of freedom.
***$p < 0.001$; **$p < 0.01$; *$p < 0.05$; +$p < 0.10$.

version: $\alpha = 0.83$). Frequency and distress sum scores were significantly predicted by anxiety, anger, depression, and shame, while no significant association between joy and any paranoia-score was found. This indicates both convergent and discriminant validity with respect to emotional state.

5. Discussion

This study aimed to derive a change sensitive state-adapted Paranoia Checklist as well as a brief version consisting of the most change sensitive items. It resulted in a thirteen item change sensitive version (revised State Paranoia Checklist) and a five and three item version of the Brief State Paranoia Checklist. Cross validation with a large population sample showed overall good psychometric qualities for all versions. An ambulatory assessment pilot study corroborated the sensitivy to change of both brief scales and provided an indicator of convergent and discriminant validity.

When compared to the full version, all three versions showed increased model fit. However, parametric estimation may only be valid for the 5 item and 3 item versions, which both included only items with an acceptable deviation from normal distribution. For the 13 item version, only non-parametric estimation yielded sufficient model fit. Implementation of the 13 item version may thus benefit from resorting to item response theories in order to calculate person parameters.

Validation of the abbreviated versions showed convergent validity with paranoia to be comparable to the 18 item version. However, all versions of the Paranoia Checklist show a medium correlation with measures of social anxiety. This is in line with previous studies that found a considerable overlap between social anxiety and paranoid ideation (Gilbert et al., 2005; Freeman et al., 2008; Lysaker et al., 2010; Newman Taylor and Stopa, 2013). Moreover, this overlap with social anxiety is in line with the way Freeman and colleagues (2005) conceptualized the hierarchy of paranoid ideation that is measured with the Paranoia Checklist. Accordingly, paranoid ideation consists of the three aspects social evaluative concerns closely related to social anxiety (e.g., fears of rejection), ideas of reference and persecutory thoughts. All aspects of the hierarchy of paranoid ideation are retained in the 13 and 5 item version of the State Paranoia Checklist. While the 5 item version still addresses ideas of control, the 3 item version does not include this aspect by omitting item 18 ("My actions and thoughts might be controlled by others"). Nevertheless, the 3 item version of the scale retains the two core elements by which persecutory thinking is defined (Freeman et al., 2007): feared harm ("I need to be on my guard against others"), and perpetrator intent ("People are trying to make me upset"). However, one of the items refers to negative evaluations by others, which is a core feature of social anxiety ("Strangers and friends look at me critically"), while item 5 asks about feared harm by self-rating safety behaviors (i.e., "I need to be on my guard against others"). Thus, content validity may be reduced in the 3 item version. The ratio of convergent and discriminant validity, however, appears similar for the full version and all abbreviated versions.

5.1. Implications for the measurement of state paranoia

The effect sizes in all presented analyses were small, even in the change-sensitive items. The effect sizes in the meta-analyses, however, may not reflect the true capability of the scales to measure change: In many of the included studies paranoia was changed by brief interventions or stressors, which may only bring about a limited amount of change.

Based on the differences between effect sizes in different subsamples, we recommend the following when working with the brief state Paranoia Checklists: (1) for all state versions of the Paranoia Checklist, a Likert scale with more than 5 points should be used to increase sensitivity to change. (2) The 3 item version may readily be used for ambulatory assessment with population samples, as it is a valid and change sensitive scale for this population. (3) Based on differences in change sensitivity for single items and in order to increase content validity, the 5 item version is the preferable choice for ambulatory assessment with people with psychosis. (4) For experiments, using the 5 item or the 13 item version may be the first choice in order to capture more aspects of paranoid ideation. It has to be noted, though, that person parameters may need to be estimated with an item-response model for the 13 item version.

Finally, the ambulatory assessment data indicates that variability can be increased by reintroducing additional dimensions such as distress (Freeman et al., 2005). Including preoccupation and conviction associated with symptoms (Peters et al., 1999) may yield similar results.

5.2. Strengths and limitations

Our analysis included a variety of studies and samples, with multiple population samples as well as samples of patients with psychosis. Consequently, we can assume to have captured variation in paranoia across different settings. The item selection can be

considered valid for all forms of changes in paranoia, including induction effects, intervention effects, and natural fluctuations.

A limitation, however, is that all samples were German-speaking. Hence, when using our item selection for the original English version (or any other translation), researchers may wish to pilot test the scale before applying it in elaborate and large-scale studies. So far, however, the original and the German version of the Paranoia Checklist have shown comparable internal consistency and validity.

Furthermore, this study lacks data that compares the State Paranoia Checklist with other state paranoia scales. Future studies are needed to complement these aspects of the scale validation. Similarly, the ambulatory assessment validation with measures of negative affect is not specific to a paranoid reaction. Given the overlap between state paranoia as measured by the Paranoia Checklist and social anxiety, future studies should test the associations between fluctuations captured with the Brief State Paranoia Checklists and fluctuations in social anxiety beliefs (discriminant validity) and specific precursors to paranoid ideation (e.g., jumping-to-conclusions bias, or perceptual anomalies).

5.3. Conclusion

With our item selection, we derived three state-adapted versions of the Paranoia Checklist consisting of 3 and 5 (*Brief state Paranoia Checklists*) as well as 13 items (*State Paranoia Checklist-R*). All scales show good reliability. Sensitivity to change, measured as the relative increase in the average effect size from the 18 item Paranoia Checklist, increases with these item selections, as does the factorial validity. Our *State Paranoia Checklist* and *Brief State Paranoia Checklists* can thus serve as validated scales for the measurement of state paranoia in experimental, longitudinal, and ambulatory assessment studies.

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Conflict of interest

None.

Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.psychres.2016.05.002.

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Supplemantal Table S1.

Overview of the studies and measures used for convergent and discriminant validation meta analyses.

Study	Sample Type	Paranoid ideation measure (convergent validity)	Social anxiety measure (discriminant validity)
Kesting et al. (2013)	Population sample	CAPE Paranoia Subscale	-
Lincoln et al. (2014a, 2014b)	Participants with Psychosis	CAPE Paranoia Subscale	Social Phobia Scale (SPS)
	Population sample		
Lincoln et al. (2012)	Population sample	CAPE Paranoia Subscale	-
Lincoln et al. (2009)	Population sample	SCL-90, Paranoia Subscale	SCL-27, Social Anxiety subscale
Moritz et al. (2015a)	Participants with Psychosis	CAPE Paranoia Subscale	WSQ
Moritz et al. (2015b)	Participants with Psychosis	CAPE Paranoia Subscale	-
Moritz et al. (2014)	Participants with Psychosis	PANSS-Item “Suspiciousness/persecution”	PANSS-Item “Active social avoidance”
Roggenbuck (unpublished)	Population sample	CAPE Paranoia Subscale	-

Note: CAPE = Community Assessment of Psychic Experiences (Stefanis et al., 2002; Schlier et al., 2015), Social Phobia Scale (Heimberg et al., 1992), SCL-90 = Symptom Checklist 90 (Derogatis and Unger, 2010), SCL-27 = Symptom Checklist 27 (Hardt et al., 2006), WSQ = Web Screening Questionnaire for common mental disorders (Donker et al., 2009), PANSS = Positive and Negative Syndrome Scale (Kay et al., 1987)

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Appendix C: Study 3

Schlier, B., Hennig, T., & Lincoln, T. M. (2017). Measuring fluctuations across the Continuum of Auditory Hallucinations. Development and validation of a state inventory. *Psychiatry Research, 253*, 325–332.

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Measuring fluctuations across the Continuum of Auditory Hallucinations. Development and validation of a state inventory

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ABSTRACT

In order to identify causes and triggers of hallucinations that can inform therapy, reliable, valid, and change-sensitive instruments to assess hallucinatory experiences in the subclinical and clinical range are needed. We developed and validated a novel scale, the Continuum of Auditory Hallucinations - State Assessment (CAHSA), to be used for repeated assessment of the subclinical factors vivid imagination, intrusive thoughts, and perceptual sensitivity as well as auditory hallucinations. After selecting items for the four factors in a first test sample (n=84), we tested factorial validity using CFA and criterion validity with self-reported psychosis-like experiences (n=534). Finally, within-subject variation of CAHSA scores over 14 days and time-lagged associations between its factors were explored (n=85). A 9-item CAHSA was selected that showed good factorial validity, criterion validity, and substantial, valid within-subject variation. Time-lagged regression showed that vivid imagination, perceptual sensitivity, and intrusive thought precede auditory hallucinations. In sum, the CAHSA validly measures fluctuation along the continuum of auditory hallucinations, is sensitive to change, and well suited for experimental studies, repeated measurement, and longitudinal research.

1. Introduction

Although there has been a wealth of research on auditory hallucinations over the past decades, we have still not understood what precedes and possibly triggers them (Stinson et al., 2010). This understanding is vital to improving therapeutic interventions. Nevertheless, it is not until recently that researchers have begun to explore the external (Delespaul et al., 2002; Verdoux et al., 2003) and internal triggers (Stinson et al., 2010) of hallucinations in daily life. A cogent next step to advance the research in this area is the development of valid and reliable instruments to assess fluctuations in hallucinatory experiences.

In contrast to widely held beliefs, hearing voices is neither a rare phenomenon nor exclusively tied to severe psychopathology. In fact, evidence points to a continuum of auditory hallucinations. The one end of the continuum consists of two groups: The clinical group, including the 60% of people diagnosed with schizophrenia spectrum disorders who repeatedly experience distressing auditory hallucinations (Lim et al., 2016), and the group of otherwise healthy people, who experience auditory hallucinations in varying frequency and comprise up to 13.8% of the general population (Beavan et al., 2011). The other end of the continuum consists of people who have never had any type of hallucinatory experience. Between these extreme ends there is a majority of people who experience "subclinical" (Serper et al., 2005) hallucination-like experiences. For example, different research groups found various factors of subclinical hallucination-like experiences such as "vivid imagination" (Morrison et al., 2002; Waters et al., 2003), "intrusive thoughts", and "sleep-related hallucinations" (Larøi et al., 2004; Preti et al., 2014) or an increased sensitivity to random auditory stimuli (Behrendt, 1998; Bell et al., 2010; Jones, 2010). If we want to explore the causes and triggers of auditory hallucinations in clinical as well as in subclinical populations, we need to extend the focus of assessment from the extreme end of the continuum of auditory hallucinations to these hallucination spectrum experiences.

Various self-report measures have been used to assess auditory hallucinations and subclinical hallucination-like experiences in the general population. The most commonly known are the Launay-Slade Hallucination Scale (LSHS) and its revised forms (Launay and Slade, 1981; Morrison et al., 2002; Larøi et al., 2004) and the Unusual Experiences subscale of the Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE; Steel et al., 1996). These questionnaires, however, assess an individual's general predisposition to experience hallucinations over a long time rather than current experiences. Moreover, many items included in these questionnaires describe experiences that are specific to a certain context (e.g., seeing one's self-image in the mirror as somewhat distorted) or content (e.g., hearing one's name being said or hearing the phone ring). These

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questionnaires are well-suited for survey studies on the prevalence of clinical and subclinical hallucinations. However, they are less suitable for measuring changes over short time intervals. Experimental research paradigms that manipulate potential causal factors to elicit changes in hallucinatory experiences need brief, less context-specific assessments. The same applies to longitudinal assessment studies that measure fluctuations in hallucinations via repeated measurements.

In the field of ambulatory assessment, auditory hallucinations are often measured with a single item, such as "I hear voices" (Delespaul et al., 2002) or "Since the last beep, I have heard or seen things others could not" (Barrantes-Vidal et al., 2013). Although this constitutes a face-valid approach, two limitations have to be noted. First, they are one item measures, which makes them susceptible to measurement error (Wilhelm and Schoebi, 2007). Second, assessing auditory hallucinations at the severe end of pathology excludes subclinical, hallucination-like experiences. In other words, these measures are suitable for a target population with frequent auditory hallucinations. For people who seldom experience hallucinations they are likely to produce floor effects. When studying at-risk populations who are predisposed to hallucinatory experiences but presently only experience subclinical phenomena along the continuum, they are unlikely to produce meaningful findings at all.

Here we report on the development of an economic measure to assess fluctuations in hallucinatory experiences along a broad spectrum of the continuum. To keep the measure brief and focused, we limited it to the continuum of auditory hallucinations and excluded other modalities like visual hallucinations, since auditory hallucinations constitute the most prevalent form of hallucinations in groups with unimodal and multimodal hallucinations (Lim et al., 2016). We conducted three studies with the respective aims of selecting, modifying, and pilot-testing items (study 1), testing factor validity and criterion validity in a cross-sectional design (study 2), and testing the measure's validity and sensitivity to change in a two week daily assessment study (study 3).

2. Study 1 – item generation and pilot testing

In the first study, we pilot tested a set of items that was generated on the basis of existing trait measures of hallucinatory experiences with the aim of selecting the most suitable items. Furthermore, within-subject variation was tested in a daily assessment pilot study in order to exclude invariant items.

2.1. Methods

2.1.1. Materials

Candidate items for the measure were generated on the basis of items from the LSHS (Launay and Slade, 1981), its revised forms (Morrison et al., 2002; Larøi et al., 2004), the O-LIFE (Steel et al., 1996; Grant et al., 2013), and the Community Assessment of Psychic Experiences (Stefanis et al., 2002). In a first step, the first author identified 25 items that dealt with subclinical, hallucination-like experiences (i.e., vivid imagination, perceptual sensitivity, and intrusive thought) or auditory hallucinations. In a second step, items were eliminated if they (a) could not be unambiguously allocated to one single form of hallucination-like experiences or auditory hallucinations (one item: "I can hear music when it is not being played", which was shown to load equally on vivid imagination and hallucinations in a previous factor analysis; Morrison et al., 2002), (b) if they mixed the experience with emotional (three items, e.g., "I have been troubled by hearing voices in my head") or cognitive appraisal (two items, e.g., interpreting a voice as being the devil), or (c) if they described a specific experience unlikely to be applicable to all circumstances (two items, e.g., "I hear the telephone ring and find that I am mistaken"), reducing the item pool to 17 items. In a third step, these remaining items were combined if they showed overlapping content, resulting in a template for the generation of a 12 item list, with three items for each of the subscales vivid imagination, perceptual sensitivity, intrusive thought, and auditory hallucinations. Finally, this item selection was discussed and approved by an expert group. For the purpose of this study, participants had to indicate how much each item applied to them for the last day (Instruction text: "Today, I had the following feelings and experiences:") on a Likert-scale ranging from 1 ("not at all") to 7 ("very much").

2.1.2. Procedure

The study was conducted online using the Questback survey platform (QuestBack GmbH, 2014). Participants were informed that the study would include a brief questionnaire about unusual experiences with an option to partake in a one week daily assessment study. All participants provided informed consent at the beginning of the study. Following this, they filled out the 12-item questionnaire, followed by a brief questionnaire on demographic data. Next, they could volunteer to take part in a daily assessment of hallucinatory experiences. In this case, they received daily e-mails with a link to the questionnaire for seven days. The baseline assessment took six minutes and the daily assessments took an average of 90 s per day. Participants received no monetary incentive for participation.

2.1.3. Participants

Eighty-four participants (60.7% female) from the general population were recruited via advertisement on facebook. Mean age was 25.49 (SD=5.51). About one third (34.5%) reported their highest education level to be the university entrance diploma, while 54.8% held a university degree (Bachelor's degree or higher). The majority of participants were students (65.5%), while 31.0% were in gainful employment. Twenty-five of these participants (60% female, age: M=24.92, SD=5.48) took part in daily assessment pilot study following the baseline assessment with 66.5% of the daily questionnaires completed.

2.1.4. Data analysis

Items were tested for their suitability for the final questionnaire in terms of factorial validity and sensitivity to daily variation. The item-pool of each of the four potential subscales (i.e., vivid imagination, perceptual sensitivity, intrusive thought, hallucinations) was subjected to a separate principal component analysis (PCA). Items were considered for removal from the item pool if they did not load consistently with the other items from their respective category.

Furthermore, within-subject variation over the one week daily assessments was calculated for each item using random-intercept regression models of assessment days (level 1) nested in participants (level 2). Similar to ICC, the percentage of within-subject variation was calculated as the fraction of residual level 1 variance (i.e., the absolute variance within subjects in the multilevel model) and total variance derived from these multilevel regression models. If an item showed low absolute within-subject variation as well as a low percentage of within-subject variation compared to the remaining items of its category, it was removed. All analyses were performed with R 3.2.2 (R Core Team, 2014).

2.2. Results

Based on PCA, one item from the vivid imagination and one item from the intrusive thoughts subscale were removed because of reversed and low loadings on principal components.

Analyses of the within-subject variation of the items showed that one item of the perceptual sensitivity scale showed considerably less within-subject variation than the other two (23.7% within-subject variation vs. > 40% within-subject variation, see Table 1), so it was removed as well, leaving a list of nine of the originally 12 items for further testing.

Table 1
Factor loadings and sensitivity to change of the Continuum of Auditory Hallucinations - State Assessment (CAHSA) and its items.

Factor Item Text	Study 1 (*N*=25×7) within-subj. variation (absolute/%)		Study 2 (*N*=534) Item loading	Study 3 (*N*=85×14) within-subj. Variation (absolute/%)	
Vivid imagination subscale	2.55	24.2%		1.02	47.4%
My fantasies were vivid and intense.	0.99	34.7%	0.738	1.25	51.3%
I daydreamed a lot.	1.03	32.6%	0.664	1.32	50.8%
Noises, tunes, or words I imagined were as clear as if they were real	0.86	23.8%	–	–	–
Perceptual sensitivity subscale	4.77	44.0%		0.55	50.9%
My hearing was so sensitive that even everyday noise became irritating.	1.61	41.7%	0.786	0.72	55.8%
I felt easily distracted by distant sounds.	1.69	40.3%	0.793	0.74	55.8%
My voice seemed to be distant or far away	0.41	23.7%	–	–	–
Intrusive thoughts subscale	2.70	34.5%		0.47	41.8%
My thoughts were so strong and vivid that I could almost hear them.	1.28	41.3%	0.793	0.68	50.2%
Ideas and thoughts hit me so fast that I could not express them all.	1.14	45.2%	0.679	0.74	50.6%
I found it difficult to control my thoughts even when I was concentrating.	0.89	42.8%	–	–	–
Auditory hallucinations subscale	1.06	13.4%		0.10	33.0%
I heard one or more voices in my head speaking my thoughts aloud, talking to each other or saying other things.	0.23	13.7%	0.459	0.31	37.1%
Meaningless noise I heard sounded like someone was saying my name or as if people were talking.	0.39	41.2%	0.605	0.19	52.4%
I heard something other people cannot hear.	0.35	23.7%	0.671	0.15	45.5%

Note. Loading=Item loading in a confirmatory factor analysis of a four-factor model; within-subj. variation=residual variance in a random intercept hierarchical regression model and percentage of total variance; (*N*=25×7)=repeated measurement, with 25 participants being assessed on 7 consecutive days.

3. Study 2 – factorial and criterion validation

In the second study, we aimed to verify the model fit of the previously derived 9-item questionnaire in a new and larger sample and to test the criterion validity with an established self-report measure of psychosis-like experiences. Moreover, we aimed to explore the structure of the continuum of hallucinations by determining how closely each of the three subclinical factors (vivid imagination, perceptual sensitivity, and intrusive thought) is related to auditory hallucinations, the upper end of the continuum.

3.1. Methods

3.1.1. Participants

For the second online-study, 534 students (67.6% female) were recruited via advertisement on the homepage of the University of Hamburg. Their mean age was 21.31 years (*SD*=1.73, Range 18–24). Participation took about ten minutes. Participants received no monetary incentive for participation.

3.1.2. Materials

The 9-item measure was presented with 7-point Likert scales and with the same brief instruction as in study 1. A full list of all items is shown in Table 1. In the further course of this validation, the 9-item questionnaire will be referred to as *Continuum of Auditory Hallucinations - State Assessment* (CAHSA).

The *Community Assessment of Psychic Experiences* (CAPE, Stefanis et al., 2002) was included for criterion validation. The CAPE is a 42-item self-report questionnaire that assesses life-time experiences of positive symptoms (e.g., “Do you ever feel as if you are being persecuted in some way?”), negative symptoms (e.g., “Do you ever feel that your emotions are blunted?”), and symptoms of depression (e.g., “Do you ever feel pessimistic about everything?”) in population samples. Participants indicated how frequently they experienced each of the feelings, thoughts, and experiences described on a 4-point Likert scale ranging from 0 (“never”) to 3 (“nearly always”). The CAPE (Stefanis et al., 2002) and its German version (Schlier et al., 2015) have been shown to be valid and reliable measures of positive symptoms, negative symptoms, and symptoms of depression in population samples.

3.1.3. Procedure

The online survey was presented on Questback (QuestBack GmbH, 2014). Participants were informed that the study included brief questionnaires about certain experiences and thoughts before they gave their informed consent. Participants answered to a brief demographic questionnaire, followed by the CAPE and the CAHSA. At the end of the study, participants could enter contact information (e-mail) if they wanted to participate in a daily assessment study (study 3).

3.1.4. Data analysis

Confirmatory factor analysis (CFA) was performed to determine model fit. Satorra-Bentler correction was used in order to compensate for skewed item distributions. A $CFI > 0.95$, a $RMSEA < 0.06$, and a $SRMR < 0.08$ served as indicators of a good model fit. The four-factor model for the CAHSA was compared to a one-dimensional and a two-dimensional model (1. subclinical factor: vivid imagination, perceptual sensitivity, and intrusive thoughts; 2. clinical factor: auditory hallucinations). The best fitting model was re-tested with fixed equal loadings of all items to their respective factors in order to determine whether calculating sum scores would validly represent the latent factor values. Finally, the fit of a model including a second-order factor was tested to validate the use of a total score representing the full continuum of auditory hallucinations.

Correlation tests of CAPE and CAHSA subscales were used to determine criterion validity. The positive symptom subscale served as an indicator of convergent validity, whereas the depression and negative symptom subscales served as indicators of discriminant validity. Finally, we explored how the CAHSA subclinical factors are related to the auditory hallucination subscale using Bonferroni-corrected partial correlation tests of the factors (controlling for all other factors, respectively).

3.2. Results

3.2.1. Confirmatory factor analysis

Factor loadings for a four-factor model are shown in Table 1. The four-factor model of the CAHSA showed good model fit according to all three fit indices (CFI=0.988, $RMSEA$=0.029, $SRMR$=0.025), while neither a one-dimensional (CFI=0.793, $RMSEA$=0.124, $SRMR$=0.070) nor a two-dimensional alternative model (CFI=0.831, $RMSEA$=0.093, $SRMR$=0.060) showed sufficient fit. Retest of the four-

Table 2
Convergent and discriminant validity of the CAHSA as indicated by correlations with the CAPE.

	CAPE positive symptoms	CAPE symptoms of depression	CAPE negative symptoms
CAHSA total	0.56***	0.33***	0.21***
CAHSA subscales			
Vivid imagination	0.34***	0.24***	0.13**
Perceptual sensitivity	0.44***	0.29***	0.23***
Intrusive thoughts	0.47***	0.27***	0.15***
Auditory hallucinations	0.43***	0.18***	0.12**

Note. CAPE=Community Assessment of Psychic Experiences, positive symptoms are an indicator of convergent validity, negative symptoms and symptoms of depression are indicators of discriminant validity. CAHSA=Continuum of Auditory Hallucinations - State Assessment.
** $p < 0.01$.
*** $p < 0.001$.

factor model with fixed equal item loadings to the respective factors still yielded good model fit (*CFI*=0.983, *RMSEA*=0.030, *SRMR*=0.030). Also, testing a four-factor model with a second-order factor showed good fit (*CFI*=0.959, *RMSEA*=0.050, *SRMR*=0.050).

3.2.2. Criterion validation

Correlations of the CAHSA total and subscale scores with CAPE positive symptoms, negative symptoms, and symptoms of depression are shown in Table 2. The CAHSA total score showed a large correlation with positive symptoms, a medium correlation with symptoms of depression, and a small correlation with negative symptoms. Furthermore, each of the CAHSA subscales showed a medium correlation with positive symptoms, and small correlations with negative symptoms and symptoms of depression. Thus, all CAHSA scales showed stronger correlations with the indicator of convergent validity (positive symptoms) than with indicators of discriminant validity (negative symptoms and depression).

3.2.3. Partial correlations of CAHSA subscales

All significant partial correlations between CAHSA subscales are shown in Fig. 1. Significant partial correlations were found between vivid imagination and perceptual sensitivity (r_{par}=0.14, t(530)=3.56, $p_{bonf\text{-}cor}$=0.007) as well as intrusive thoughts (r_{par}=0.42, t(530) =10.74, $p_{bonf\text{-}cor} < 0.001$). Furthermore, perceptual sensitivity and intrusive thoughts correlated significantly (r_{par}=0.22, t(530)=5.15, $p_{bonf\text{-}cor} < 0.001$). Finally, auditory hallucinations showed partial correlation with perceptual sensitivity (r_{par}=0.23, t(530)=5.58, $p_{bonf\text{-}cor} < 0.001$) and intrusive thoughts (r_{par}=0.35, t(530)=8.65, $p_{bonf\text{-}cor} < 0.001$), but not with vivid imagination (r_{par}=−0.02, t(530) =−0.36, $p_{bonf\text{-}cor} \approx 1.000$).

4. Study 3 – application in daily assessment

The third study served to validate the CAHSA in a repeated measurement design. We aimed (1) to replicate the four-factor model in a multilevel model, (2) to test sensitivity to change, (3) to validate that daily assessments and fluctuations between days correspond with retrospective reports of having more psychosis-like experiences prior to the assessment period, and (4) to explore time-lagged associations between the CAHSA subscales.

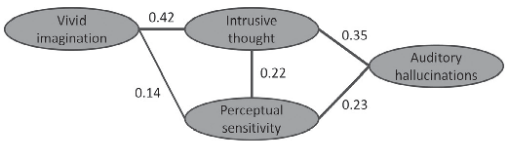

Fig. 1. Association between the Continuum of Auditory Hallucinations - State Assessment (CAHSA) subscales, based on partial correlations controlling for all other subscales. Only significant partial correlations are shown.

Specifically, we tested to which extent the CAHSA captures daily variation in hallucinatory experiences in a population sample comprising people with elevated baseline levels of positive symptoms and those with no history of experiencing positive symptoms. Moreover, we explored whether the self-reported life-time experience of positive symptoms at baseline was associated with the mean levels of the CAHSA scores over an extended assessment period (indicating that averaged daily assessments correspond with retrospective reports of psychosis proneness). Additionally, we tested whether life-time experience of positive symptoms at baseline (i.e., retrospectively reporting frequent psychosis-like experiences) corresponds with the amount of fluctuations in a person's daily assessments. This association would indicate that the observed within-subject variation of CAHSA scores validly represents fluctuations between experiencing and not experiencing hallucination-like events.

Finally, based on the partial correlations found in study 2, we tested which subclinical subscales predicted other subclinical subscales and auditory hallucinations at the same time-point (cross-sectional analyses) and at the next time-point (time-lagged analyses). We expected to find a pattern of cross-sectional and time-lagged associations similar to the partial correlations in study 2 (see Fig. 1), with subclinical factors being a stronger precursor of more pronounced hallucination-like experiences and auditory hallucinations than vice versa (i.e., vivid imagination predicts perceptual sensitivity and intrusive thoughts in the time-lagged analyses and perceptual sensitivity and intrusive thoughts predict auditory hallucinations).

4.1. Methods

4.1.1. Participants

Eighty-five participants were recruited from the pool of participants from study 2, based on their CAPE positive symptoms score. Participants were included in the no symptom group (NoS Group; n=43), if their CAPE positive symptoms score was at or below the 25%-quantile (i.e., ≤5), and in the attenuated symptoms group (AtS Group; n=42), if their CAPE positive symptoms score was at or above the 75%-quantile (i.e., ≥13). Norm data to calculate the quantiles was derived from the population sample used in the German CAPE validation study (Schlier et al., 2015). Demographic characteristics of the two groups are summarized in Table 3. Participants received 20€ for their participation.

4.1.2. Materials

During screening for this study (i.e., study 2), participants filled out a demographic questionnaire and the CAPE (Stefanis et al., 2002). During the assessment period, participants were presented with the CAHSA in the same way as in the previous two studies. Additional daily assessment measures not relevant for this analysis but included in the daily questionnaires were 5 items on paranoid ideation (Schlier et al., 2016), 10 items on current mood (Stemmler et al., 2001; Wilhelm and Schoebi, 2007), a 12-item questionnaire on emotion regulation (Ebert et al., 2013) and an 11-item sleep questionnaire (based on Hoffmann et al. (1997)).

4.1.3. Procedure

Participants were informed about the study and provided informed consent during a baseline session at the University of Hamburg. Thereafter, they received daily E-mails containing a link to the daily questionnaire for 14 days. Participants were instructed to fill out the questionnaires in the evening of the respective day. Completing a daily assessment took about nine minutes. The questionnaires were presented in randomized order each day.

Table 3
Demographic characteristics and reported psychosis-like experiences of the sample in study 3.

	M; SD or %		*T*-test or Chi²-test
	AtS Group (n=42)	NoS Group (n=43)	Between group difference
Age	21.35; 1.38	21.35; 1.51	$T(67.11)=0.01$, $p=0.989$
Female	62.8%	64.3%	$\chi^2(1)=0.02$, $p=0.886$
Born in Germany	93.0%	95.2%	$\chi^2(1)=0.19$, $p=0.664$
CAPE			
Positive symptoms	18.19; 5.19	3.19; 1.06	$T(45.61)=18.54$, $p<0.001$, d=4.02
Negative symptoms	16.98; 6.30	9.00; 3.76	$T(66.94)=7.05$, $p<0.001$, d=1.53
Depression	9.79; 4.03	4.90; 1.75	$T(57.61)=7.28$, $p<0.001$, d=1.58
CAHSA			
Assessment adherence	96.51%	96.26%	$\chi^2(1)=0.05$, $p=0.815$
total score	2.01; 0.78	1.32; 0.29	$T(53.27)=5.43$, $p<0.001$, d=1.18
vivid imagination	2.82; 1.21	1.89; 0.73	$T(69.30)=4.33$, $p<0.001$, d=0.94
perceptual sensitivity	1.81; 0.90	1.21; 0.39	$T(57.19)=4.00$, $p<0.001$, d=0.87
intrusive thought	2.08; 0.95	1.14; 0.23	$T(47.00)=6.29$, $p<0.001$, d=1.36
Auditory hallucinations	1.34; 0.60	1.04; 0.11	$T(45.51)=3.22$, $p=0.002$, d=0.70
CAHSA MSSD scores			
total score	0.46; 0.47	0.10; 0.10	$T(46.03)=4.98$, $p<0.001$, d=1.05
vivid imagination	1.81; 1.60	0.95; 0.93	$T(67.79)=3.07$, $p=0.003$, d=0.66
perceptual sensitivity	1.52; 2.04	0.20; 0.34	$T(44.42)=4.20$, $p<0.001$, d=0.90
intrusive thought	1.15; 1.16	0.16; 0.32	$T(48.61)=5.36$, $p<0.001$, d=1.16
Auditory hallucinations	0.25; 0.46	0.05; 0.20	$T(58.04)=2.54$, $p=0.014$, d=0.56

Note. AtS Group=attenuated positive symptom group; NoS Group=control group with no history of experiencing positive symptoms; CAPE=Community Assessment of Psychic Experiences; Assessment adherence=percentage of completed daily questionnaires; CAHSA=Averaged scores of the Continuum of Auditory Hallucinations - State Assessment over the 14 days assessment period; MSSD=Mean squared successive differences.

4.1.4. Data analysis

The four factor structure was tested with a CFA of two level hierarchical data using MPLUS 7.3 (Muthén and Muthén, 2012). As an indicator of daily fluctuation, within-subject variation (i.e., the proportion of variance in CAHSA scores at the within participant level) was calculated based on random intercept multilevel regression models with assessment days (level 1) nested in participants (level 2) and CAHSA scores as dependent variables.

In order to test for specific associations of the CAHSA scores and positive symptoms, the CAPE factors positive symptoms, negative symptoms, and symptoms of depression were simultaneously entered as level 2 predictors into multilevel regression models of the CAHSA scores.

For the validation of the within-subject fluctuations in CAHSA scores, we calculated the average of all squared differences between successive observations at occasions T_{n-1} and T_n (MSSD; Jahng et al., 2008) for each participant. The resulting MSSD score served as an indicator of fluctuation in CAHSA scores at the participant level. We then tested for group differences in MSSD scores and whether baseline CAPE factors predicted MSSD scores.

To identify significant predictors of each of the CAHSA subscales, two sets of random intercept, fixed slope multilevel regressions were calculated. In the first set (cross-sectional analyses) all other subscales at the same time-point T_n were entered as predictors. In the second set (time-lagged analyses) all four subscales at the previous timepoint T_{n-1} were entered as predictors in multilevel regression models.

4.1.5. Power considerations

Simulation studies have shown that a sample between 50 and 100 participants suffices for unbiased estimation of regression coefficients, variance components, and standard errors (Maas and Hox, 2005). Because we aimed to test associations between CAHSA subscales, sufficient test-power was needed to detect associations equivalent to the medium to small effects found in study 2 (i.e., $r_{par} \geq 0.1$). Using the multilevel power calculation program PinT (Snijders and Bosker, 1993), we found that based on variance and covariance estimates from the multilevel data in study 1, a sample of 80 participants with 14 measurement points suffices to detect all of these effects with an α-error and β-error of 0.05, respectively, in random intercept, fixed slope multilevel models.

4.2. Results

4.2.1. Confirmatory factor analysis and within-subject variation

The two-level CFA of the CAHSA yielded good model fit for the four-factor model (*CFI*=0.957, *RMSEA*=0.031, $SRMR_{within}$=0.038, $SRMR_{between}$=0.077). The model-fit remained acceptable when a second order factor was included (*CFI*=0.902, *RMSEA*=0.044, $SRMR_{within}$=0.064, $SRMR_{between}$=0.097).

Within-subject variation of the CAHSA total score was 0.223 (33.12% of total variation). Within-subject variation at subscale and item level is shown in Table 1.

4.2.2. Validity of daily reports and fluctuation in daily reports

Participants in the AtS Group showed significantly higher averaged CAHSA scores over the assessment period than participants in the NoS Group (see Table 3, $0.70 \leq d \leq 1.18$). When entering all three CAPE baseline scores into the multilevel regression models, the CAPE positive symptoms score was a significant predictor of the CAHSA total scores ($b=0.04$, $t(79.94)=3.74$, $p<0.001$), and also predicted the individual subscales vivid imagination ($b=0.04$, $t(79.73)=2.63$, $p=0.010$), perceptual sensitivity ($b=0.04$, $t(79.76)=3.69$, $p<0.001$), intrusive thoughts ($b=0.04$, $t(79.98)=3.73$, $p<0.001$), and auditory hallucinations ($b=0.02$, $t(80.02)=2.47$, $p=0.016$). Negative symptoms did not predict any of the subscales, while depression significantly predicted intrusive thoughts ($b=0.06$, $t(80.26)=2.03$, $p=0.046$).

Similarly, the AtS-group showed larger MSSD scores than the NoS-group (see Table 3, $0.56 \leq d \leq 1.16$). When the CAPE factors were entered in linear regression models of the fluctuations in CAHSA total score and subscales, positive symptoms were a trend-level predictor for vivid imagination and a significant predictor for all other subscales and the total score (see Table 4). Moreover, fluctuations in CAHSA total

Table 4
Linear regression of MSSD scores of all CAHSA subscales predicted by life-time positive symptoms, negative symptoms, and symptoms of depression reported at baseline (study 3).

Independent variables	Dependent variable				
	CAHSA total score B (SE)	Vivid imagination B (SE)	Perceptual sensitivity B (SE)	Intrusive thoughts B (SE)	Auditory hallucinations B (SE)
CAPE positive symptoms	−0.016**	−0.039+	0.102***	0.029*	0.017**
	(0.006)	(0.020)	(0.022)	(0.014)	(0.005)
CAPE negative symptoms	−0.003	−0.001	−0.026	−0.001	0.004
	(0.008)	(0.033)	(0.035)	(0.022)	(0.009)
CAPE depression	0.031*	0.064	0.060	0.084*	−0.008
	(0.013)	(0.051)	(0.055)	(0.035)	(0.013)
R^2	0.285	0.131	0.299	0.247	0.153

Note. Multifactorial regression models with all three independent variables entered to predict the respective dependent variable; CAPE=Community Assessment of Psychic Experiences; B=regression coefficient, SE=standard error.
+ $p < 0.10$.
* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.

scores and intrusive thoughts were significantly predicted by depression.

4.2.3. Time-lagged associations of the CAHSA subscales

The results of the cross-sectional and time-lagged analyses are summarized in Table 5. As can be seen, standardized estimates for vivid imagination and intrusive thoughts were of similar strength in the time-lagged analyses (vivid imagination predicted by intrusive thought: β=0.10, t(1034)=2.87, p=0.004; intrusive thoughts predicted by vivid imagination: β=0.10, t(1035)=6.71, $p < 0.001$). No time-lagged associations were found between vivid imagination and perceptual sensitivity, while intrusive thoughts was a stronger predictor for perceptual sensitivity (β=0.15, t(1035)=3.87, $p < 0.001$) in the time-lagged analyses than vice versa (β=0.07, t(1033)=2.56, p=0.011). Similarly, time-lagged analyses showed auditory hallucinations to be more strongly predicted by previous perceptual sensitivity (β=0.07, t(1006)=2.65, p=0.008) and intrusive thoughts (β=0.13, t(1002)=4.19, $p < 0.001$) than the other way round (β=0.03, t(750.4)=0.71, p=0.476, and β=0.11, t(744.4)=3.57, $p < 0.001$, respectively).

5. Discussion

This study developed and validated a Continuum of Auditory Hallucination State Assessment (CAHSA) that measures fluctuations in hallucination spectrum experiences ranging from subclinical, hallucination-like experiences to auditory hallucinations. We derived a 9-item scale comprising four factors. Consistent with previous research on the structure of the continuum of hallucinations (Morrison et al., 2002; Waters et al., 2003; Larøi et al., 2004; Bell et al., 2010), these factors include three facets of subclinical, hallucination-like experiences (i.e., vivid imagination, intrusive thought, and perceptual sensitivity) and auditory hallucinations. Each factor is measured with two or three items. Confirmatory factor analyses showed good fit for a four-factor model, suggesting that the four subscales represent valid latent variables. Furthermore, a four-factor model with a second-order factor showed good model fit, suggesting that the four subscales are part of a common latent variable, representing the continuum of auditory hallucinations. Criterion validity of the CAHSA was demonstrated by its specific association with life-time experiences of positive symptoms in a cross-sectional study and in a prospective ambulatory assessment study.

Confirmatory factor analysis showed sufficient model fit when items were forced to have an equal loading to the respective factors. This indicates that the sum scores validly represent their associated latent variables, rendering the CAHSA scores easily to calculate without any trade-off in terms of validity.

Furthermore, a repeated measurement study with daily assessments showed all subscales and the CAHSA total score to capture daily

Table 5
Random-intercept, fixed slope multilevel regression of CAHSA subscales with all respective other CAHSA subscales as predictors (study 3).

Independent variables	Dependent variable			
	Vivid imagination	Perceptual sensitivity	Intrusive thoughts	Auditory hallucinations
Predictors from timepoint n	B (SE)	B (SE)	B (SE)	B (SE)
Vivid imagination	–	0.07* (0.03)	0.42*** (0.02)	−0.01 (0.03)
Perceptual sensitivity	0.05* (0.03)	–	0.10*** (0.02)	0.23*** (0.02)
Intrusive thoughts	0.54*** (0.03)	0.14*** (0.04)	–	0.21*** (0.03)
Auditory hallucinations	−0.07 (0.10)	0.36*** (0.03)	0.22*** (0.03)	–
Predictors from timepoint n−1	B (SE)	B (SE)	B (SE)	B (SE)
Vivid imagination	0.25*** (0.03)	0.02 (0.04)	0.10** (0.03)	0.01 (0.03)
Perceptual sensitivity	−0.01 (0.03)	0.21*** (0.03)	0.07*** (0.03)	0.07*** (0.03)
Intrusive thoughts	0.10*** (0.03)	0.15*** (0.04)	0.22*** (0.03)	0.13*** (0.03)
Auditory hallucinations	0.08* (0.03)	0.03 (0.04)	0.11*** (0.03)	0.19*** (0.03)

Note. All estimates are based on z-standardized dependent and independent variables. Group (lifetime experience of attenuated symptoms vs. no lifetime experience of symptoms) and assessment day were controlled for in all regression models. B=regression coefficient, SE=standard error.
* $p < 0.05$.
*** $p < 0.001$.
** $p < 0.01$.

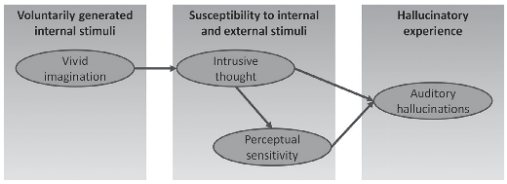

Fig. 2. Continuum of auditory hallucinations. Process model based on the results from the partial correlation and multilevel regression analyses.

variation in hallucinatory experiences, indicating that the CAHSA measures changes in auditory verbal hallucinations over time. Finally, more fluctuations in CAHSA scores were shown to correspond with more frequent positive psychosis-like experiences in a preceding retrospective report. This indicates that observed fluctuations represent valid changes in daily hallucination-like experiences.

5.1. Continuum of auditory hallucinations

The partial correlation analyses and the time-lagged multilevel regression analyses yielded fairly consistent results regarding the internal structure of auditory hallucinations and preceding experiences. Based on the associations found, we assume a process model of the continuum of auditory hallucinations as shown in Fig. 2. The model includes two interrelated pathways to auditory hallucination. The first pathway includes the distal precursor vivid imagination and the proximal precursor intrusive thought, while the second path includes perceptual sensitivity. This model bears some resemblance to the differentiation of a subtype of hallucinations that stems from internally generated stimuli (i.e., intrusive thoughts and memories) and a subtype that stems from susceptibility to external random noise, which is perceived as a voice speaking or other auditory hallucinations (Jones, 2010).

Multiple models exist to explain the causal path from vivid mental imagery to intrusive thought, which in turn predicts auditory hallucinations. Possible cognitive and neuro-cognitive etiological factors include an anomalous activation of the auditory cortex by internal events that cause hypersalient auditory signals (i.e., unusually vivid thoughts) without external stimuli (Waters et al., 2012). Moreover, rumination and thought suppression processes that lead to experiences of intrusive thought (Jones and Fernyhough, 2009) constitute a potential cognitive factor, as do meta-cognitive beliefs and an associated perturbation in the control of internally generated events (Larøi et al., 2005). Finally, source monitoring deficits may play a significant role (Bentall, 1990), for example reduced sensory attenuation of self-initiated action (Frith, 2000) or source memory errors for internal verbal thoughts and perception (Brébion et al., 2010, 2012), which lead to self-generated auditory signals (i.e., vivid, intrusive inner monologues and thoughts) being perceived as an alien, externally generated perception.

Perceptual sensitivity formed a second direct path to auditory hallucinations – separate, but not independent of intrusive thoughts. This hallucination subtype may be rooted in bottom-up processes that lead to the erroneous detection of complex meaning in random auditory experiences, and deficits in top-down processes, such as sensory gating deficits (Smith et al., 2013) or deficits in executive control to shift attention between stimuli (Hugdahl, 2009). Further research is needed to investigate whether the aforementioned etiological factors are associated with these specific hallucination spectrum experience factors.

5.2. Limitations

Some limitations should be noted. First, we conducted our studies on population samples with limited age and demographic range. Thus, a substantial part of the upper end of the continuum of hallucinations was not represented in our validation study. Although the factor structure of the continuum of hallucinations has already been shown to be equal for clinical and non-clinical populations when trait-measures are used (Serper et al., 2005), there might be differences in symptom fluctuation. Future research should aim to replicate the CAHSA factor structure and within-subject variation in patient samples and more diverse population samples.

Second, we used well-established trait measure items as templates for our scale to ensure content-validity, which possibly entailed a trade-off in terms of maximizing sensitivity to change. While the daily assessment served as a first indicator of within-subject variation, it included comparatively long measurement intervals that do not capture momentary variations over shorter periods. It has to be noted that etiological models differ in the time-frame assumed for a hallucination-like experience (e.g., intrusive thought) to become a hallucinatory experience. Some models suggest brief momentary intervals in which an intrusive thought may become a hallucination (e.g., Jones and Fernyhough, 2009). Consequently, our time-lagged analyses that reflected the evolution of hallucination-like experiences over several days (e.g., vivid imagination yesterday preceding intrusive thoughts today predicting hallucinatory experiences tomorrow) may not be the most accurate time-frame to capture the relationship between these variables. While the results of our daily assessment study are promising, future research needs to investigate whether shorter assessment intervals increase the magnitude of effect sizes in time-lagged association of vivid imagination, intrusive thought, perceptual sensitivity, and auditory hallucinations.

Finally, validation with established ambulatory assessment measures of psychosis symptoms is needed to confirm the promising results on criterion validity we found with a trait measure. A direct comparison of different measures in future research could serve to cross-validate each of these measures while simultaneously comparing their respective sensitivity and reliability.

5.3. Conclusion

The CAHSA constitutes a brief state measure of hallucination spectrum experiences. It measures the frequency of these experiences without restrictions in terms of specific context or content and without being confounded with emotional appraisal or (religious or other) interpretation of the experience in the item text. It covers a wide range of phenomena, so it can be used to explore precursors of hallucinations and subclinical hallucination-like experiences in general population samples with varying vulnerability to experiencing hallucinations. Moreover, the inclusion of subclinical hallucination-like experiences is likely to increase the measure's sensitivity in those clinical samples that do not frequently experience auditory hallucinations at the clinical level. Both the auditory hallucinations subscale alone and the full questionnaire are likely to be useful for research in voice-hearer populations, but this requires further confirmation. In sum, the CAHSA is a valid assessment tool for future experimental and repeated measurement studies, which we hope will contribute to the understanding of the continuum of auditory hallucinations.

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Conflict of interest

None.

Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.psychres.2017.03.051.

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[Supplements]

Information and recommendations:

- The following instruction was for daily repeated measurement of hallucination like experiences. For differing Time-intervals, we recommend changing the brief instruction at the beginning.

- For momentary assessment, item text may be changed to present tense (e.g., "my fantasies are vivid and intense"); Given that hallucinations and hallucination-like experiences are episodic, it is recommended to use time-interval (e.g., asking for any experiences during preceding 90 min. time interval). Note that momentary assessment with the CAHSA was not tested in the validation article mentioned above.

- For repeated measurement, we recommend randomizing the order of the items for every assessment.

- For the first presentation of the items, we recommend the item order shown below so participants start their first assessment with items that ask for more common internal experiences.

[Supplements]

Instruction and items

CAHSA

Today, I had the following feelings and experiences:

1. My fantasies were vivid and intense.

Not at all						Very much
1	2	3	4	5	6	7

2. I daydreamed a lot.

Not at all						Very much
1	2	3	4	5	6	7

3. My hearing was so sensitive that even everyday noise became irritating.

Not at all						Very much
1	2	3	4	5	6	7

4. I felt easily distracted by distant sounds.

Not at all						Very much
1	2	3	4	5	6	7

5. My thoughts were so strong and vivid that I could almost hear them.

Not at all						Very much
1	2	3	4	5	6	7

6. Ideas and thoughts hit me so fast that I could not express them all.

Not at all						Very much
1	2	3	4	5	6	7

7. I heard one or more voices in my head speaking my thoughts aloud, talking to each other or saying other things.

Not at all						Very much
1	2	3	4	5	6	7

8. Meaningless noise I heard sounded like someone was saying my name or as if people were talking.

Not at all						Very much
1	2	3	4	5	6	7

9. I heard something other people cannot hear.

Not at all						Very much
1	2	3	4	5	6	7

[Supplements]

Scoring

Calculation of the the CAHSA – factor:

"Vivid imagination"	=	(Item 1 + Item 2)/2
"Perceptual sensitivity"	=	(Item 3 + Item 4)/2
"Intrusive thought"	=	(Item 1 + Item 2)/2
"Auditory hallucinations"	=	(Item 7 + Item 8 + Item 9)/3

The calculation of the total score is based on the mean scores of the four factors:

CAHSA-total	=	(Vivid imagination + Perceptual sensitivity+ Intrusive thought + Auditory hallucinations)/4

Appendix D: Study 4

Schlier, B., Krkovic, K., Clamor, A., & Lincoln, T. M. (submitted for publication). Autonomic arousal during psychosis spectrum experiences: results from a high resolution ambulatory assessment study over the course of symptom on- and offset.

Autonomic arousal during psychosis spectrum experiences: results from a high resolution ambulatory assessment study over the course of symptom on- and offset.

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Abstract

Introduction: Ecological momentary assessment (EMA) studies show that stressors trigger the onset or increase of psychotic positive symptoms. These studies, however, predominantly rely on large sampling intervals and self-report assessment. This study aims to identify the autonomic stress-response to positive psychosis-spectrum experiences by using a one-day high-resolution EMA with continuous skin conductance and heart rate monitoring in a sample with attenuated positive symptoms.

Methods: Sixty-two participants were equipped with a smartphone and wearable sensors to monitor skin conductance level (SCL) and heart rate variability (HRV) for 24 hours. Every 20 minutes, participants answered questions on current stress, hallucination spectrum experiences (HSE), and paranoia. Sampling intervals were categorized into no event, pre-onset, event, pre-offset, and post-offset phases. We contrasted stress, SCL, and HRV between phases using multilevel regression models of sampling intervals nested in participants.

Results: For paranoia, we found alterations in the autonomic and self-reported stress response prior to the onset that persisted until the episodes had ended. For HSE, we found no effects. Exploratory separate analyses of the different items aggregated into HSE yielded diverging results for intrusive thoughts, perceptual sensitivity, and hallucinations.

Conclusion**:** Physiological parameters are sensitive indicators of the onset of paranoia, which holds implications for preventive mobile interventions. To further explore the autonomic stress-response associated with HSE, further studies of the different HSE are needed.

Keywords: stress; autonomic arousal; psychosis; ambulatory assessment; hallucinatory experiences; paranoia

Introduction

Traditional (Nuechterlein and Dawson, 1984; Zubin and Spring, 1977) and more recent (Howes and Murray, 2014; Walker and Diforio, 1997) etiological models converge in the assumption that stressors trigger and maintain psychotic symptoms such as paranoia and hallucinations. Evidence from numerous ecological momentary assessment (EMA) studies supports this hypothesis. In these studies, the participants spend about a week reporting state-stress and symptoms levels multiple times per day, usually in 90-minute intervals. Based on this approximation to real-time assessment, EMA studies found self-reported stress and symptom intensity levels to co-vary (Peters et al., 2012; Reininghaus et al., 2016; Udachina et al., 2014; Varese et al., 2011) and self-reported stress to predict increases in positive symptom levels at the subsequent assessment-point (e.g., Ben-Zeev et al., 2011).

Only few studies have simultaneously investigated stress-levels prior to, during, and following momentary symptom episodes. A few notable exceptions (Delespaul et al., 2002; Oorschot et al., 2012; Thewissen et al., 2011) employed a symptom-phase approach: Based on the self-reported symptoms before and after each 90 minute EMA sampling interval, they categorized intervals into different phases (i.e., the last phase before onset, symptom phases, and the phases before and after offset). However, 90-minute sampling intervals only provide a rough picture of the total symptom-fluctuations in everyday life. In 50% of the people who experience hallucinations or delusions, symptoms occur only for seconds or minutes at a time (Steel et al., 2007). In other words, the majority of symptom episodes begins and ends well within one standard 90-minute sampling interval. There is thus considerable potential to improve the symptom-phase approach. Shorter sampling intervals will enable a more precise analysis of symptoms, precursors, and consequences.

Related to this, assessing stress-levels by self-report merely provides a state-indicator for one moment every 90 minutes or a retrospective report of the last 90 minutes. Thus, a considerable amount of momentary stress-fluctuations remains undetected in conventional EMA. Recent technical innovations, however, have enabled researchers to supplement EMA with continuous monitoring of autonomic arousal (Cella et al., 2017), which further increases the temporal resolution

of stress parameter assessment. This is of particular interest as autonomic hyperarousal has been considered a core feature in the traditional vulnerability-stress-models of schizophrenia (Nuechterlein and Dawson, 1984), in which it is assumed to contribute to the deficient processing of stimuli. Furthermore, several cognitive models postulate an affective pathway to psychosis, in which negative emotions trigger symptom onset (Garety et al., 2001; Myin-Germeys and van Os, 2007). Finally, recent conceptualizations of psychosis posit that difficulties in down-regulating negative emotions may be related to altered autonomic regulation (Clamor et al., 2015).

In support of these conceptualizations of the role of altered autonomic regulation in psychosis, an increased tonic skin conductance level (SCL), which is an indicator of sympathetic autonomic arousal, is found during acute psychotic states (Dawson et al., 2010; Maina et al., 1995; Schell et al., 2005). Moreover, laboratory studies showed that SCL increases prior hallucination onset in patients with psychosis (Levine and Grinspoon, 1971) and during anomalous bodily experiences (i.e., the rubber hand illusion; Braithwaite et al., 2014) in healthy participants. Hence, momentary hyperarousal co-occurs with anomalous experiences across the continuum of psychotic experiences. Another prominent focus of autonomic deregulation research in schizophrenia is heart rate variability (HRV). HRV is an indicator of parasympathetic activity regulated by central-peripheral neural feedback mechanisms that allow individuals to adapt physiological, perceptional, and cognitive processes (Thayer and Siegle, 2002). A meta-analysis of 34 studies found HRV to be reduced in psychosis relative to controls (Clamor et al., 2016). Furthermore, a review outlined that reduced HRV correlates with the severity of suspiciousness, feelings of persecution, and psychotic symptoms in general (Montaquila et al., 2015). Finally, low levels of HRV have been shown to prospectively predict the onset of hallucinations in an EMA study with patients with psychosis (Kimhy et al., 2017). Thus, there is some evidence that autonomic stress indicators co-vary with and predict positive symptoms, but so far, no study has investigated the autonomic stress-response over the full course of psychotic symptom episodes.

There is a particular dearth of research on the autonomic stress-response prior to and after symptom *off*set, for which several hypotheses appear theoretically plausible: The first of these is rooted in etiological models that conceptualize positive symptoms as a reaction to stress (Howes and Murray, 2014; Nuechterlein and Dawson, 1984; Walker and Diforio, 1997; Zubin and Spring, 1977): Based on these models, successful adaptation to stress or cessation of the stressor precedes symptom offset. Thus, one would hypothesize that stress-parameters return to resting levels *before* symptom offset. A second hypothesis can be deduced from the fact that symptoms themselves often, but not always, lead to distress (Birchwood, 2003; Peters et al., 1999). Extending on this, we can define psychotic symptoms as stressors in their own right. People with psychosis who are confronted with a stressor in a laboratory environment show a prolonged self-reported (Perry et al., 2011) and autonomic stress-reaction (Castro et al., 2008) after the stress induction had ended. Thus, we could hypothesize that the stress response persists even *after* symptom offset. Finally, it is also conceivable that different symptoms elicit differing stress-responses. For example, hallucinations are experienced as sensory events (i.e., as self-generated stressors), thus their onset may be more likely to induce a stress-response that persists after symptom offset. In contrast, paranoia was shown to have positive short-term effects, such as the relief that comes with having an explanation (Maher, 1988) or the short-term preservation of self-esteem by blaming others (Lincoln et al., 2014). In this regard, paranoia could be understood as a dysfunctional cognitive coping strategy to deal with external stressors In this case, we would expect reduced stress-levels prior to symptom offset.

This study aimed to identify the stress-response over the course of psychosis-spectrum experiences (PSE) in a one-day high-resolution EMA with 20-minute sampling intervals and continuous SCL and heart rate monitoring in a community sample with attenuated levels of positive psychotic symptoms. We assessed fluctuations in PSE, including paranoia and hallucination spectrum experiences (HSE; ranging from subclinical experiences to auditory hallucinations). We examined self-reported and physiological stress-reactions during (1) phases without PSE events, (2) phases prior to PSE onset, (3) phases with continuously reported PSEs, (4) PSE phases prior to offset, and (5) post-offset phases. We expected to find (A) increases in self-reported stress and SCL and a decrease

in HRV preceding the onset of PSE and (B) coinciding with PSE symptom-phases. Moreover, for all PSE, we explored whether (C1) self-reported stress and SCL will continue to be elevated and HRV will continue to be reduced or (C2) whether these parameters decrease in the pre-offset and the post-offset phases.

Methods

Procedure

Potential participants were screened for attenuated positive symptoms. Participants with an extent of self-reported symptoms above the median of a large German reference sample (i.e., *Med*=8.00; Schlier et al., 2015) were invited to our lab for a baseline assessment. After providing informed consent, the participants were equipped with an electrocardiogram sensor and an electrodermal activity sensor. Next, the participants completed a battery of self-report questionnaires on emotion-regulation (Ebert et al., 2013; Loch et al., 2011), cognitive schemata (Fowler et al., 2006), and traumatic experiences (Hooper et al., 2011), which are reported elsewhere (e.g., Krkovic et al., 2018). Following this, they were equipped with a Motorola Moto G smartphone with a pre-installed movisensXS EMA application (movisens GmbH). The smartphones were programmed to allow only for the use of the EMA application.

After a demonstration of the alarm followed by the EMA-questionnaires, the participants were able to ask questions about the EMA procedure. Subsequently, participants left the laboratory and the 24-hour EMA started. During this time, the sensors recorded continuously whereas the EMA questionnaires were presented every 20 minutes (±60 seconds random variation), starting at 9am and ending/pausing at 10pm. Each participant received prompts to provide self-report data at 38 time-points. The participants were instructed to follow their normal daily routine during the assessment period, but to abstain from taking a shower, bathing, or partaking in straining physical activity in order to guarantee continuous sensor-readings. After 24 hours, the participants returned to the lab to finish the study and to return the sensors and smartphone.

The project was approved by the local ethics committee and the participants were compensated with 15€. Psychology students received partial course credit for participation.

Materials

Screening. Attenuated positive symptoms at baseline were measured with the 20 item positive symptoms frequency scale of the Community Assessment of Psychic Experiences (CAPE; Stefanis et al., 2002). Participants rated the life-time frequency of experiences of paranoia, bizarre experiences, hallucinations, grandiose ideas, and magical thinking on four-point Likert scales (0="never", 1="sometimes", 2="often", 3="nearly always"). The positive symptom scale of the CAPE and its German translation were shown to be sufficiently valid and reliable (Schlier et al., 2015).

EMA questionnaires. Paranoia was assessed with the three item state version (Schlier et al., 2016) of the Paranoia Checklist (Freeman et al., 2005). Participants indicated to what extent each item (e.g., "I need to be on my guard against others") applied to them "at the moment before the beep" on an 11-point scale (0="not at all"; 10="very much"). The multilevel reliability was acceptable for the within-subject-level (α=0.62), and excellent for the between-subject-level (α=0.92).

HSEs were assessed with an abbreviated version of the Continuum of Auditory Hallucinations – State Assessment (CAHSA; Schlier et al., 2017a) that was developed for this study. It included the following four items: (1) "Fantasies, daydreams or thoughts I have had were vivid and intense" for vivid daydreaming, (2) "My thoughts seemed almost real or overwhelming (e.g., Thoughts came faster than I could express them or seemed as if I could really hear them)" for intrusive thoughts, (3) "My hearing has been sensitive (e.g., I felt distracted by everyday noise or distant sound)" for perceptual sensitivity, and (4) "I have heard something others could not hear (e.g., random noise sounding like someone mumbling or hearing a voice in my head)" for auditory hallucinations. Participants indicated to what extent each statement applied to them during the 20-minute interval preceding the beep on an 11-point scale (0="not at all"; 10="very much"). The multilevel reliability for the scale was poor at the within-subject-level (α=0.51), whereas it was good at the between-subject-level (α=0.83).

Self-reported stress was assessed with four items referring to the previous 20 minutes rated on 11-point scales (0=”not at all”; 10=”very much”). The items (based on Gaab *et al.* 2005) included self-ratings of arousal and stress (two items: “the situation stressed me”, “I was calm and relaxed”) and of subjective control (two items: “I could influence the situation”, “I felt helpless in face of the situation”). The multilevel reliability was acceptable for the within-subject-level (α=0.73) and the between-subject-level (α=0.64).

Physiological data. Heart rate and SCL were measured with the Movisens ecgMove and Movisens edaMove, respectively. Both devices are small 62.3 x 38.6 x 11.5 mm ambulatory sensors. The reusable, non-polarizing sintered Ag/AgCl-EDAmove-electrodes were attached to the inner wrist of the non-dominant arm with a wristband and recorded SCL using a sample rate of 32 Hz. The ecgMove was attached to the left side of the chest with two disposable, self-adhesive Ag/AgCl -electrodes (Ambu® BlueSensor VL). For electrodermal activity, the range-corrected SCL was calculated for each participant. For HRV, the root mean square of successive normal-to-normal interval differences (RMSSD) was calculated, which reflects parasympathetic activity (Bauer et al., 2008) and was shown to be a more homogenous measure in psychosis than the alternative high frequency HRV (Clamor et al., 2016). Automated calculation of SCL and RMSSD and correction for potential artifacts (e.g., by disturbances in electrode connection) was performed in DataAnalyzer (Movisens GmbH) and yielded one-minute intervals, which were then averaged for 20(±2) minute intervals between two successive assessment alarms.

Participants

Prescreening of 292 participants from the community with the CAPE positive symptom scale yielded 67 participants with a sum score ≥8 who were recruited for this study. Five participants were excluded from the analyses because they failed to respond to at least half of the EMA self-assessments. This resulted in a final sample of 62 participants (71.6% female, age: *M*=23.01, *SD*=4.63). The majority of the participants were of German nationality (85.5%). Most participants were currently enrolled in university (79.0%) and 46.8% of the sample worked for six or more hours

per week. Eight participants reported a mental illness diagnosis at some point in their life. The average CAPE sum-scores were 15.89 (*SD*=4.31) for positive symptoms, 15.87 (*SD*=6.35) for negative symptoms, and 10.03 (*SD*=3.80) for symptoms of depression.

In the final sample, 84.95% of all EMA self-reports were completed. Heart rate was successfully recorded for 95.82% and SCL for 98.59% of the time-intervals, resulting in combined self-report and heart rate for 81.46% and combined self-report and SCL for 83.93% of all time-segments.

Data Analysis.

Data was analyzed using R 3.2.2 (R Core Team, 2015). All analyses were random intercept, fixed slope multilevel-regression analyses of assessment intervals (level 1) nested in participants (level 2). Dependent variables were self-reported stress, SCL, and RMSSD. As the independent variables, five-category factors of PSE interval type were calculated based on the Paranoia Checklist and CAHSA mean scores, respectively, in a two-step procedure. First, we calculated the 95%-reliable difference score for the CAHSA- and Paranoia-Checklist-mean scores based on the within-subject reliability, and the full sample standard deviations. All intervals with CAHSA-scores ≥2.33 (i.e. reliably different from 0) were marked as intervals with HSEs reliably present, whereas intervals with CAHSA-scores below 2.33 were marked as intervals with no HSEs reported. Similarly, all intervals were marked as intervals with paranoia reliably present for Paranoia Checklist scores ≥1.51) or not present when Paranoia Checklist scores were below 1.51). Thereafter, and separately for HSE and paranoia, each of the 20 minute intervals was categorized as belonging to one of the following five different phases (see also Figure 1):

- "*no event phase*" (reference category), when the respective PSE was not reported at the time interval itself, the preceding time-interval, and the following time interval,
- *"pre onset phase"* if the respective PSE was not reported for the time interval itself, but was followed by a time interval with PSE reliably present,
- "*event phase*" if the PSE was reliably present at the time interval itself and the following interval,

- "*pre offset phase*" if the PSE was reliably present during the time interval itself, but not at the following interval,
- "*post offset phase*" if the PSE was reported at the preceding phase, but neither during the time interval itself nor at the following interval.

Self-reported stress, SCL, and RMSSD were analyzed in three random-intercept, fixed slope multilevel analyses of time intervals nested in participants for HSEs and paranoia, respectively; stress levels in pre-onset, event, pre-offset, and post-offset phases were contrasted with the stress levels in the no-event phases. To provide an estimate of potential bias due to alpha-error-inflation, Bonferroni-Holm corrected p-values were calculated. We performed all analyses on the full sample first, but controlled for conflation of between- and within-subject effects by excluding participants who either experienced no PSE at all during the assessment period (i.e., participants with only no event phases) or constantly experienced PSE (i.e., participants without no event phases) and repeating the multilevel regressions.

Finally, due to the low internal consistency of the CAHSA, we added four exploratory analyses based on the four CAHSA-items. All procedures mirrored the main analysis for HSE and paranoia, with the exception that since no reliable difference scores were available for single item measures, all item scores above zero were defined as the presence of the respective experience (i.e., "event phase").

Results

Descriptive results

The grand means and frequency of the stress indicators and PSE recording during EMA are summarized in Table 1. Regarding phase prevalence for paranoia, 21 participants reported no paranoia or had insufficient data to identify any event-related paranoia phase and 2 participants did not report any no-event-phase; regarding HSEs, 22 participants reported no HSEs or insufficient data to identify the event-related phases and 6 participants did not report any no-event phase.

Autonomic arousal in relation to paranoia phases

For paranoia, we found roughly u-shaped curves for all stress parameters over the course from no event to post-offset phases (see Figure 2, right). As can be seen in Table 2, pre-onset phases were associated with increased self-reported stress and decreased RMSSD. Furthermore, event phases yielded significant increases in self-reported stress and SCL and a significant decrease in RMSSD. Finally, we found continuing differences from no-event phases in self-reported stress, SCL, and RMSSD at pre-offset. In the post event phase, no stress parameter was significantly different from the corresponding no event phase level (see Table 2), indicating a decrease in stress with symptom offset. All results remained stable when the participants with no and constant PSEs were excluded (see online supplementents, Table S1).

Autonomic arousal in relation to HSE phases

Regarding HSE-phases, no significant differences in self-reported stress, SCL levels or RMSSD were found (see Table 2, left and Figure 1, left). When the four items were analyzed separately, we found decreased RMSSD in intrusive thought event (b=-6.102, T=-3.61, p_{corr}=0.015) and pre-offset phases (b=-7.239, T=-4.02, p_{corr}=0.003), increased SCL in perceptual sensitivity pre-onset (b=0.094, T=4.02, p_{corr}=0.003), event (b=0.088, T=3.96, p_{corr}=0.004) and pre-offset phases (b=0.089, T=3.60, p_{corr}=0.016), and increased self-reported stress in perceptual sensitivity event (b=0.600, T=4.20, p_{corr}=0.001) and pre-offset phases (b=0.576, T=3.90, p_{corr}=0.004) as well as hallucination event (b=0.920, T=4.22, p_{corr}=0.001) and pre-offset phases (b=0.812, T=4.18, p_{corr}=0.001, see online supplements, Table S2)

Discussion

In this study, we found a consistent pattern of alterations in self-report and autonomic parameters over the course of paranoia event phases, but no consistent results regarding HSEs.

Paranoia as a potentially dysfunctional stress-response

There was an autonomic response in the form of a combined increase in self-reported stress and a decrease in parasympathetic activity prior to the start of the paranoia episodes that persisted over the course of the episode but ended with the offset. Moreover, these alterations were accompanied by a delayed increase in sympathetic activity (i.e., SCL) during event-phases. This is in

line with Montaquila et al.'s (2015) recent review on the interplay between the parasympathetic and sympathetic nervous systems in psychosis. Their findings converge on the assumption that diminished levels of parasympathetic activity constitute a vulnerability for psychosis: Low levels of parasympathetic activity reduce vulnerable people's capacity to recover from stress, which leads to a dominant state of sympathetic arousal over the course of the disorder. Arguably, our findings show a micro-level version of this autonomic response mechanism at the level of singular paranoia episodes.

Of importance, all stress-parameters returned to baseline-levels at post-offset, which may point towards a short-term self-regulatory function of paranoid thinking. In line with this, short term benefits of paranoid beliefs have been demonstrated in terms of reduced self-reported negative affect (Lincoln et al., 2014) and a lower subsequent heart rate (Clamor and Krkovic, 2018). This pattern of findings is in line with the notion that paranoia may be a cognitive coping style that yields relief (Bentall et al., 1994; Maher, 1988) in the short term, which contributes to symptom persistence in the long-term. More research into the cognitive, emotional, and autonomic processes associated with the offset of paranoid thinking is needed to further corroborate this hypothesis and test it in clinical populations.

Hallucination spectrum experiences as potential stressors

In contrast to the clear picture for paranoia phases, the results appear to become more complicated in phases of HSEs. For the HSE mean score, no significant results were found. This is in contrast to a previous study with patients with psychosis, in which significant decreases in parasympathetic activity predicted (i.e., preceded) auditory hallucination onset (Kimhy et al., 2017). One interpretation for these results based on the low within-subject reliability could be that we may have assessed the spectrum of hallucinatory experiences too broadly – as it was particularly constructed to assess the continuum. In line with this, our exploratory analysis shows that "mild" subclinical HSE (i.e., vivid daydreams) yield no stress-response, whereas more severe HSE (i.e. intrusive thoughts, perceptual sensitivity) are accompanied by autonomic alterations. Contrary to this thought, auditory hallucinations were only accompanied by self-reported stress but not

autonomic alterations. Possibly, non-clinical-populations experience less distress due to hallucinations, which results in the well-recorded lack of need for treatment of these experiences (Larøi et al., 2012).

In sum, HSE in general neither classified as stressors nor as stress-responses. However, the in-depth analysis of separate types of HSE yielded significant differences from baseline stress levels - mainly in event and pre-offset phases. Thus, we speculate that some HSE (e.g., intrusive thoughts, perceptual sensitivity, hallucinations) classify as stressors in themselves that elicit an subjective and/or autonomic stress-responses when experienced (Castro et al., 2008). If this is the case, these types of HSEs could contribute to the emergence of further symptoms via stress-sensitization: For example, previous research has linked differences in baseline or average HRV to problems in functional coping (e.g., greater self-reported difficulties in emotion regulation; Clamor et al., 2015; Williams et al., 2015). Consequently, the momentary decreases in HRV following some HSEs could increase the likelihood that the next stressor will trigger other symptom episodes, thus contributing to the stress-sensitization mechanism central to recent etiological models of psychosis (Howes and Murray, 2014; Walker and Diforio, 1997). Thus, further research on different types of HSEs with a more detailed (i.e., multiple item) assessment and in a clinical sample with potentially more symptom distress is warranted in order to fully understand the association between HSEs and autonomic stress parameters.

Strengths and Limitations

The brief sampling interval and the continuous assessment of physiological parameters constitute strengths of our approach. Furthermore, using reliable differences for threshold-calculation is a less arbitrary form of determining the presence of PSEs than previous procedures (e.g., scores above mid-scale: Delespaul et al., 2002; or scores above 0; Schlier et al., 2017b). However, some limitations need to be considered. The battery life of the autonomic monitoring limited the assessment period to one day of continuous, uninterrupted monitoring, which comes at the cost of reducing representativeness of the EMA for real life. Furthermore, 20-min sampling intervals possibly constitute stressful interferences with everyday life which increases the risk of

measurement-reactivity. However, even if measurement reactivity reduced the external validity of the results (e.g., mean stress-levels over the assessment period exceeding the usual stress-levels in everyday life), we can still assume internal validity of the comparison between the different event phases in the multilevel models. Finally, some limitations of the HSE assessment need to be considered: The abbreviated assessment with single items per experience did not allow for event-phase classification based on reliable difference scores. Furthermore, the retrospective assessment for these experiences may have introduced some memory bias into the assessment, although this seems unlikely given the high frequency sampling procedure.

Conclusion

This is the first EMA study of experiences along the psychosis continuum that includes a high-resolution assessment of psychotic experiences and an assessment of both self-reported and physiological stress responses over the course of PSE episodes. Our results show that autonomic arousal parameters can be readily assessed using ambulatory devices and constitute informative additions to self-report to explore the predictors and immediate effects of positive symptoms as well as potential symptom-specific stress signatures underlying paranoia and HSEs. Furthermore, for paranoia there is considerable overlap in the results based on autonomic indicators and self-reported stress measures, hence there is a potential to replace self-report EMA with autonomic assessment and develop a feasible early warning-sign for symptom onset with high-time resolution and no need of user-input. Future studies could build on these findings and replicate these results in patient samples, establish a threshold for a sufficiently specific prediction of symptoms based on autonomic parameters alone, and explore the potential of physiological stress parameters to optimize ecological momentary interventions.

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Legend of Figures

Figure 1. Definition of event-phases based on the symptom status prior to, during, and following the interval from which stress-indicators were analyzed (bold lines and dots).

Figure 2. Stress-response in event-phases of hallucination spectrum experiences and paranoia (predicted values from multilevel regression and 95% confidence intervals).

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Conflict of interest

None.

Contributors

BS and KK conceptualized and conducted the study. BS analyzed the data and wrote the first draft of the manuscript. AC contributed to the analysis of the physiological data. TML contributed to interpreting and discussing the results. All authors edited and contributed to the manuscript and have approved of the final version.

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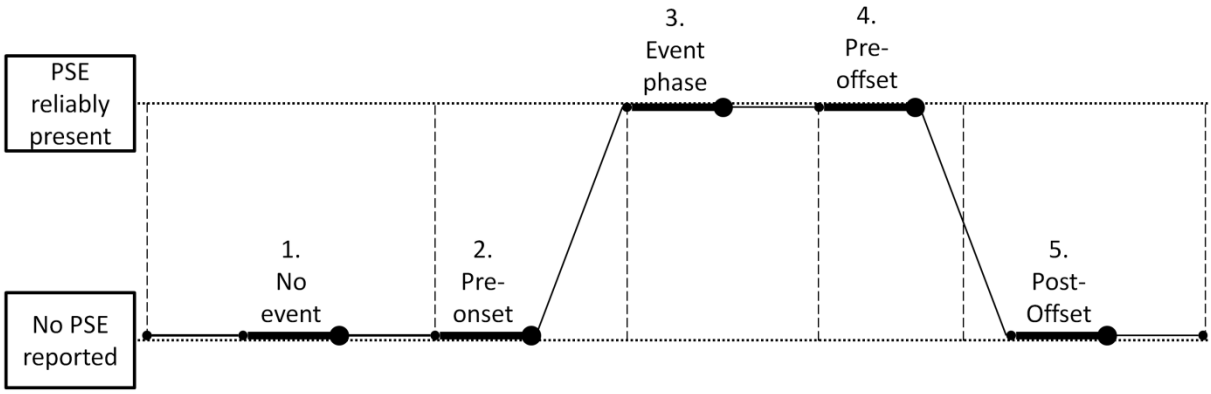

Figure 1. Definition of event-phases based on the symptom status prior to, during, and following the interval from which stress-indicators were analyzed (bold lines and dots).

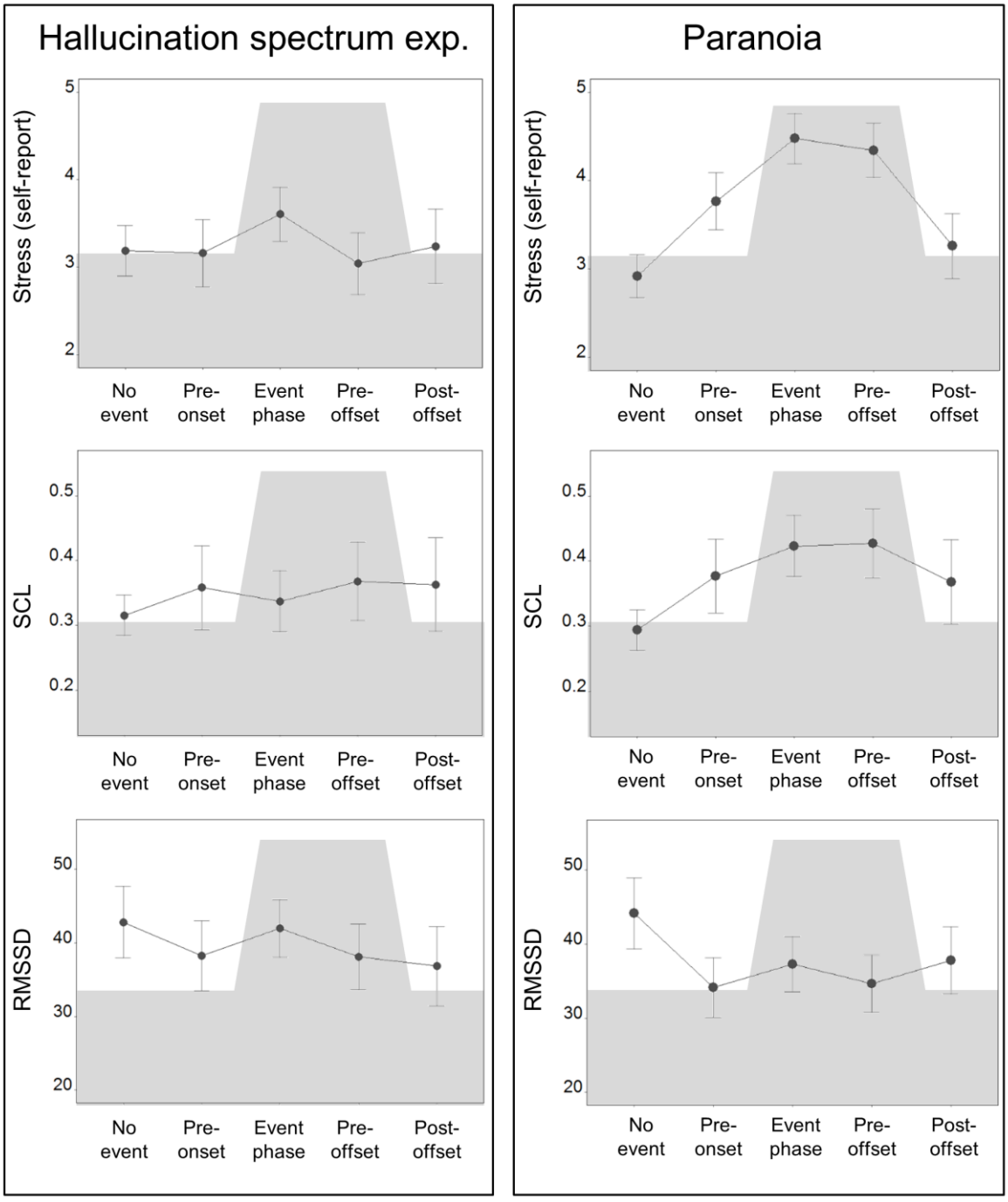

Figure 2. Stress-response in event-phases of hallucination spectrum experiences and paranoia (predicted values from multilevel regression and 95% confidence intervals).

Table 1.

Mean, standard deviation, skew, range, and frequency of psychosis-spectrum experiences during EMA assessment.

Variable					Intervals with PSE reliably reported		Participants with at least one interval with PSE reported	
	M	SD	Skew	Range	n	%	n	%
Self-reported stress	3.33	1.80	-0.43	0-10	-	-	-	-
SCL (range corrected)	0.35	0.27	0.8	0-1	-	-	-	-
RMSSD (ms)	40.85	23.74	1.49	3.55-149.03	-	-	-	-
Hallucination spectrum experiences	1.55	1.70	1.09	0-9	539	27.07%	40	64.52%
Paranoia	0.75	1.25	1.92	0-7	400	20.09%	43	69.35%

Table 2.

Self-reported and physiological reaction to psychosis-spectrum experience phases. Results of multilevel regression models symptom phase (level 1 predictor) on the respective stress parameter.

		Paranoia				Hallucination spectrum experiences			
Stress indicator	Phase	b	SE	T	p_{corr}	b	SE	T	p_{corr}
Self-report	No event[1]	2.916	0.124	23.48	-	3.186	0.147	21.72	-
	Pre onset	***+0.850***	***0.165***	***5.15***	***<0.001***	-0.025	0.197	-0.13	0.900
	Event	***+1.561***	***0.146***	***10.71***	***<0.001***	*+0.419*	*0.159*	*2.63*	*0.200*
	Pre offset	***+1.425***	***0.156***	***9.16***	***<0.001***	-0.144	0.181	-0.80	≈1
	Post offset	+0.344	0.188	1.83	0.871	+0.053	0.217	0.24	≈1
SCL	No event[1]	0.294	0.016	18.95	-	0.315	0.016	19.74	-
	Pre onset	*+0.083*	*0.029*	*2.88*	*0.101*	+0.043	0.033	1.28	≈1
	Event	***+0.129***	***0.024***	***5.26***	***<0.001***	+0.022	0.024	0.90	≈1
	Pre offset	***+0.133***	***0.027***	***4.87***	***<0.001***	+0.053	0.031	1.75	0.976
	Post offset	*+0.074*	*0.033*	*2.25*	*0.517*	+0.048	0.037	1.28	≈1
RMSSD	No event[1]	44.151	2.446	18.05	-	42.777	2.484	17.22	-
	Pre onset	***-10.008***	***2.065***	***-4.85***	***<0.001***	-4.562	2.431	-1.88	0.851
	Event	***-6.879***	***1.912***	***-3.60***	***0.009***	-0.823	2.001	-0.41	≈1
	Pre offset	***-9.526***	***1.980***	***-4.81***	***<0.001***	*-4.684*	*2.285*	*-2.05*	*0.608*
	Post offset	*-6.351*	*2.318*	*-2.74*	*0.149*	*-5.954*	*2.744*	*-2.17*	*0.574*

Note. Multilevel regression with the independent variable symptom phase. SCL=range-corrected skin conductance level, RMSSD=root mean square of successive differences, p_{corr}=Bonferroni-Holm corrected p-values. [1] = All other phase are contrasted to the respective “no event”-phase (intercept). Significant results are printed in bold.

Table S1.

Self-reported and physiological reaction to psychosis-spectrum experience phases. Results of multilevel regression models symptom phase (level 1 predictor) on the respective stress parameter, based on subsamples who reported at least one phase with and without the respective experience.

		Paranoia (*n*=39)				Hallucination spectrum experiences (*n*=34)			
Stress indicator	Phase	b	SE	T	p_{corr}	b	SE	T	p_{corr}
Self-report	No event (intercept)	3.067	0.158	19.38	-	3.263	0.199	16.43	-
	Pre onset	**+0.820**	**0.177**	**4.65**	**<0.001**	-0.052	0.199	-0.26	≈1
	Event	**+1.516**	**0.159**	**9.56**	**<0.001**	+0.373	0.168	2.22	0.648
	Pre offset	**+1.395**	**0.166**	**8.38**	**<0.001**	-0.170	0.183	-0.93	≈1
	Post offset	+0.316	0.200	1.58	≈1	+0.031	0.218	0.14	≈1
SCL	No event (intercept)	0.264	0.020	13.22	-	0.306	0.023	13.46	-
	Pre onset	**+0.093**	**0.029**	**3.20**	**0.034**	+0.045	0.034	1.32	≈1
	Event	**+0.136**	**0.026**	**5.31**	**<0.001**	+0.020	0.028	0.72	≈1
	Pre offset	**+0.142**	**0.027**	**5.20**	**<0.001**	+0.056	0.031	1.77	≈1
	Post offset	+0.083	0.033	2.53	0.267	+0.050	0.038	1.32	≈1
RMSSD	No event (intercept)	45.819	3.372	13.59	-	44.485	4.041	11.01	-
	Pre onset	**-10.130**	**2.262**	**-4.48**	**<0.001**	-4.664	2.560	-1.82	≈1
	Event	**-7.041**	**2.112**	**-3.33**	**0.022**	-0.839	2.162	-0.39	≈1
	Pre offset	**-9.652**	**2.170**	**-4.45**	**<0.001**	-4.771	2.408	-1.98	≈1
	Post offset	-6.471	2.538	-2.55	0.263	-6.060	2.876	-2.11	0.852

Note. Multilevel regression with the independent variable symptom phase. SCL=range-corrected skin conductance level, RMSSD=root mean square of successive differences, p_{corr}=Bonferroni-Holm corrected p-values. All other phase are contrasted to the respective “no event”-phase. Significant results are printed in bold.

Table S2.

Self-reported and physiological reaction to hallucination-spectrum experience phases. Estimates based on the results of multilevel regression models symptom phase (level 1 predictor) on the respective stress parameter.

		Phase				
HSE type	Stress parameter	No event	Pre-onset	Event phase	Pre offset	Post offset
Vivid daydreams	Self-report	3.36	3.50	3.25	3.24	3.05
	SCL	0.29	0.35**	0.35**	0.33^{+}	0.27
	RMSSD	45.38	41.08*	40.97*	41.30*	41.27
Intrusive thoughts	Self-report	3.25	3.28	3.36	3.27	3.26
	SCL	0.30	0.37**	0.35**	0.33	0.36^{+}
	RMSSD	46.02	42.10*	**39.92*** **	**38.78*** **	38.98**
Perceptual sensitivity	Self-report	3.00	3.22	**3.59*** **	**3.57*** **	3.09
	SCL	0.28	**0.38*** **	**0.37*** **	**0.37*** **	0.35**
	RMSSD	43.89	39.95*	40.71^{+}	40.42^{+}	39.97^{+}
Auditory hallucinations	Self-report	3.13	3.34	**4.05*** **	**3.94*** **	3.89**
	SCL	0.32	0.38*	0.39*	0.35	0.29
	RMSSD	42.11	36.92*	40.02	36.53*	33.92**

Note. Results are based on multilevel regression with the independent variable symptom phase. SCL=range-corrected skin conductance level, RMSSD=root mean square of successive differences. For no-event-phase the difference to zero is tested for significance; all other categories are contrasted to the “no event”-phase, with significant differences printed in bold. Uncorrected significance levels: *** - $p < 0.001$; ** - $p < 0.01$; * - $p < 0.05$; $^{+}$ - $p < 0.10$, significant differences after Bonferroni-Holm-correction ($p_{cor}<0.05$) are printed in bold.

Appendix E: Study 5

Schlier, B., Winkler, K., Jaya, E. S., & Lincoln, T. M. (2018). Fluctuations in Hallucination Spectrum Experiences Co-vary with Social Defeat but not with Social Deafferentation. A 3-Week Daily Assessment Study. *Cognitive Therapy and Research, 42*, 92-102.

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Fluctuations in hallucination spectrum experiences co-vary with social defeat but not with social deafferentation. A three-week daily assessment study

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Abstract

The social deafferentation hypothesis proposes social isolation to be a risk factor for hallucinations, whereas the social defeat hypothesis postulates that only negatively appraised experiences of social exclusion constitute a risk factor. In a community sample, we tested whether social isolation and social defeat coincide with or precede hallucination spectrum experiences (HSE; i.e. auditory hallucinations and their subclinical precursors vivid imagination, perceptual sensitivity, and intrusive thought). Once daily for three weeks, 75 participants answered questionnaires on social contact, social exclusion, and HSE during the last 24 h. Multilevel-regressions were calculated. Social exclusion was associated with the subclinical precursors of auditory hallucinations on the same and following day but not with auditory hallucinations as such. Thus social exclusion coincides with and potentially triggers HSE. Further research needs to expand on these findings in ESM studies with clinical samples to test whether these findings extend to brief time-intervals and clinical hallucinations.

Keywords: Schizophrenia; Psychosis like experiences; Social defeat; Social deafferentation; Hallucinatory experiences

Auditory hallucinations, mostly in the form of voices, are a core symptom of schizophrenia spectrum disorders and have been the subject of clinical research for decades. Much has been done to understand the neurobiological basis of auditory hallucinations, and increasing attention is paid to cognitive and emotional etiological factors (Beck et al. 2009). Nevertheless, our knowledge about the social causes and triggers of hallucinations is still limited. Given that social factors may be a fairly accessible therapeutic target at any point of the course of the disorder, a more detailed knowledge about which social factors contribute to the etiology of hallucinations can help us to develop effective psychosocial interventions.

In recent years, researchers have begun to investigate the social environment and specifically social contact as a potential cause for auditory hallucinations. Two distinct hypotheses were generated to explain how social contact (or the lack thereof) causes hallucinatory experiences: The social defeat hypothesis (Selten and Cantor-Graae 2005; Selten et al. 2013) and the social deafferentation hypothesis (Hoffman 2007, 2008). Both theories postulate that certain social factors make people vulnerable to psychosis and constitute stressors that trigger psychotic experiences such as hallucinations. Whereas evidence from epidemiological studies has been accumulated for both models' macro-level notion that a history of social adversity adds to the underlying vulnerability for psychosis, far less attention has been given to the role of social factors as stressors that directly trigger hallucinations at the micro-level in the context of daily life. Previous ambulatory assessment studies indicate that social interactions with unfamiliar individuals precede anomalous experiences in population samples with a preexisting vulnerability to psychosis (Verdoux et al. 2003), whereas social engagement intensifies hallucinations in people with a psychotic disorder (Delespaul et al. 2002). Thus, the existing studies support the idea that social factors trigger hallucinatory experiences in daily life. However, to date, no study has investigated social factors as triggers of hallucinations within the framework of the social defeat or the social deafferentation hypothesis.

The social defeat hypothesis

The social defeat hypothesis (Selten and Cantor-Graae 2005; Selten et al. 2013) is based on epidemiological findings that identified urbanicity, migration, childhood trauma, low IQ, and drug abuse as risk factors for schizophrenia (Selten et al. 2013). According to the social defeat hypothesis, the negative experience of exclusion from a majority group is the common denominator of these five risk factors. In essence, the hypothesis proposes that "any characteristic that defines a person as different from their environment may increase their risk for psychosis" by facilitating "one type of exposure, namely the negative experience of being excluded from the majority group" (Selten et al. 2013). According to the social defeat hypothesis, accumulated negative experiences of being excluded increase the risk for psychosis by sensitizing the mesolimbic dopamine system, leading to an enhanced dopamine response to subsequent social defeat. In line with this hypothesis, cross-sectional studies found an association of social defeat/social exclusion and psychotic symptoms (Jaya and Lincoln 2016; Stilo et al. 2013; Valmaggia et al. 2015; van Nierop et al. 2014). Specifically, people with psychosis who hear distressing voices report social and interpersonal cognitions characterized by an appraisal of their social rank as subordinate as well as a low sense of group identification and belonging, which indicates prior social defeat (Birchwood et al. 2000). Moreover, experimental studies that simulate social defeat have shown that experiencing social exclusion induces psychotic experiences (Kesting et al. 2013; Westermann et al. 2012). Finally, an fMRI-study showed that an anomalous activation of the medial prefrontal cortex in response to increasing levels of simulated exclusion in participants with schizophrenia was associated with the severity of delusions, grandiosity, and hallucinations (Gradin et al. 2012).

The social deafferentation hypothesis

Whereas the social defeat hypothesis postulates that exposure to negative (or negatively appraised) social interactions constitutes the key social risk factor for schizophrenia, the social deafferentation hypothesis (Hoffman 2007, 2008) postulates that the lack of social interaction as such is the key risk factor: Much like certain brain regions respond to the loss of neural input due to a lost limb by internally generating a phantom limb sensation from spurious neural activity, neural

networks associated with social cognition begin to process spurious neural information in absence of external social stimuli (i.e. social withdrawal or isolation). This results in “complex, emotionally compelling hallucinations and delusions representing” (Hoffman 2007) other social agents. This hypothesis is supported by epidemiological findings that identify social withdrawal (Kwapil 1998) and isolated living conditions (van Os et al. 2000) as risk factors for schizophrenia spectrum disorders. Moreover, it has long been known that hallucinations can be induced by extreme sensory deprivation (Schulman et al. 1967).

Suitability of social defeat and social deafferentation as triggers for hallucinations

The social deafferentation hypothesis primarily stems from observations regarding the emergence of distressing hallucinations (Hoffman 2007), which makes hallucinations the prototypical symptom to this hypothesis. The social defeat hypothesis, by contrast, postulates social defeat/social exclusion to be a risk factor for psychosis in general without further elaborating on single symptoms. Evidence from research on social rank threat in voice hearers, however, shows that social-cognitive beliefs indicative of recurring social defeat are associated with hearing distressing voices (Birchwood et al. 2004, 2000).

A striking similarity of both hypotheses is their focus on a vulnerability-stress mechanism consisting of immediate and long-term exposure to certain social stimuli: According to the social defeat hypothesis, an increased risk of psychosis results from continued exposure to an adverse social situation (e.g., belonging to a minority in a majority-dominated neighborhood), which increases a person’s vulnerability to future events of social stress (Selten et al. 2013). Similarly, the social deafferentation hypothesis postulates that prolonged social isolation, especially during critical developmental periods, induces cortical changes that increase the likelihood that future experiences of social isolation will trigger hallucinations (Hoffman 2007). As we mentioned before, the bulk of evidence for both theories comes from epidemiological and neurological studies of long-term risk-factors that support the vulnerability-part of both theories (Hoffman 2007, 2008; Selten and Cantor-

Graae 2005; Selten et al. 2013). However, there is also correlational (Jaya and Lincoln 2016) and experimental (Kesting et al. 2013; Westermann et al. 2012) evidence supporting the idea that immediate social defeat or social deafferentation triggers psychosis symptoms.

Of importance, Selten et al. (2013) described a potential overlap between social defeat and social deafferentation. Social isolation could be a consequence of repeatedly experiencing social defeat. For example, after feeling excluded, a person may decide to withdraw from a certain peer-group leading to less social interaction. Furthermore, social isolation may be appraised as defeating (e.g., if a person attributes the absence of social contact as not 'fitting in'). In consequence, both theories have to be tested together. Otherwise, any association between social defeat and hallucinations could result from the confounding influence of social deafferentation or vice versa.

In sum, experimental evidence points toward a potential dose-response or trigger effect of social defeat and social deafferentation. Conclusive evidence for one hypothesis, however, requires a direct comparison of the influence of both social factors on hallucinations. Elucidating which of these two hypotheses holds true in daily life is not only of theoretical importance, but also yields crucial clinical implications. If social isolation is found to be the underlying social risk factor, interventions and prevention strategies could be improved by focusing on the client's social network and increasing social interactions. If, however, negative appraisal (i.e., social defeat) is found to be the most important social risk factor, interventions should focus on modifying negative social cognitions and teaching functional ways of relating to others.

Aims of this study

In this study, we tested whether indicators of social deafferentation and social defeat reported once per day are associated with hallucination spectrum experiences (HSE; i.e., auditory hallucination along with the subclinical precursors vivid imagination, perceptual sensitivity, and intrusive thoughts) in a community sample. We aimed to identify social factors that co-vary with

HSEs and may thus constitute potential triggers for first episodes of auditory hallucinations and their subclinical predecessors.

The rationale for using a community sample is that psychotic experiences such as hallucinations appear to exist along a continuum - with people who never had any psychosis-like experiences on the one end and people who fulfil all diagnostic criteria for a psychotic disorder on the other. Between these extreme ends, there is a large group of people with unusual experiences (e.g. vivid daydreams, perceptual sensitivity, and intrusive thoughts; Bell et al. 2010) and experiences below the diagnostic threshold (Johns and van Os 2001). These psychosis-spectrum experiences have been shown to predict transition to psychosis (Mark and Toulopoulou 2015). Furthermore, they share environmental and psychopathological causal factors with clinical symptoms (Van Os and Linscott 2012). Accordingly, it is possible to investigate the etiology of hallucinations based on HSE in community samples. In fact, community samples are advantageous for research on causal factors because compared to clinical groups, they allow to test for etiological factors that contribute to an eventual onset of clinical symptoms without the risk of confounding etiological factors with factors that follow clinical symptoms (e.g. medication, stigma, decline in functioning).

Methods

Participants

Participants were recruited via online-advertisement on facebook.com (*n*=34) as well as via posters and leaflets distributed on the campus (*n=41)*. Psychology students were granted partial course credit for participating. Other participants could take part in a raffle and win one of four 25 Euro amazon.com gift cards. A participation in the raffle was only possible after completing the whole study.

A sample of 75 participants was recruited for this study (26 men and 49 women). The age ranged from 18 to 66 years (*M*=25.03, *SD*=8.82). The sample was a convenience sample consisting of adults from the general population. There were no particular eligibility criteria. All participants were

German native speakers. Fifty-four participants (72%) provided data on their ethnic background. A majority of them (88.9%) reported to be German or white/Caucasian. Three participants (5.6%) reported to be German with Asian roots, one participant reported to have Arabic roots, and two participants reported to have a mixed ethnic background. The majority of participants (65.3%) reported their highest education level to be the university entrance diploma ("Abitur"), 16 participants (21.3%) held a university degree, and 8 participants (10.7%) had completed a vocational training. Most participants (81.3%) were students (57.3% psychology students), and 13.3% were gainfully employed. The majority of participants (81.3%) reported to never have had a mental disorder. The other participants most frequently reported having been diagnosed with depression (14.7%), whereas others reported anxiety disorders (4%), PTSD (4%), panic disorders (2.7%), personality disorders (2.7%), eating disorders (2.7%), OCD (1.3%) and sleeping disorders (1.3%).

Design & Procedure

This longitudinal study consisted of an introductory questionnaire and a three-week daily diary assessment. All questionnaires were presented in Questback EFS-Survey (QuestBack GmbH 2014).

The introductory questionnaire comprised information on the study and informed consent, self-report assessments of psychosis-like experiences and HSE, and a demographic questionnaire. Completion of the introductory questionnaire took the participants 25 min on average. Participants could complete the introductory questionnaire either at home from their own computer (*n*=34) or in our laboratory (*n*=41). The first daily questionnaire was sent to the participants via email 24 h after they had completed the introductory questionnaire. The daily questionnaires included self-report items about HSE (nine items), social isolation (three items), social defeat (five items), and general mood (six items). Over 21 consecutive days, the participants received daily emails containing the link to the online-questionnaire. Participants were instructed to complete the questionnaire on the day it was sent to them, preferably in the evening. If participants failed to complete a daily questionnaire

by the end of the respective day, they were instructed to omit it. After completing the last daily questionnaire, all participants were debriefed and thanked for their participation.

Materials

Introductory assessment. The introductory questionnaire included the Community Assessment of Psychic Experiences (CAPE; Schlier et al. 2015; Stefanis et al. 2002) and the Launay-Slade Hallucination Scale (LSHS-R; Bentall and Slade, 1985), which were presented in the aforementioned order.

The CAPE measures the lifetime prevalence of psychosis-like experiences. It consists of 42 items that tap into positive symptoms (20 items, e.g., “Do you ever hear voices when you are alone?”), negative symptoms (14 items, e.g., “Do you ever feel that you have no interest to be with other people?”), and symptoms of depression (8 items, e.g., "Do you ever feel pessimistic about everything?”). Participants rated how often they had experienced each symptom over the course of their life. The items are answered on a four-point Likert scale (0=“never”, 1=“sometimes”, 2=“often”, 3=“nearly always”). The CAPE and its German translation have been shown to be sufficiently valid and reliable (Schlier et al. 2015; Stefanis et al. 2002).

The LSHS-R (Bentall and Slade 1985) assesses hallucination proneness in community samples. The scale includes twelve items. Participants answer on five-point Likert scales ranging from 0= „certainly does not apply to me” to 4=„certainly applies to me”. The LSHS taps into different aspects of hallucinatory experiences (Waters et al. 2003), including auditory and visual hallucinations (e.g. "I have been troubled by hearing voices in my head.”), vivid daydreams (e.g. "The sounds I hear in my daydreams are usually clear and distinct.”) and religious hallucinations (e.g. "In the past I have heard the voice of God speaking to me.”). In the present study, a validated German version of the LSHS-R was used, for which good reliability (*Cronbach’s* α= 0.83-0.87) and an acceptable criterion and construct validity has been shown (Lincoln et al. 2009).

Daily assessment. The daily questionnaires included the nine-item Continuum of Auditory Hallucinations - State Assessment (CAHSA), the six-item Multidimensional Mood Questionnaire (MDMQ), as well as four indicators of social interactions, ranging from a strong indicator of social isolation to a strong indicator of social defeat (see Fig. 1).

The CAHSA (Schlier et al. 2017) assesses HSE and was specifically developed for repeated measurement. It includes three subclinical precursors of auditory hallucinations, namely vivid imagination (two items, e.g., „I daydreamed a lot“), perceptual sensitivity (two items, e.g., „Even distant noises distracted me“), intrusive thoughts (two items, e.g., „My thoughts were so powerful and vivid that I could almost hear them“), and auditory hallucinations (three items, e.g., „I heard something other people could not hear“). Participants answered to the question how much each item applied to them for the last 24 h on 7-point Likert-scales ranging from 1=“not at all” to 7=“very much”. The questionnaire shows good criterion validity and is sensitive to change. Previous research showed a good fit of a four-factor model with a second-order general factor (Schlier et al. 2017). In the present study, model fit was acceptable according to two out of three fit-indices (*CFI*=0.854; *RMSEA*=0038; $SRMR_{within}$=0.050, $SRMR_{between}$=0.081). The CAHSA sum score was used as primary outcome measure.

The MDMQ (Wilhelm and Schoebi 2007) is a six-item questionnaire that has been shown to reliably and validly measure mood in everyday life. Using six-point bipolar scales to answer to the question “over the past day, I felt…”, it assesses calmness (“agitated–calm”, “relaxed–tense”), valence (“unwell–well”, “content–discontent”), and energetic arousal (“full of energy–without energy”, “tired–awake”).

The four indicators of social interactions included two variables indicative of social isolation and two variables indicative of social defeat (see Fig. 1). The first indicator was “time spent alone” (two items: “Today, I have been alone” and “today, I have been in company of others”, rated on 7-point Likert scales ranging from 1=”not at all” to 7=”all the time”). As a second “weak” indicator of

social deafferentation (see Fig. 1) the amount of social interactions (one item: “How often did you talk or interact with one or more other people today?”, rated on 7-point Likert scales ranging from 1=”not at all” to 7=”all the time”) was assessed. The items for these two indicators were developed for the purpose of this study: Initially, prototype items were constructed based on the environment and functioning items from the computerized Ecological Momentary Assessment Questionnaire (EMAc; Granholm et al. 2007). The items and answer options were adapted to a one-day sampling interval, presented to a group of experts and finalized based on their feedback.

As a first indicator for social defeat, we included the three-item group fit subscale of the Social Comparison Scale (Allan and Gilbert 1995) which measures social exclusion (i.e. the defining type of experience of the social defeat hypothesis; Selten et al. 2013). In this scale, participants rated their subjective experience of feeling accepted vs. excluded by their peer group on 10-point semantic differentials (e.g., “In relationship to others I feel: left out – accepted“).For this study, we translated the three items into German and adapted the scale to daily assessment by changing the instruction “In relationship to others I feel” to “Today, in relationship to others I felt”. Good internal consistency was shown in previous studies (Allan and Gilbert 1995). As a second “weak” indicator for social defeat we asked for the amount of unpleasant social interactions” (two items: “How many of your interactions with others today were enjoyable?” and “How many of your interactions with others today were unpleasant?”). Participants answered on 7-point Likert scales ranging from 1=”none” to 7=”all of them”. Internal consistencies for the indicators are shown in Fig. 1. Mean scores were calculated for all indicators except the one-item measure “few interactions with others”. If necessary, items were reversed so that higher values indicate higher levels of social deafferentation/defeat.

Data analysis

Based on EFS-Survey time logs, daily questionnaires were checked for consecutively made entries outside the daily assessment schedule. Any questionnaires completed immediately after the

previous one were treated as a missing value. All analyses were carried out using R 3.1.3 (R Core Team 2014) . Multilevel models were estimated using the R packages lme4 (Bates et al. 2015) and lmerTest (Kuznetsova et al. 2016). For all analyses, we originally aimed to calculate linear multilevel regression models. However, the hallucination-spectrum experiences in our community sample showed a skewed, non-normal distribution that could have biased findings in linear regression (see Table 1 and online supplements to this article). Thus, we switched to binomial logistic regression analyses. For this purpose the respective dependent HSE variable was dichotomized, with the low end of the scale "1" (i.e. having not at all experienced the HSE in question) set to 0 and all other values (i.e. having experienced the HSE to some degree) set to 1.

For our main analyses, we calculated random-intercept, random-slope multilevel regression analyses of daily assessments nested in participants. HSE (i.e., CAHSA scores) were the dependent variable and the independent variable was one out of the 4 social deafferentation/social defeat indicators: Four separate regression models were calculated for (1) time spent alone, (2) few social interactions, (3) social exclusion, and (4) unpleasant interactions. In the first set of analyses, predictors from the same day (cross-sectional analyses) were entered. In a second set, four time-lagged regression analyses were carried out to test whether changes in social factors preceded the occurrence of HSE. The respective social isolation/social defeat predictor from the previous day was the independent variable in these models and the CAHSA score from the previous day served as a covariate. Additionally, the reverse patterns of HSE predicting social isolation or social defeat on the following day were tested.

Furthermore, any significant association between social defeat indicators and HSE was tested again while controlling for general mood (MDMQ-subscales), in order to rule out that the influence of social defeat is just a by-product of overall negative mood. Finally, the association between social isolation/social defeat and HSE was further explored by repeating the cross-sectional analyses with the four CAHSA-subscales vivid imagination, perceptual sensitivity, intrusive thoughts, and auditory hallucinations as dependent variable.

Results

Baseline assessment and compliance

Baseline and mean daily assessment scores are summarized in Table 1. All participants indicated to experience at least one CAPE-symptom of each subscale at least “sometimes”. Forty-seven participants (62.67%) indicated to experience at least one positive symptom “often” or “nearly always”, 56 participants (74.67%) indicated the same for at least one negative symptom and 48 participants (64%) for at least one symptom of depression. The mean total score of the LSHS was 7.64 (*SD*=6.65), with 34 participants (45.33%) indicating that at least one item “possibly” or “certainly” applies to them. Valid data was available for 1291 of 1575 days. Thus, the compliance rate was 81.97%. Participants omitted daily assessments on an average of 3.79 days (*SD*=5.16; Range: 0-17).

Regarding the daily assessments, all HSE variables were positively skewed, with the auditory hallucination subscale showing the most deviation from normal distribution (5.06). Based on the dichotomized HSE variables, the majority of participants experienced some degree of vivid imagination on at least one day (90.7%), about three quarter reported perceptual sensitivity (78.7%) and intrusive thoughts (74.7%) on one or more days, whereas 37.3% reported some degree of auditory hallucinations on at least one day. Further details regarding the distribution of all independent and dependent variables can be found in the online-supplements to this article.

Cross-sectional prediction of HSE by social deafferentation vs. defeat

Logistic multilevel regression models yielded neither significant results for the two social deafferentation variables (time spent alone; *OR*=1.06, *z*=0.52, *p*=0.601; few interactions: *OR*=1.16, *z*=1.09, *p*=0.275) nor for the amount of unpleasant interactions (*OR*=1.04, *z*=0.32, *p*=0.748). However, social exclusion was associated with more HSE at the same day (*OR*=1.27, *z*=2.10, *p*=0.036).

Time-lagged and reversed time-lagged prediction models

In time-lagged logistic regression, again neither the indicators of social deafferentation nor the social defeat indicator unpleasant interactions predicted HSE on the following day. However, social exclusion was significantly associated with the presence of HSE on the next day (*OR*=1.46, *z*=2.37, *p*=0.018). In comparison, reversed time-lagged models showed that HSE did not predict any of the social deafferentation or social defeat indicators on the next day (see Table 2).

The influence of social deafferentation and social defeat after controlling for potential covariates

The cross-sectional and time-lagged effects of social exclusion on HSE remained significant when the MDMQ scales were entered as control-variables (cross-sectional: *OR*=1.24 *z*=2.75, *p*=0.006; time-lagged: *OR*=1.20, *z*=2.14, *p*=0.032). Furthermore, all other indicators in cross-sectional, time-lagged and reversed time-lagged analyses remained non-significant when mood was controlled for. Similarly, the pattern of results remained the same when gender and age of the participants were controlled for.

Exploratory analyses of continuum of auditory hallucinations subscales

Separate analyses for the CAHSA-subscales vivid imagination, intrusive thoughts, perceptual sensitivity, and auditory hallucinations are summarized in Table 3. There were no significant associations between the indicators of social deafferentation and any of the CAHSA subscales. Regarding the indicators of social defeat, social exclusion was associated with increased vivid imagination (*OR*=1.18, *z*=, *p*=0.023), perceptual sensitivity (*OR*=1.27, *z*=2.28, *p*=0.014) and intrusive thoughts (*OR*=1.24, *z*=2.70, *p*=0.007) in the cross-sectional analyses. Time-lagged analyses further showed that social exclusion was associated with vivid imagination (*OR*=1.12, *z*=2.46, *p*=0.014) and intrusive thought (*OR*=1.27, *z*=2.44, *p*=0.015) on the following day. Finally, one reversed time-lagged analysis was significant: vivid imagination was associated with increased reports of social exclusion (*b*=0.31, *t*=3.09, *p*=0.002).

Discussion

In this study, we investigated whether social defeat and social deafferentation co-vary with HSE in healthy participants. We found that social defeat, but not social deafferentation was associated with self-reported HSE on the same day. This association was not accounted for by general mood. Moreover, feeling socially excluded was consistently associated with HSE, whereas having unpleasant social interactions per se was not. This is in line with the social defeat hypothesis (Selten and Cantor-Graae 2005; Selten et al. 2013), which posits that experiencing social exclusion is more strongly related to HSE than social stress in general. Possibly, this result provides a framework to explain why social engagement (rather than social withdrawal) predicted hallucinatory experiences in previous ambulatory assessment studies (Delespaul et al. 2002; Verdoux et al. 2003)

Moreover, the same pattern was found regarding a temporal order of social risk factors preceding an increase of HSE on the following day: Social exclusion was the sole significant predictor of later HSE in the logistic regression models. This further highlights that social exclusion is the most promising candidate as a potential trigger of HSE. Given the covariation of HSE and social exclusion for this comparatively long time-interval of 24 h, one may speculate that the cause-and-effect relationship between social exclusion and subsequent HSE may be even more pronounced over a narrow time-interval. Time-lagged associations between days may already be subject to further moderating variables.

Regarding social deafferentation, time-lagged analyses indicated no significant associations with HSE at all. We need to take into account, however, that we approximated isolation with the relative time spent alone and few social interactions. The social deafferentation hypothesis proposes that extreme forms of social isolation trigger hallucinatory experiences. Possibly, social isolation needs to reach a critical threshold before it contributes to HSE, with only severe forms of social isolation that include sensory deprivation triggering HSE. Another possibility is that the critical threshold for social isolation depends on a person’s negative appraisal of the situation in the sense that only unpleasant or unwanted social isolation triggers HSE.

Finally, analyses of the CAHSA subscales revealed that the social defeat indicators were primarily associated with subclinical hallucination-like experiences such as intrusive thoughts and perceptual sensitivity. Hallucinations constituted a comparatively scarce phenomenon in our community sample. From a methodological point of view, one could thus argue that the variation in auditory hallucination scores was too small to detect any associations. However, one could also interpret that these findings are in line with the social defeat hypothesis: Present exposure to social exclusion has a base effect (i.e. triggering subclinical, unusual experiences), which is short-lived in healthy people. Possibly, the very same experience leads to more severe HSE or clinical auditory hallucinations in a person with a history of recurring social defeat that lead to a sensitization of the mesolimbic system (Selten et al. 2013). Moreover, although vivid imagination, perceptual sensitivity, and intrusive thoughts have been frequently associated with hallucinations as subclinical variations (Bell et al. 2010; Larøi et al. 2004; Waters et al. 2003), distractibility and intrusive thoughts have also been referred to as facets of a cognitive-attentional factor that is predictive of psychosis symptoms in general (e.g., Brett et al., 2007). Thus, the results pertaining to the subclinical factors are relevant to psychosis. However, further research is needed to explore the specificity with respect to hallucinations.

In sum, we found initial evidence for an association between daily variation in subclinical HSE and concurring as well as preceding experiences of social exclusion. However, no direct evidence extending to full-blown auditory hallucinations was found. While these findings do not confirm the hypothesis that an experience of social defeat triggers hallucinations in people with psychotic disorders or people at risk, they warrant further tests in more suitable samples.

Implications for research and clinical practice

In order to directly test the hypothesis that episodes of social defeat trigger hallucinations, future studies could investigate a social-defeat vulnerability-stress model by comparing the response to momentary experiences of social defeat in people with low risk vs. high risk of experiencing repeated

social defeat (e.g., non-migrants vs. first and second generation migrants; Egerton et al. 2017) or for developing psychosis (e.g., first-degree relatives of people with psychosis). Furthermore, to further corroborate the assumption that social defeat triggers HSE, ambulatory assessment studies with multiple assessments per day would be helpful. Specifically, we need to assess the fleeting experience of a hallucination when it occurs and test for correlations with immediately preceding social experiences.

Irrespective of whether feelings of social defeat ultimately trigger HSE or coincide with them, their association has practical implications: People with more frequent HSE experience distressing social exclusion more frequently, which is known to lead to reduced well-being and a lower level of functioning (Björkqvist 2001). Possibly, interventions that focus on functional ways of relating to others meet a specific need of people with frequent HSE. For example, psychosis-specific cognitive-behavioral therapy based on social rank theory (Birchwood et al. 2002; Trower et al. 2004) or focused on relating assertively to others (Hayward et al. 2009) could be adapted to reduce the impact of social defeat in people with HSE. If future studies continue to find a consistent link between social defeat and HSE, such prevention strategies may prove to reduce the burden of HSE and prevent the transition to psychosis.

Limitations

It has to be noted that the sample is an ad-hoc community sample and no prescreening criteria were used. Although our study seems to adequately capture early stages in which social defeat co-varies and potentially triggers subclinical precursors of hallucinations, a community sample may not suffice to reliably estimate the relationship of social factors and auditory hallucinations. Moreover, the analyses comprise a large number of significance tests. This is no limitation for the effect of social exclusion on HSE, which is found consistently in all variations of the analyses. However, isolated effects (e.g., vivid imagination being the only HSE-factor preceding social exclusion) with a comparatively large exact p-value need to be treated carefully. We cannot rule out

that these latter effects are false positives due to multiple comparisons. Finally, this study focused on one type of psychotic experiences, whereas the social defeat and social deafferentation hypotheses are used to explain psychotic experiences in general (Hoffman 2007; Selten et al. 2013). We limited our research to HSE to keep the daily assessments brief and to minimize the content overlap between independent and dependent variables (e.g. paranoid thoughts and feeling socially excluded, negative symptoms and social isolation). Needless to say, further research focusing on the social defeat and the social deafferentation hypotheses has to extend the focus to other symptom categories in order to comprehensively test their validity.

Conclusion

In sum, this study shows that short-term variation in HSE is associated with experiences of social defeat. Whereas previous epidemiological studies provided evidence for the long-term effect of repeatedly experiencing social defeat, we were able to show covariation of experiencing social defeat and subclinical hallucination spectrum experiences over the course of days. This opens the door for future ambulatory assessment and ambulatory intervention studies targeting negative social interactions and social exclusion.

Compliance with ethical standards

Conflict of interest

Björn Schlier, Katharina Winkler, Edo Sebastian Jaya, Tania Marie Lincoln declare that they have no conflict of interest..

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Animal Rights

No animal studies were carried out by the authors for this article.

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Table 1.

Descriptive values of baseline and daily assessment instruments.

	M	SD	Skew	Range (min-max)	Possible range (min-max)
Baseline Assessment					
CAPE					
Positive symptoms	7.77	4.67		1 - 23	0 - 60
Negative symptoms	13.03	5.61		3 - 31	0 - 42
Symptoms of depression	7.75	3.92		1 - 19	0 - 24
LSHS Total Score	7.64	6.65		0 – 29	0 - 48
Daily Assessments					
Time spent alone	2.78	1.62	0.79	1 – 7	1 – 7
Few social interactions	3.14	1.37	0.36	1 – 7	1 – 7
Social exclusion	3.23	1.77	0.73	1 – 10	1 – 10
Unpleasant interactions	2.30	1.16	0.80	1 - 7	1 – 7
HSE global score	1.47	0.64	1.78	1 – 4.67	1 – 7
HSE vivid imagination	1.95	1.33	1.75	1 – 7	1 – 7
HSE perceptual sensitivity	1.48	0.97	2.54	1 – 7	1 – 7
HSE intrusive thoughts	1.36	0.78	2.74	1 – 5.5	1 – 7
HSE auditory hallucination	1.10	0.39	5.06	1 – 4.67	1 – 7

Note. CAPE=Community Assessment of Psychic Experiences; LSHS=Launay-Slade Hallucination Scale; HSE = hallucination spectrum experiences

Table 2.

Cross-sectional and time-lagged multilevel regression of hallucination spectrum experiences, social defeat indicators, and social deafferentation indicators.

	OR/B (95%-Confidence-interval)		
	Cross-sectional Social factors predicting HSE (OR)	Time lagged Social factors predicting HSE (OR)	HSE predicting social factors (B)
Social deafferentation			
Time spent alone	1.06 (0.87; 1.29)	1.22 (0.99; 1.49)	0.11 (-0.11, 0.33)
Few social interactions	1.16 (0.89; 1.50)	1.15 (0.93; 1.42)	0.03 (-0.16; 0.22)
Social defeat			
Social exclusion	1.27* (1.02; 1.59)	1.46* (1.06; 1.88)	0.03 (-0.16; 0.23)
Unpleasant interactions	1.04 (0.82; 1.31)	1.03 (0.79; 1.35)	-0.05 (-0.24; 0.14)

Note. HSE=Hallucination spectrum experiences, OR = Odds ratio, B = linear regression estimate; * - $p<0.05$

Table 3.

Associations between hallucination spectrum experiences subscales and indicators of social deafferentation and social defeat.

Social contact variable	Analysis type	*hallucination spectrum experiences subscale*			
		vivid imagination	perceptual sensitivity	intrusive thought	auditory hallucinations
Social deafferentation					
Time spent alone	Cross-sectional (OR)	1.07	1.00	0.90	0.69
	Time-lagged (OR)	1.04	1.09	0.85	1.20
	Rev. time-lagged (B)	0.19	-0.03	-0.04	-0.04
Few social interactions	Cross-sectional (OR)	1.08	1.05	0.87	0.70
	Time-lagged (OR)	1.04	1.08	0.95	0.75
	Rev. time-lagged (B)	0.04	0.04	0.18	0.18
Social defeat					
Social exclusion	Cross-sectional (OR)	1.18*	1.27*	1.24**	0.99
	Time-lagged (OR)	1.21*	0.95	1.27*	1.07

	Rev. time-lagged (B)	0.31**	0.02	0.05	0.05
Unpleasant interactions	Cross-sectional (OR)	0.97	1.15	0.96	1.01
	Time-lagged (OR)	1.05	0.86	1.17	1.28
	Rev. time-lagged (B)	0.01	-0.01	0.01	0.20

Note: OR = Odds ratio based on logistic multilevel regression; B = estimate based on linear multilevel regression; ** - $p<0.01$; * - $p<0.05$;

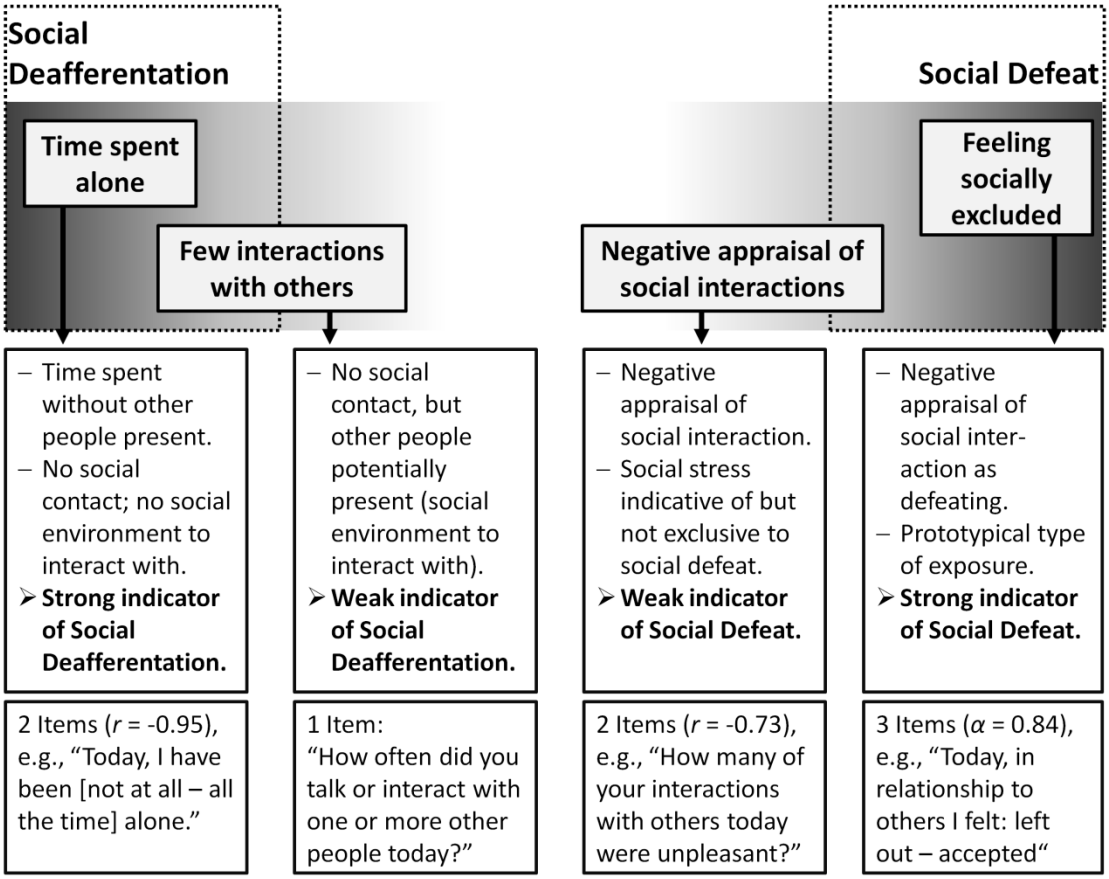
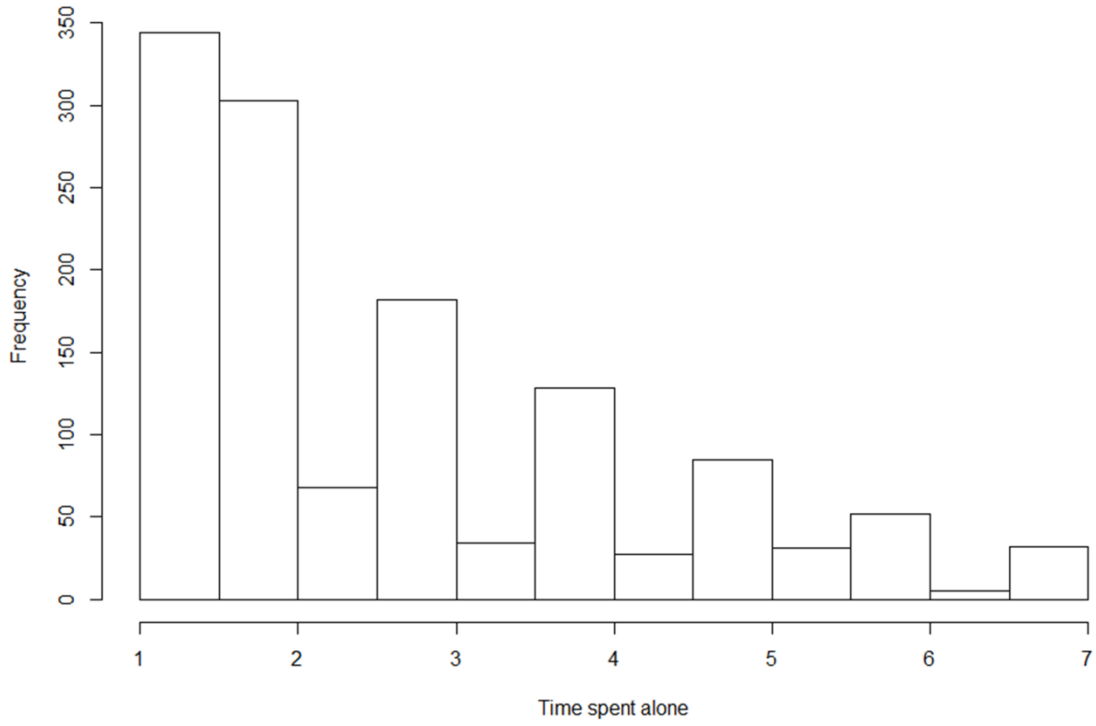
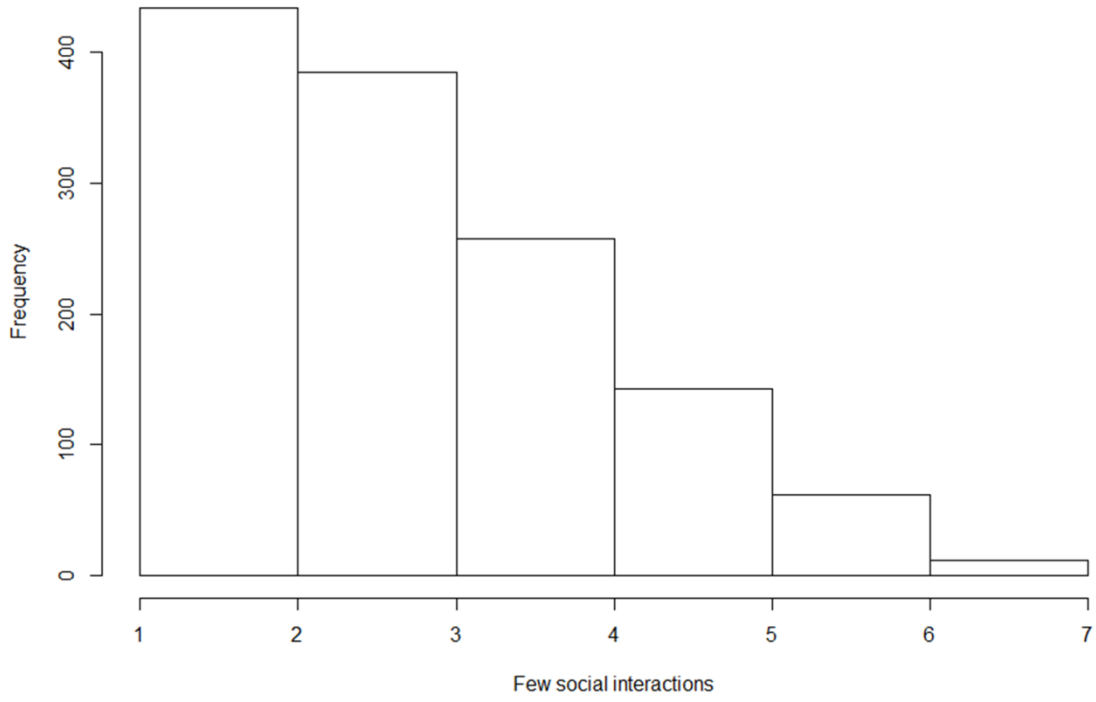


Figure 1. Conceptual proximity of the independent variables to the constructs social deafferentation and social defeat

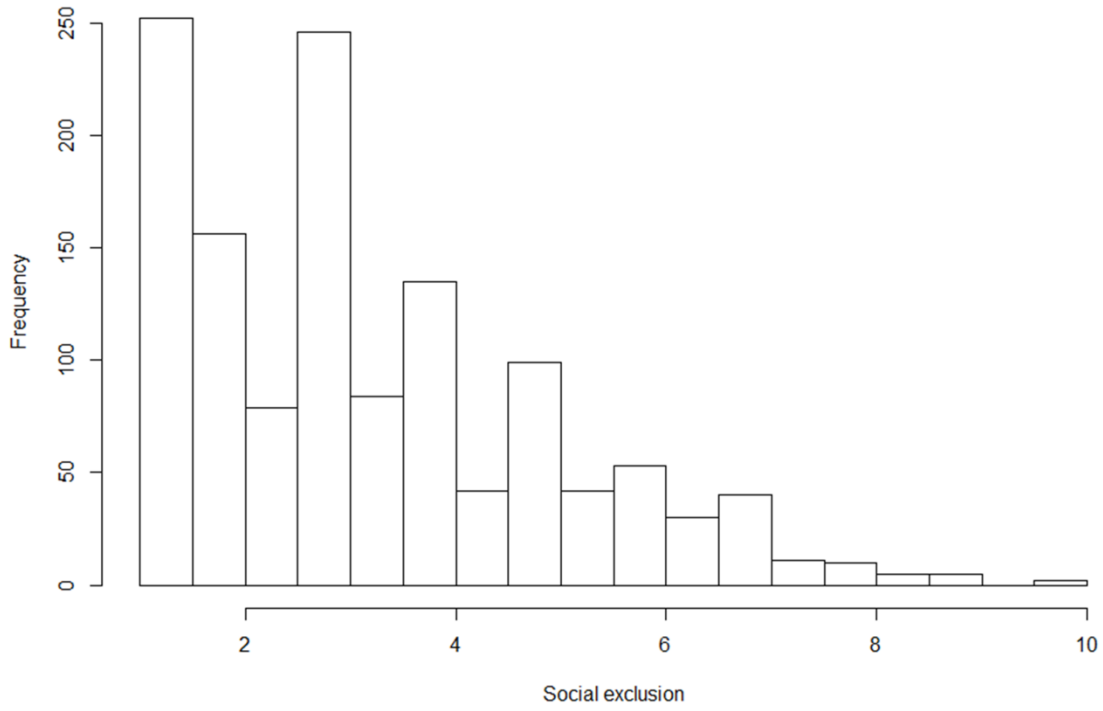
Supplement 1: Distribution of the independent and dependent variables



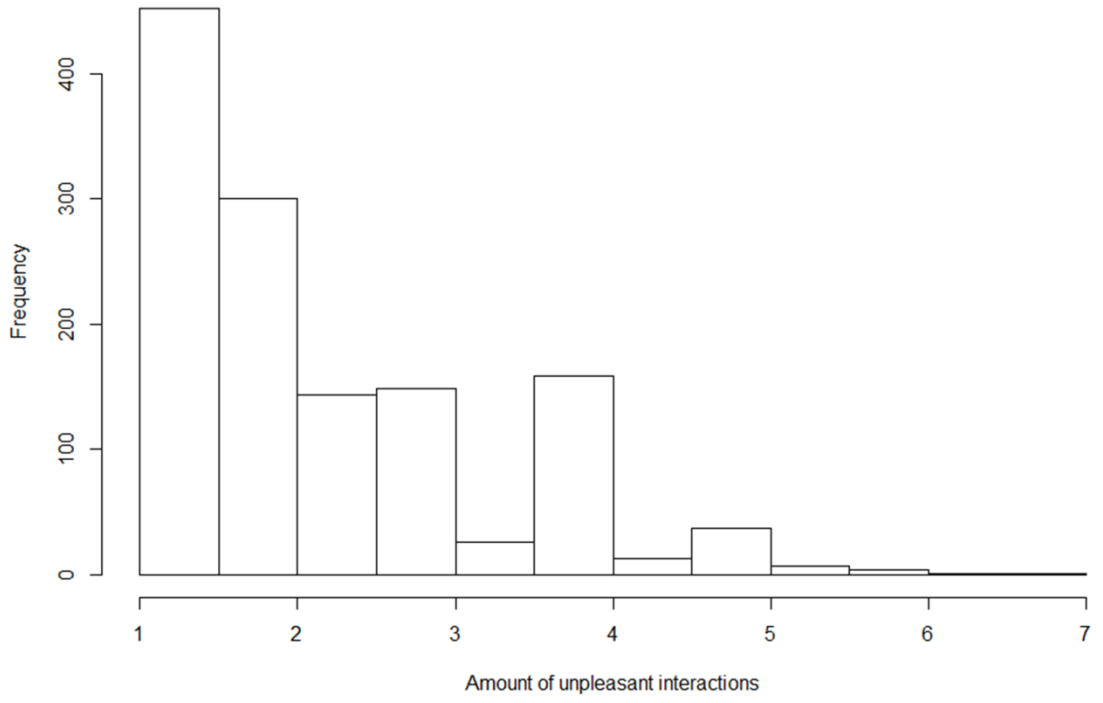
Suppl. Figure 1. Distribution of the variable “time spent alone”



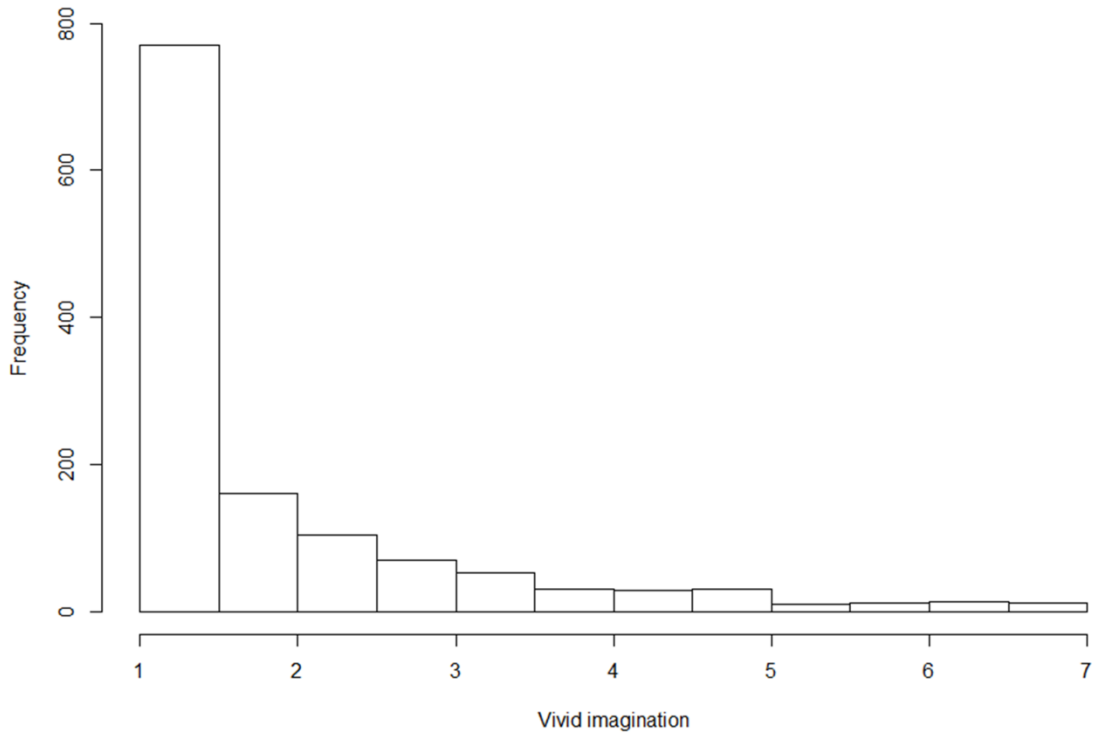
Suppl. Figure 2. Distribution of the variable “few social interactions”



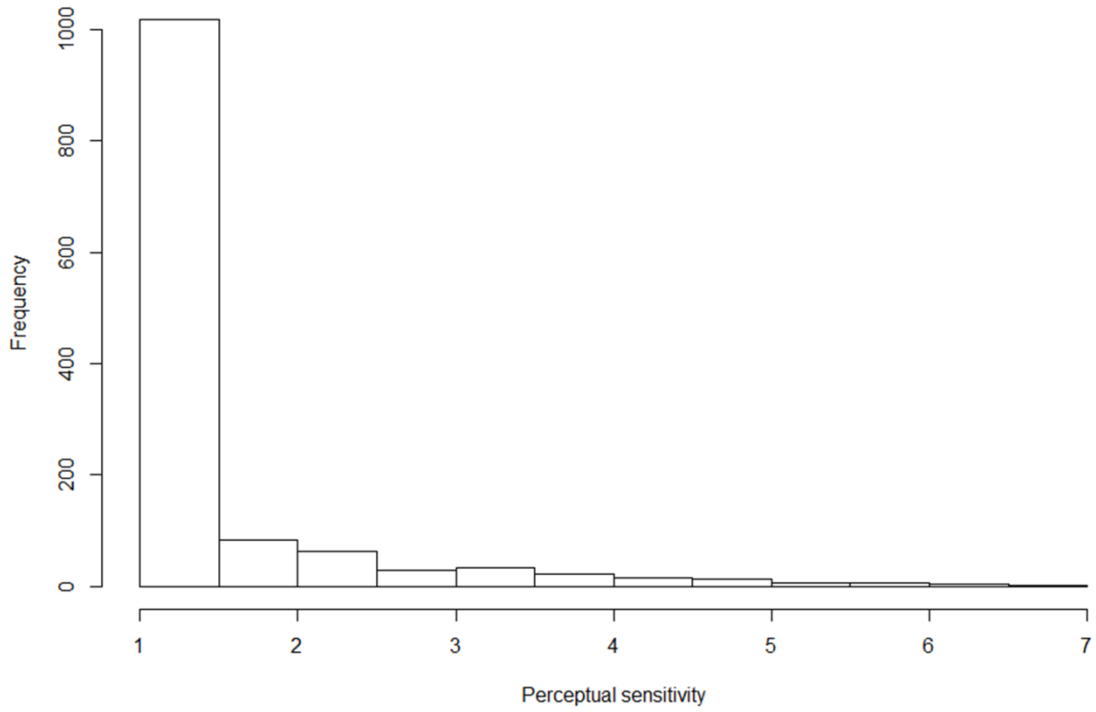
Suppl. Figure 3. Distribution of the variable “social exclusion”



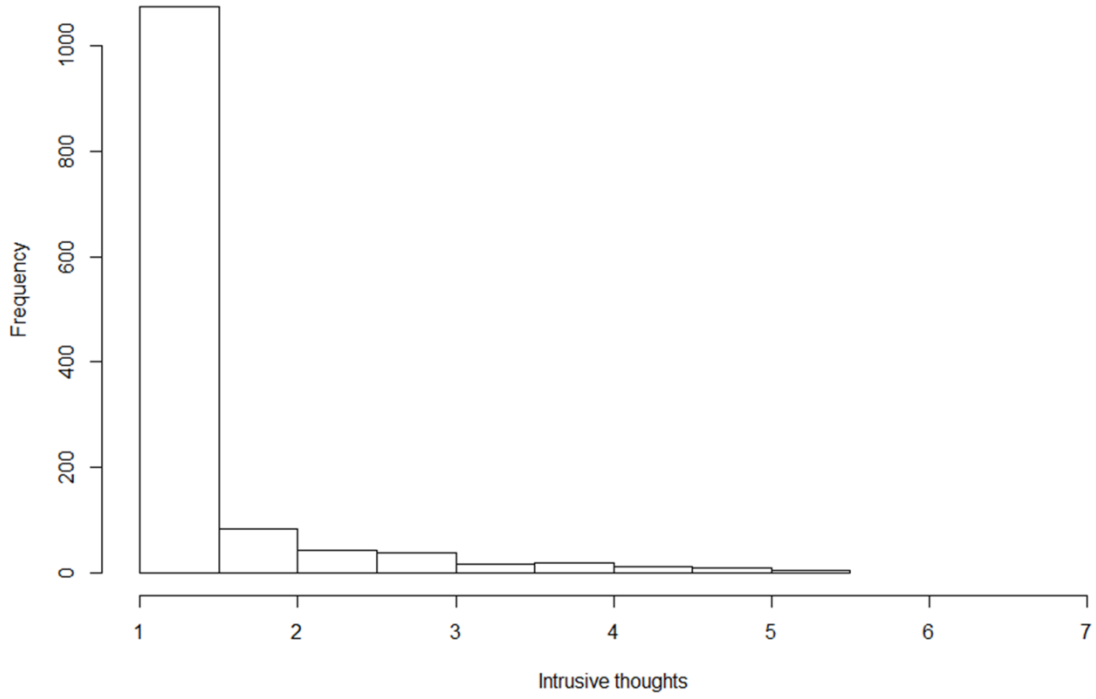
Suppl. Figure 4. Distribution of the variable “amount of unpleasant interactions”



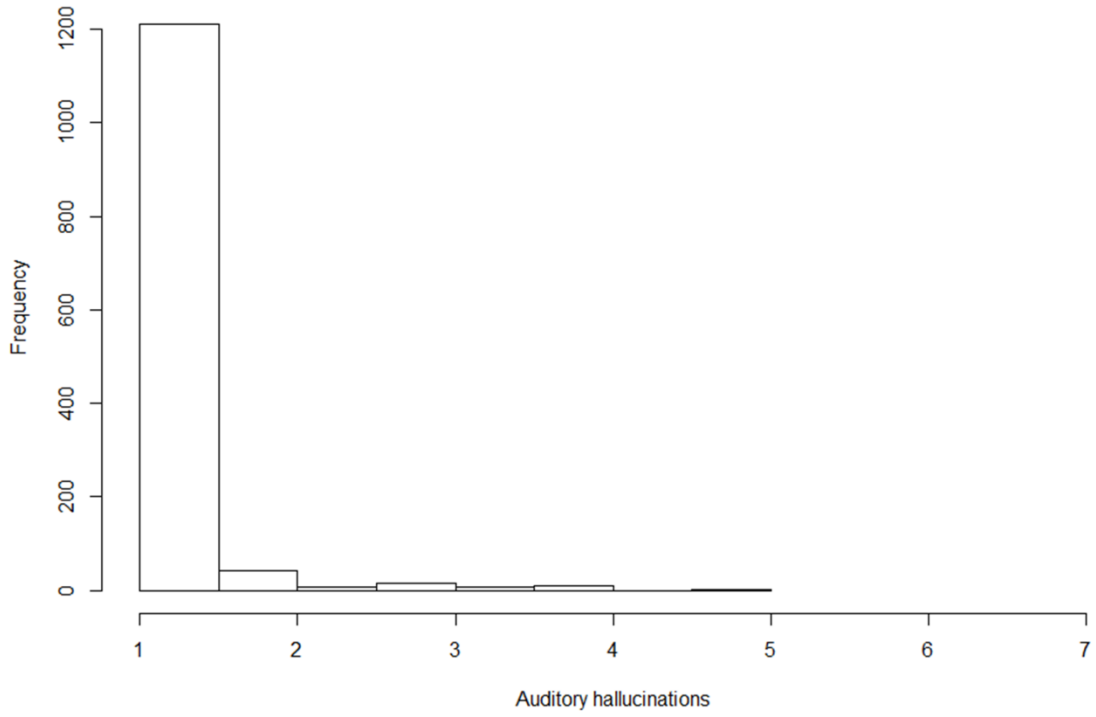
Suppl. Figure 5. Distribution of the variable “vivid imagination”



Suppl. Figure 6. Distribution of the variable “perceptual sensitivity”



Suppl. Figure 7. Distribution of the variable “intrusive thought”



Suppl. Figure 8. Distribution of the variable “auditory hallucinations”

Appendix F: Study 6

Schlier, B., Ludwig, L., Wiesjahn, M., Jung, E., & Lincoln, T. M. (submitted for publication). Fostering coping as a mechanism of symptom change in cognitive behavioural therapy for psychosis.

Fostering coping as a mechanism of symptom change in cognitive behavioural therapy for psychosis

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Abstract

Introduction: Cognitive behavioural therapy for psychosis (CBTp) has been repeatedly shown to ameliorate psychotic symptoms. However, so far we have little understanding of the mechanisms of change in CBTp. In this study, we tested whether improved *cognitive and behavioural efforts to manage taxing external or internal demands (=coping)* constitute a mechanism of change in CBTp.

Methods: We tested whether the continuous symptomatic improvement of patients (n=57) who received 45 sessions of CBTp and completed weekly self-assessments of symptoms (i.e., suspiciousness, individualised positive and negative symptoms, and individualised symptoms of depression) was mediated by preceding improvement in self-assessed coping using multilevel analysis. A reverse model in which symptom improvement predicted improved coping was also tested.

Results: Continuous improvement in some positive symptoms (suspiciousness, bizarre experiences, and hallucinations), negative symptoms, and depression over the course of CBTp was preceded by improvement of coping. Improvement in positive symptoms did not predict subsequent improvement in coping, whereas improvement in negative symptoms and depression predicted subsequent improvement in coping.

Conclusion: Coping constitutes a mechanism of change, albeit to a different extent for different symptom clusters. Further research needs to explore how best to utilise this mechanism and optimise its integration with other active ingredients of CBTp to maximise therapeutic gain.

Keywords: Cognitive behavioral therapy; therapy mechanism; working mechanisms; Coping;

Introduction

Numerous reviews and meta-analyses converge on the finding that cognitive behavioural therapy for psychosis (CBTp) results in small to medium improvements in positive symptoms (Turner et al., 2014; Wykes et al., 2008; Zimmermann et al., 2005), particularly in delusions and hallucinations (Lincoln and Peters, 2018; van der Gaag et al., 2014), in symptoms of depression and general levels of functioning (Wykes et al., 2008), and –albeit with less consistent results– in negative symptoms (Turner et al., 2014; Velthorst et al., 2014; Wykes et al., 2008). There is a wide consensus that adding CBTp to medical treatment is more effective than medical treatment alone. Despite broad agreement on the question *whether* CBTp works, the question *how* it works has remained largely unanswered. A detailed understanding of the working mechanisms of CBTp on the various symptoms of psychosis (including positive symptoms, such as delusions and hallucinations, negative symptoms, such as motivational problems and affective flattening, and symptoms of depression), however, is necessary in order to further develop and optimise treatment.

The improvement of coping is likely to constitute a common denominator and general mechanism of effect for the variety of existing CBTp-interventions. In a broad sense, coping can be understood as the "*cognitive and behavioural efforts to manage specific external and/or internal demands that are appraised [as] taxing"* (Lazarus and Folkman, 1984). Early conceptualisations of CBTp focused exclusively on coping and problem solving strategies to enable patients to deal with their symptoms (Tarrier et al., 1993). Thereafter, coping with symptoms continued to be an important element of CBTp. For example, the NICE guidelines' (NCCMH, 2014) definition of CBTp encompasses cognitive interventions to "establish links between […] thoughts, feelings or actions with respect to the current or past symptoms, and/or functioning" and to re-evaluate "perceptions, beliefs or reasoning in relation to the target symptoms" (NCCMH, 2014, p. 222). These interventions often involve enhancing functional cognitive processing of precipitant stressors that trigger symptoms (e.g., daily hassles, negative emotions). Accordingly, the NICE definition of CBTp stresses the "promotion of alternative ways of coping with the target symptom" and the "reduction of distress" in general (NCCMH, 2014, p. 222). Thus, despite their heterogeneity, CBT-interventions all

include elements to foster coping, either in the sense of effectively dealing with stressors in everyday life or by strengthening the ability to cope with psychotic symptoms including their external (e.g., everyday stressor) or internal (e.g. affective processes) antecedents or consequences.

Correspondingly, attempts to summarise the essential components of CBTp from a service user perspective include learning "to cope with ongoing unusual psychological experiences" (Byrne and Morrison, 2014). In a Delphi study, in which individuals with lived experience of psychosis were asked about their views on what defines recovery, 89% considered adaptive "coping […] with mental or emotional problems on a day to day basis" to be essential (Law and Morrison, 2014). In line with this, coping is a core component in the "CHoice of Outcome In Cbt for psychosEs" (CHOICE, Greenwood et al., 2010), a self-report assessment developed with service-users in order to assess their priority goals when evaluating therapeutic progress. Items tapping into the "behavioural (coping) [oriented aspects] (e.g., A sense of being in control of my life, ways of dealing with unpleasant feelings and emotions […])" (Greenwood et al., 2010, p. 7) show the highest loadings in factor analysis of the CHOICE, which indicates them to be the most representative of the scale's underlying construct. Finally, retrospectively reported gains in coping resources (e.g., coping with one's main problems, moods, and everyday problems) were the only significant predictors of service-users' satisfaction with CBTp (Miles et al., 2007).

However, to date no study has prospectively tested whether an improvement in coping explains the effect of individualised CBTp on symptom improvement. Using data from a therapy trial with weekly symptom assessment to map the symptomatic improvement over the progress of 45 sessions of CBTp (Lincoln et al., 2016), we tested whether the improvement in core symptoms of psychosis (positive symptoms, negative symptoms, and symptoms of depression) can be explained by preceding changes in effective coping. Specifically, we first tested whether therapy progress (i.e., the number of therapy sessions up to a given time) predicts the positive symptom (i.e., suspiciousness, paranoid delusions, hallucinations, bizarre experiences, grandiosity, and magical thinking), negative symptom (i.e., amotivation, flat affect, and social withdrawal), and depression levels at this time. Second we tested whether effects of the number of therapy sessions on current symptom levels are

mediated by preceding change in effective coping with everyday problems, symptoms, and emotions (see Figure 1). Finally, we tested for directionality of effects with a reverse model (i.e., symptom improvement predicting coping one week later, see Figure 2).

Methods

Study Design

This study was conducted with data from the first wave of an ongoing longitudinal therapy trial on CBTp (for information on the studies main outcomes, see Lincoln et al., 2016). The study was conducted in a German university-associated outpatient clinic. Participants applied for and received individualised CBTp as covered by German insurance companies following an expert review of the indication for CBTp, the individual therapy rationale and goals. For all participants included in the study, an application for 45 sessions of CBTp à 50 minutes was approved by the participants' respective health insurance company.

Inclusion criteria for the trial were (1) a diagnosis of a psychotic disorder, (2) presence of one or more positive or negative symptoms based on observer rating using the Positive and Negative Syndrome Scale (PANSS, respective symptom-rating of 3 or more; Kay et al., 1987), (3) age between 18 and 65 years, (4) sufficient German language skills, (5) no acute suicidality, (6) no substance dependency. Furthermore, to be included in the analyses for this study, participants needed to have provided at least two brief symptom assessments following two consecutive therapy sessions.

The local Ethical Committee of the Department of Psychology approved the trial. All participants or their legal guardian provided informed consent prior to participating in the study.

Participants

Out of a full sample of 58 patients, one patient was excluded due to not having taken part in any of two consecutive brief symptom assessments. Thus, a final sample of 57 patients (59.7% male; age: *M*=35.93, *SD*=12.65; years of formal education: *M*=14.05, *SD*=3.71, *range*=6-23) was analysed. Based on the Structured Clinical Interview for DSM-IV (SCID; (Wittchen et al., 1997)), 61.4% of the patients (*n*=35) received a diagnosis of schizophrenia, 31.6% (*n*=18) a diagnosis of schizoaffective disorder, 3.5% (*n*=2) a diagnosis of brief psychotic disorder, and 3.5% (*n*=2) a diagnosis of delusional

disorder. Comorbid diagnoses were present in 35.1% (*n*=20) and 19.3% (*n*=11) of the patients were currently not taking antipsychotic medication.

The participants received individualised CBTp by one of eleven study therapists (73% female). All therapists were psychologists who had received at least basic CBT training at trial outset and were enrolled in ongoing training throughout the trial as part of their post-master level clinical training. Moreover, they had received a minimum of 16 hours of specific training in CBTp. For the full duration of the trial, all therapists received regular psychosis specific group supervision as well as monthly group supervision. All therapists were trained in conducting the SCID.

Procedure

The participants received an average of 4.8 probatory sessions (i.e. pre-therapy sessions for case formulation mandatory in Germany), which included the assessment with the SCID (Wittchen et al., 1997) and the Positive And Negative Syndrome Scale (PANSS; Kay et al., 1987). Thereafter, participants received CBTp for a maximum duration of 45 sessions, which were usually held in weekly intervals. Following each session, participants completed a brief assessment of coping and symptoms, which took about 2-5 minutes.

Intervention. The individualised CBTp was delivered according to a published German-language manual (Lincoln, 2014). The manual included interventions for building rapport and facilitating engagement using a normalising approach to psychotic symptoms; gaining a detailed understanding of the individual symptom development, culminating in a case formulation based on cognitive models of psychosis; a range of established cognitive and behavioural techniques to work with distressing symptoms as well as their antecedents and consequences, including (1) changing maintaining factors with problem-solving, social-skill training, exposure, socratic questioning, and behavioural experiments, (2) modifying delusional beliefs and dysfunctional beliefs about hallucinations using cognitive interventions such as socratic questioning, reviewing the evidence for the beliefs, and behavioural experiments, and (3) cognitive interventions to modify dysfunctional beliefs about the self and others, and (4) relapse prevention. Therapists formulated individualised therapy plans from which they derived the interventions to focus on for each patient individually.

Materials & Measures

Baseline assessment. Psychotic symptoms at the start of the therapy were assessed via interview with the PANSS (Kay et al., 1987) and via self-report with the Community Assessment of Psychic Experiences (CAPE, Stefanis et al., 2002). Each of the 28 items/symptoms of the PANSS was rated on a seven-point scale by the respective therapist conducting the interview. High interrater reliability for all subscales of the PANSS (range: r=0.86 positive symptoms to r=0.77 general psychopathology) was found based on a second rating of a subsample (n=37) of video-documented PANSS-interviews. With 42 items rated on two four-point Likert-scales for frequency and distress, respectively, the CAPE assesses a range of different positive symptoms (paranoid beliefs, bizarre experiences, hallucinations, grandiosity, magical thinking), negative symptoms (amotivation, flat affect, social withdrawal), and depression. In addition to the aforementioned measures, participants also completed questionnaires on a range of putative mediators of change at baseline and after therapy session 5, 15, 25, and 45, and were invited for a second PANSS interview at the end of their therapy (see Lincoln et al., 2016).

Brief assessment after every session. The brief assessment inventory included measures of (1) the patients' abilities to cope, (2) a range of general symptoms, and (3) an individualised list of each patient's most prevalent symptoms of psychosis. All items referred to the week prior to the respective assessment.

Coping was assessed with three items derived from the CHOICE (Greenwood et al., 2010) that assessed coping with everyday problems (i.e., „I had ways of dealing with everyday life stresses"), coping with symptoms (i.e., „I had ways of dealing with distressing experiences (e.g. beliefs, thoughts, voices)"), and emotion regulation (i.e., „I had ways of dealing with unpleasant feelings and emotions (e.g. depression, worry, anger)"). Participants were asked to indicate how much each of the items applied to them for the last seven days on a ten-point scale ranging from 1="not at all" to 10="absolutely". The items showed sufficient internal consistency at the within subject (α=0.78) and between subjects level (α=0.95), so the mean score of these items was calculated.

All participants answered the item “Feeling that others are watching you or talking about you” (referred to as “suspiciousness”) from the nine item short form of the Symptom Checklist (SCL-K-9; Klaghofer and Brähler, 2001) on a five point Likert scale. Suspiciousness served as a standardised psychosis symptom assessment (i.e., presented to all patients).

Additionally, an individualised psychosis symptom assessment for each patient was devised based on the CAPE: For each patient, the ten items with the highest combined frequency and distress baseline scores were selected. Patient preference was the secondary selection step in case the item-score yielded a list of more than ten items (e.g., if the eighth to eleventh highest ranking items had the same score). For every following assessment, patients indicated how often they experienced each symptom over the last seven days on ten-point scales ranging from 1=”not at all” to 10=”all the time”. For each participant, the items selected from the positive symptom, negative symptom, and depression dimension were aggregated in three individualised mean scores.

Data analysis

To test for continuous improvement in coping (Figure 2, path c_{rev}) and symptoms (Figure 1, path c_{1-4}) over the course of therapy, we calculated multilevel regression models of assessment points nested in participants. For all models, therapy session number was entered as an independent variable and one of the variables of interest (i.e., CHOICE-coping, SCL-suspiciousness, and the CAPE positive symptom, negative symptom, and depression scores) was entered as dependent variable. Multilevel regressions were calculated in R 3.4.2 (R Core Team, 2017) using the packages lme4 (Bates et al., 2015) and lmerTest (Kuznetsova et al., 2016).

To test for the mediation (Figure 1) and reverse mediation models (Figure 2), we used structural equation modelling in MPlus (Muthén and Muthén, 2012) to calculate multilevel mediation models . In the mediation model, the number of the therapy session prior to a given time-point (t) was entered as independent variable (X), coping was entered as mediator (M), and suspiciousness as well as positive symptoms, negative symptoms, and depression were entered as dependent variables (Y_{1-4}, see Figure 1). We tested for the unconflated within subject pathways (a: X to M; b_{1-4}: M to Y_{1-4}; c'_{1-4}, X to Y_{1-4} controlled for M, Figure 1, bottom) and indirect effects of therapy session via coping on

suspiciousness (ab_1), positive symptoms (ab_2), negative symptoms (ab_3), and depression (ab_4). To test for a reverse temporal order (i.e., symptom change preceding change in coping), a separate model was calculated (see Figure 2), in which symptom scores at t served as mediators for the effect of the number of therapy sessions (t) on coping at t+1.

Additionally, where results for a CAPE symptom dimension were inconclusive, we separately explored mediation effects for individual symptoms to test whether mediation effects vary within symptom clusters. Based on previous factor-analytic results (Schlier et al., 2015), the positive symptom dimension was to be divided into a paranoia (five items), bizarre experiences (seven items), hallucinations (four items), grandiosity (two items) and magical thinking subscore (two items). The negative dimension was divided into an amotivation (seven items), flat affect (three items), and social withdrawal subscore (four items).

Results

Clinical data at trial start and compliance

At the beginning of the trial, participants had an average of *M*=14.98 (*SD*=5.39) on the PANSS positive symptom scale, *M*=16.95 (*SD*=6.26) on the PANSS negative symptom scale, and *M*=35.82 (*SD*=9.23) on the PANSS general psychopathology scale.

The full 45 sessions of therapy were completed by 36 participants. Therapist initiated discontinuation for two participants (at session 15 and 28, respectively) due to substance use problems and need for inpatient care, respectively. Further 19 participants finished treatment earlier (*n*=5) or discontinued (*n*=14; for more details, see Lincoln et al., 2016). All available data from all patients were included in the analyses. Compliance rates regarding the post-session assessments based on the total number of therapy sessions was 86.30%.

Improvements during the course of therapy

As can be seen in Table 1, there was a significant incremental improvement in coping, suspiciousness, positive symptoms, negative symptoms, and depression as therapy progressed.

Mediation effects via coping on symptom factors

Table 2 shows the direct effects (paths c'_{1-4}), individual pathways (paths a, b_{1-4}), and the indirect effects (paths ab_{1-4}) of the mediation model (Figure 1). As can be seen, the path from therapy sessions received prior to the assessment (t) to current coping levels (path a) was significant, as were the paths from coping at t to suspiciousness (path b_1), negative symptoms (path b_3), and depression (path b_4) at the next therapy sessions, t+1. Correspondingly, the indirect effects of therapy session on suspiciousness (path ab_1), negative symptoms (path ab_3), and depression (path ab_4) were significant. However, no significant mediation was found for positive symptoms.

Reversed mediation via symptoms on coping

The analyses of reversed mediation effects (Figure 2) yielded no significant reverse mediation of coping by prior changes in suspiciousness or positive symptoms. However, changes in negative symptoms and depression mediated later changes in coping over the course of therapy (see Table 3).

Mediation models of single symptoms

Exploratory mediation models of single positive symptoms yielded heterogeneous effects: For paranoia (n=40), there was a significant direct effect of the number of the therapy session (t) on symptom improvement (c'=-0.021, SE=0.008, Z=2.95 p=0.003), but no mediation. However, there were significant indirect effects via coping on hallucinations (n=11, ab=-0.009, SE=0.005, Z=-1.99, p=0.046) and bizarre experiences (n=22, ab=-0.005, SE=0.002, Z=-2.48, p=0.013; see online suppl. 1 for detailed results of the single symptom mediation analyses).

Discussion

We found improvement in coping with everyday problems, symptoms, and negative emotions over the course of therapy to be a predictor for improvement in suspiciousness and some individual positive symptoms, negative symptoms, and symptoms of depression. Furthermore, improvements in negative symptoms and in depression also predicted later improvement in coping. However, for positive symptoms we found no indication of a reverse mediation, so that the necessary conditions to assume causality (correlation and time-order; Schwartz and Susser, 2006) were fulfilled. Thus, fostering the ability to cope with everyday problems, symptoms, and negative emotions in everyday life appears to be a uni-directional mechanism of change for some positive

symptoms in CBT. This corresponds to the service users' perspective, in which coping has been highlighted as one of the most important parts of CBTp (Miles et al., 2007).

Coping and positive symptoms

The standardised assessment of positive symptoms (suspiciousness-item in the SCL-9) yielded a full mediation, whereas the individualised assessment did not, which warranted a closer inspection. When sum-scores for all five symptom groups were tested separately, we found uni-directional mediation effects for the 'experiential' positive symptoms (hallucinations and bizarre experiences), but not for the less "proto-typical" positive symptoms, such as magical thinking or grandiosity. Possibly, this is due to the small patient subgroups available for the analyses of magical thinking and grandiosity. Additionally, the small item pool (2 items, respectively) for these symptoms may have added to potentially underestimating the effects. Future studies need a more balanced symptom assessment.

A more puzzling finding pertains to the individualised assessment of paranoia: In contrast to the mediation effect for the SCL-9 item suspiciousness, there was a direct effect without mediation for the individualised paranoia score. For most patients at least one CAPE paranoia item was selected, so it is unlikely that we failed to detect a mediation effect due to a too small sample size. However, a possible explanation may be that the suspiciousness item and the five CAPE paranoia items differ substantially in item content. The majority of the CAPE paranoia items tap into more "severe" paranoid beliefs (e.g., item 6 "people are not what they seem to be" and item 7 "feeling persecuted") or even mark the "top of the hierarchy" (Freeman et al., 2005) of paranoid beliefs (i.e., item 10 "believing in a conspiracy against oneself"). One could speculate that these severe paranoid beliefs require a combination of cognitive interventions for delusions (e.g., gathering evidence; weighing benefits and costs of keeping vs. abandoning a delusional belief, etc.; Lincoln, 2014) that tap into other mechanisms of change. Suspiciousness, "feeling that others are watching you or talking about you", by comparison, can be categorised as a relatively "mild" form of paranoid beliefs (i.e., ideas of reference, Freeman et al., 2005). Possibly, "mild" forms of paranoid beliefs are more readily changed by fostering coping alone. However, such a hypothesis needs further testing, for

example by directly comparing the effects of interventions targeting different putative cognitive and emotional mechanisms of change.

Other putative mechanisms of change for positive symptoms include changes in meta-)cognitive processing, in core schemas, and in social cognition. A growing body of research shows that the reduction of reasoning biases, in particular the jumping to conclusion bias, in computerised reasoning trainings (Garety et al., 2015) and individual or group-based metacognitive therapy (Aghotor et al., 2010; Moritz et al., 2011a, 2011b) constitute a symptom specific intervention for delusions, although diverging results exist (Mehl et al., 2018). Furthermore, initial tests confirmed an association between change in self-schema and symptom improvement (e.g., Morrison et al., 2012). However, meta-analytic evidence yielded no significant effect of CBT for psychosis on the core self-schema outcome self-esteem (Jones et al., 2012). Similarly, tests for the putative mechanisms of changing theory of mind deficits (Ventura et al., 2013) and attribution biases (Garety and Freeman, 2013; Mehl et al., 2014) have put these potential mechanisms of change in question: For example, a recent reanalysis of a therapy trial shows symptomatic improvement in CBTp without co-occurring change in theory of mind or attribution biases (Mehl et al., 2018). In sum, there are varying levels of evidence for some (meta-)cognitive mechanisms of change in CBTp, but results for other putative mediators are mixed. Possibly, improvement in positive symptoms is better understood as the result of a convergence of change in cognitive factors (e.g., social cognition, core schemas) and behavioural factors (e.g. coping). Thus, future research not only has to quantify the amount of symptomatic improvement explained by different mechanisms, but also needs to explore the effects of combined approaches that target multiple mechanisms of change.

Coping and negative symptoms/depression

For negative symptoms and depression, there were more consistent indirect effects showing a time-lagged association between improvement in coping and later symptomatic improvement. The lack of a clear uni-directional temporal association for negative symptoms and depression could be interpreted as a recursive mechanism, where changes in negative affect and motivational problems affect coping resources and vice versa. One could speculate that a vicious cycle of residual

(negative/depression) symptoms and a decrease in successful coping with taxing experiences explains why higher levels of negative symptoms predict relapse (i.e., the re-emergence of positive symptoms, Bowtell et al., 2017). A clinical implication of this finding would be that optimised interventions for negative symptoms should include both, interventions that directly target negative symptoms (e.g., setting goals and increasing motivation, Velligan et al., 2015) as well as enhancing coping skills for setbacks and taxing situations.

Limitations

Our study was a non-controlled study with a moderate sample size, which was further decreased for some positive symptoms (e.g. hallucinations, grandiosity, magical thinking), which resulted in a lack of test-power for some models. Moreover, the assessment of coping was not accompanied by an assessment of the corresponding stressors that were present in the respective week. Consequently, we are unable to disentangle whether high coping-ratings stem from a change in coping resources or from a change in environmental demands. Finally, we did not assess the specific coping strategies used by patients, so there is a chance that patients based their coping rating on both functional and dysfunctional strategies, leading to an underestimation of the link between (functional) coping and symptom improvement.

Conclusion

Adaptive coping constitutes a uni-directional mechanism of change for some positive symptoms and is intertwined with changes in negative symptoms and depression. This opens up the question of the magnitude of this effect in comparison to other putative mechanisms of change, including those specific to CBTp and general predictors of therapeutic success (e.g. the therapeutic alliance, Jung et al., 2014) Further exploration of the differential mechanisms of change for different symptoms is needed, so we can optimise interventions to instigate the changes in behaviour and cognition that are crucial for recovery and increase the efficacy of CBTp.

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Legend of Figures

Figure 1. Mediation model of ongoing therapy session number predicting symptom change via coping

Figure 2. Reverse mediation model of ongoing therapy session number predicting coping via symptom change

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Conflict of interest

None.

Contributors

BS analyzed the data and wrote the first draft of the manuscript. BS and LL conceptualized the re-analysis. MW and EJ collected the data. TML supervised all steps and contributed to interpreting and discussing the results. All authors edited and contributed to the manuscript and have approved of the final version.

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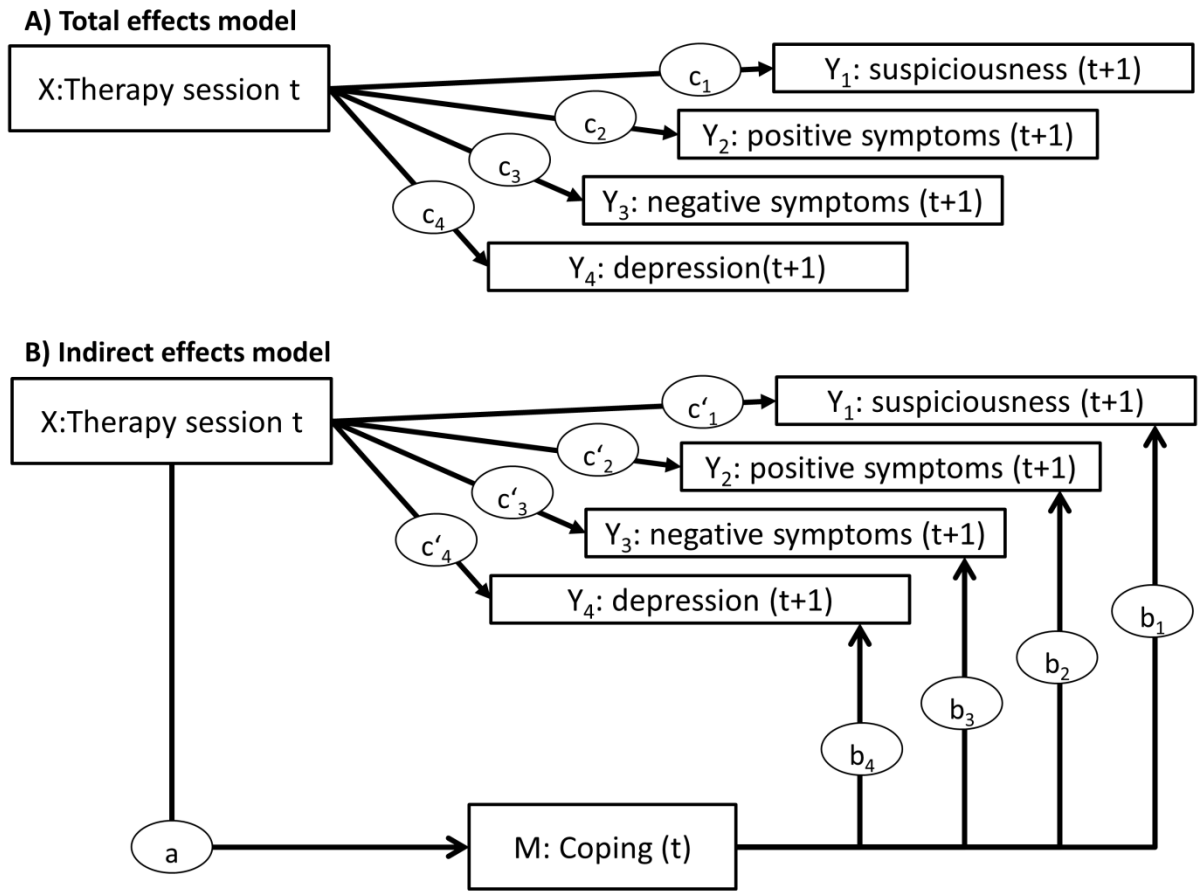


Figure 1. Mediation model of ongoing therapy session number predicting symptom change via coping

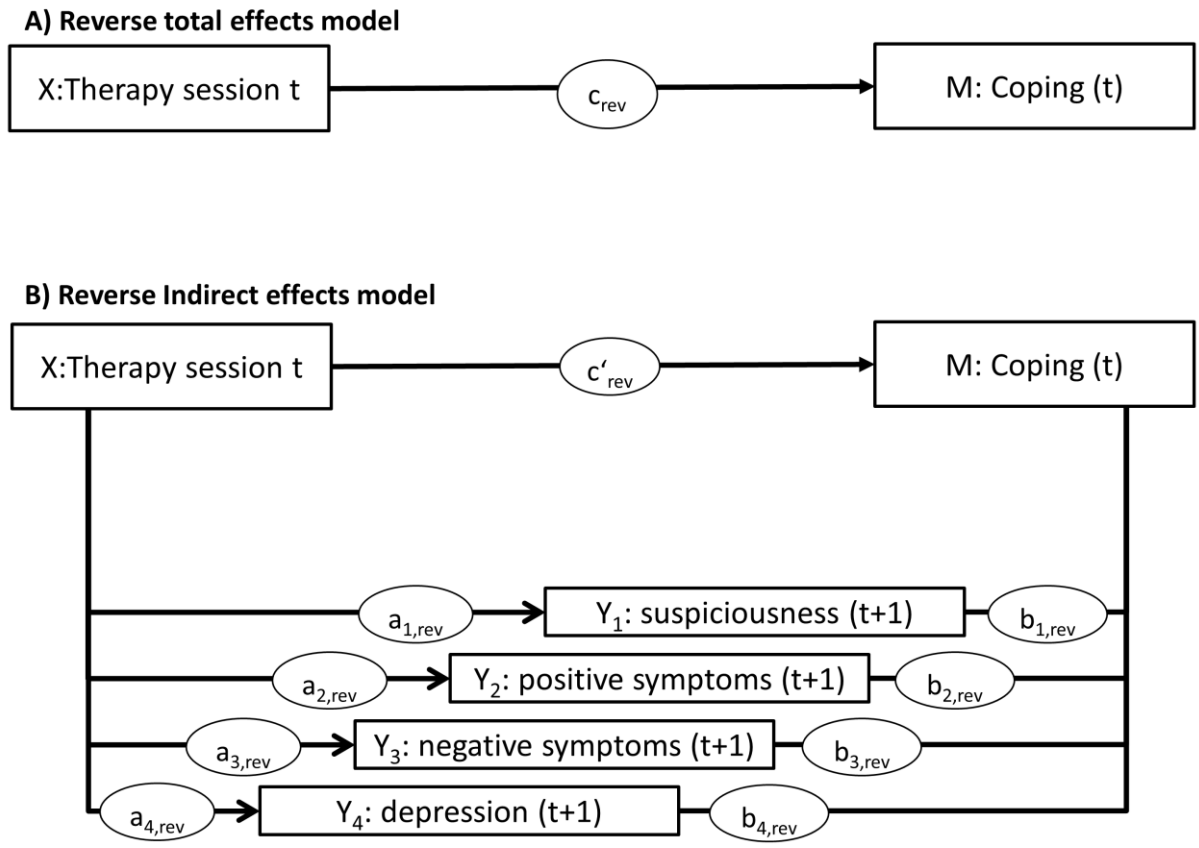


Figure 2. Reverse mediation model of ongoing therapy session number predicting coping via symptom change

Table 1.

Multilevel regression models of therapy sessions nested in participants. Effects of therapy session no. (range 1-45) on coping and symptom factors.

Dependent variable	n	k	Estimate	SE	T	p
Coping	57	1543	0.026***	0.003	9.13	<0.001
Suspiciousness (SCL)	57	1544	-0.004*	0.002	-2.42	0.016
Positive symptoms (CAPE)	47	1306	-0.010**	0.003	-3.14	0.002
Negative symptoms (CAPE)	57	1547	-0.037**	0.003	-12.03	<0.001
Depression (CAPE)	54	1448	-0.022***	0.003	-6.23	<0.001

Note. n= participants included in the respective analysis; k= assessment points included in the respective analysis; SE= standard error; SCL=Symptom Checklist; CAPE= Community Assessment of Psychic Experiences,

* p<0.05; ** p<0.01; *** p<0.001

Table 2.

Estimates for the multilevel structural equation model of therapy session (independent variable X) predicting later symptom change at t+1 (dependent variables Y_i) via coping at t (mediator M).

		Path coefficient				Indirect effect			
Outcome variable	Predictor	name	estimate	SE	Z	name	estimate	SE	Z
coping	Session no. t	path a	0.026***	0.006	4.15	-	-	-	-
suspiciousness [1]	Coping	path b_1	-0.049*	0.021	-2.29	ab_1	-0.001**	<0.001	-2.87
	Session no. t	path c'_1	-0.002	0.004	-0.66				
positive symptoms[2]	Coping	path b_2	-0.073	0.061	-1.18	ab_2	-0.002	0.001	-1.29
	Session no. t	path c'_2	-0.011	0.009	-1.22				
negative symptoms[2]	Coping	path b_3	-0.201***	0.061	-3.29	ab_3	-0.005**	0.002	-3.00
	Session no. t	path c'_3	-0.030***	0.009	-3.46				
symptoms of depression[2]	Coping	path b_4	-0.190***	0.058	-3.30	ab_4	-0.005**	0.002	-2.65
	Session no. t	path c'_4	-0.016*	0.008	-2.11				

Note. All estimates at within level. [1] Assessment based on Symptom Checklist 9 item paranoia; [2] assessment based on individual selection of items from the respective Community Assessment of Psychic Experiences (CAPE) dimension; 95% confidence interval; p<0.10 ; * p<0.05; ** p<0.01; *** p<0.001

Table 3.

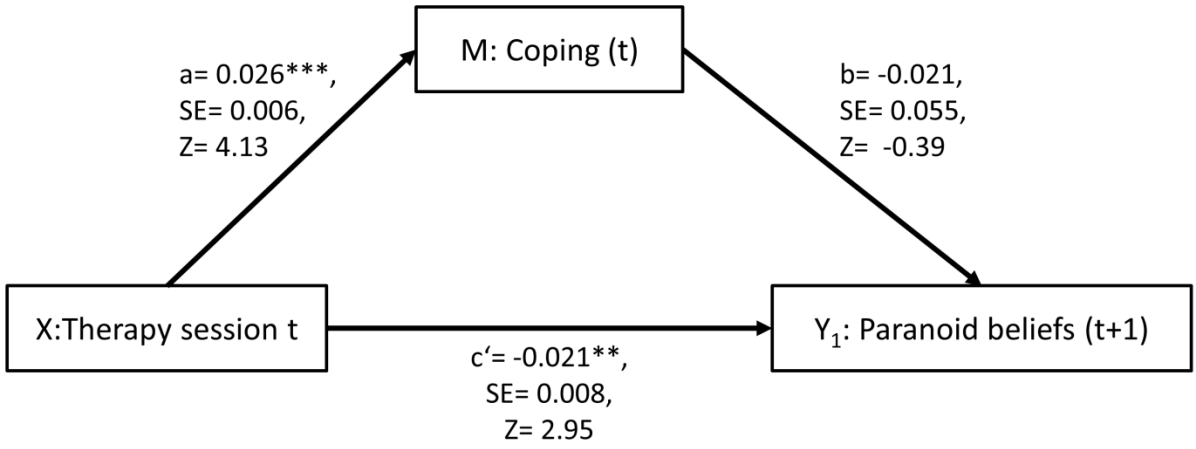
Estimates for the reverse multilevel structural equation model of therapy session predicting later change in coping at timepoint t+1 via symptom i at timepoint t.

			Path coefficient			Corresponding indirect effect			
Outcome variable	Predictor	name	estimate	SE	Z	name	estimate	SE	Z
Suspiciousness[1]	Session no. t	path $a_{1,rev}$	-0.002	0.004	-0.57	$a_1b_{1,rev}$	0.000	<0.001	-0.33
Coping	Suspiciousness[1]	path $b_{1,rev}$	0.020	0.043	0.46				
positive symptoms[2]	Session no. t	path $a_{2,rev}$	-0.010	0.009	-1.14	$a_2b_{2,rev}$	0.000	<0.001	0.17
Coping	positive symptoms[2]	path $b_{2,rev}$	-0.008	0.045	-0.17				
negative symptoms[2]	Session no. t	path $a_{3,rev}$	-0.037***	0.009	-4.21	$a_3b_{3,rev}$	0.003*	0.001	2.45
Coping	negative symptoms[2]	path $b_{3,rev}$	-0.090**	0.032	-2.85				
symptoms of depression[2]	Session no. t	path $a_{4,ev}$	-0.021*	0.008	-2.47	$a_4b_{4,rev}$	0.003*	0.001	2.18
Coping	symptoms of depression[2]	path $b_{4,rev}$	-0.156***	0.029	-5.43				
Coping	Session no. t	path c_{rev}	0.017**	0.006	3.09	-	-	-	-

Note. All estimates at within level. [1] Assessment based on Symptom Checklist 9 item paranoia; [2] assessment based on individual selection of items from the respective Community Assessment of Psychic Experiences (CAPE) dimension; * p<0.05; ** p<0.01; *** p<0.001

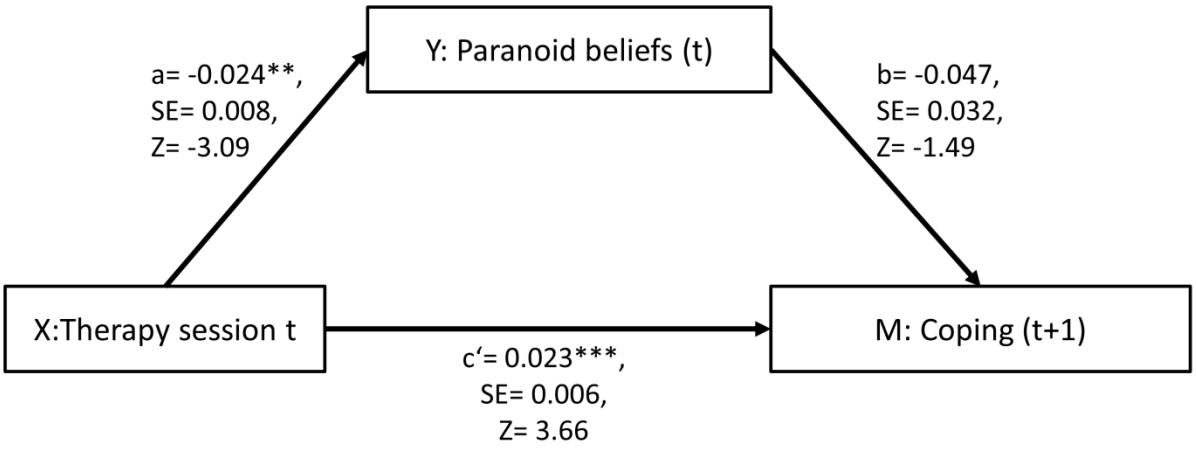
1.1 - Positive symptoms: Paranoia

Mediation model:



Indirect effect ab= -0.001, SE= 0.001, Z= -0.39

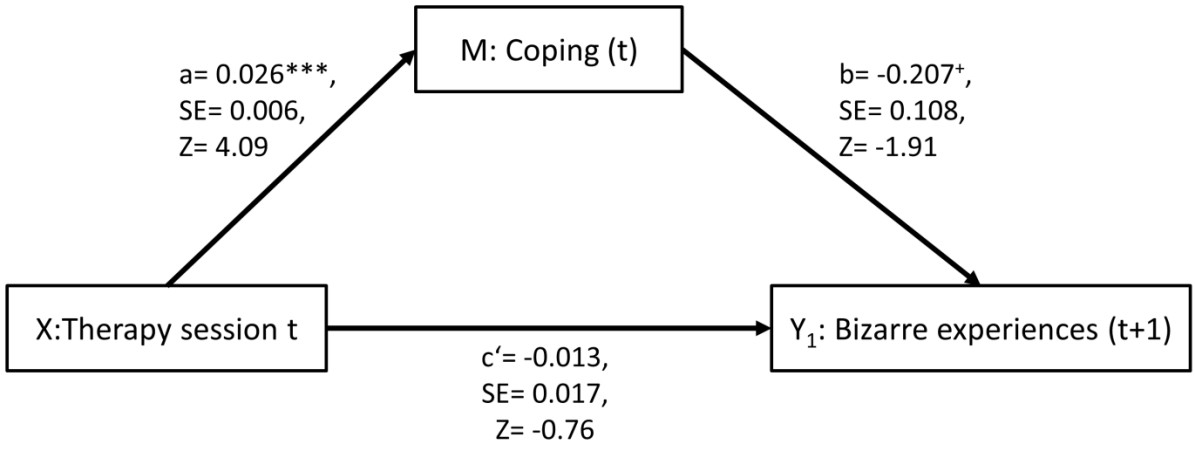
Reverse Mediation model:



Indirect effect ab= 0.001, SE= 0.001, Z= 1.22

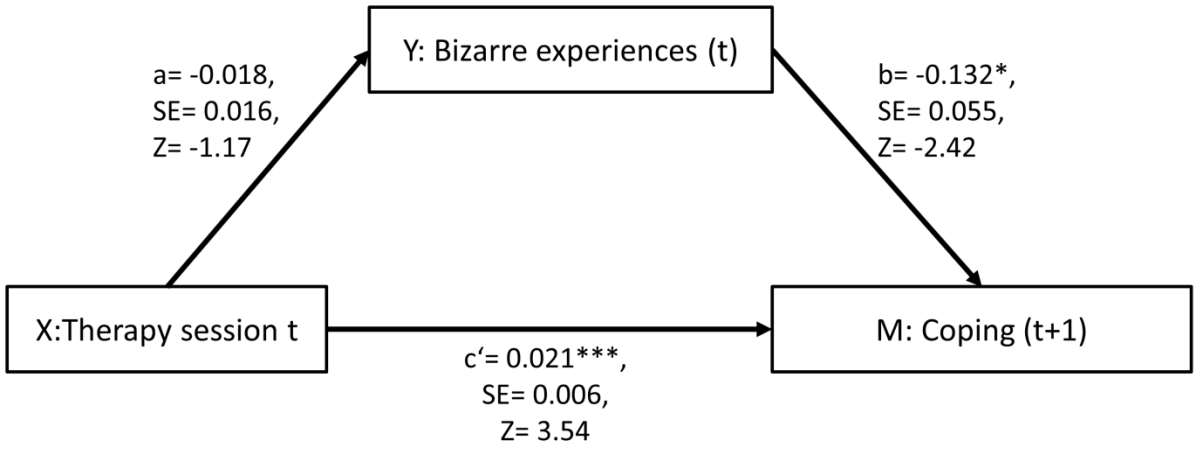
1.2 - Positive symptoms: Bizarre experiences

Mediation model:



Indirect effect ab= -0.005*, SE= 0.002, Z= -2.48

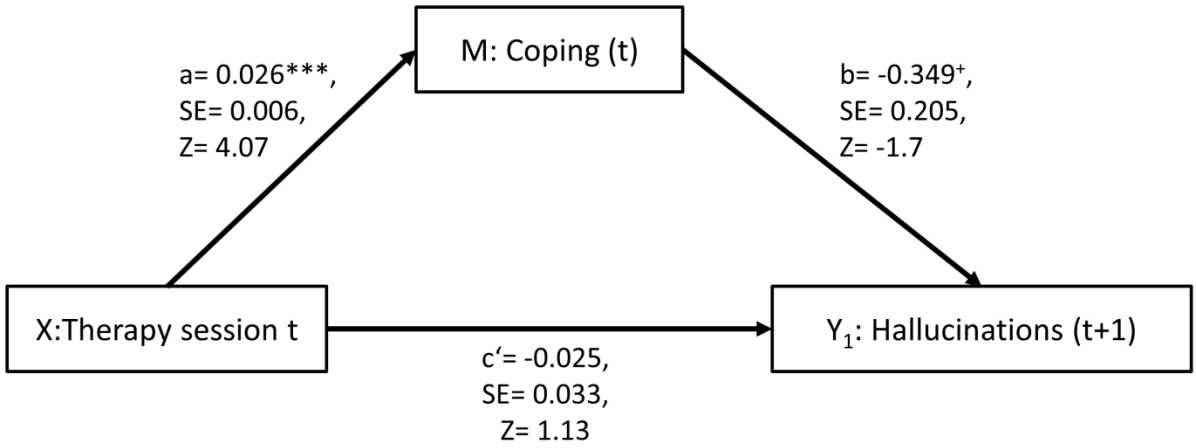
Reverse Mediation model:



Indirect effect ab= 0.002, SE= 0.002, Z= 1.32

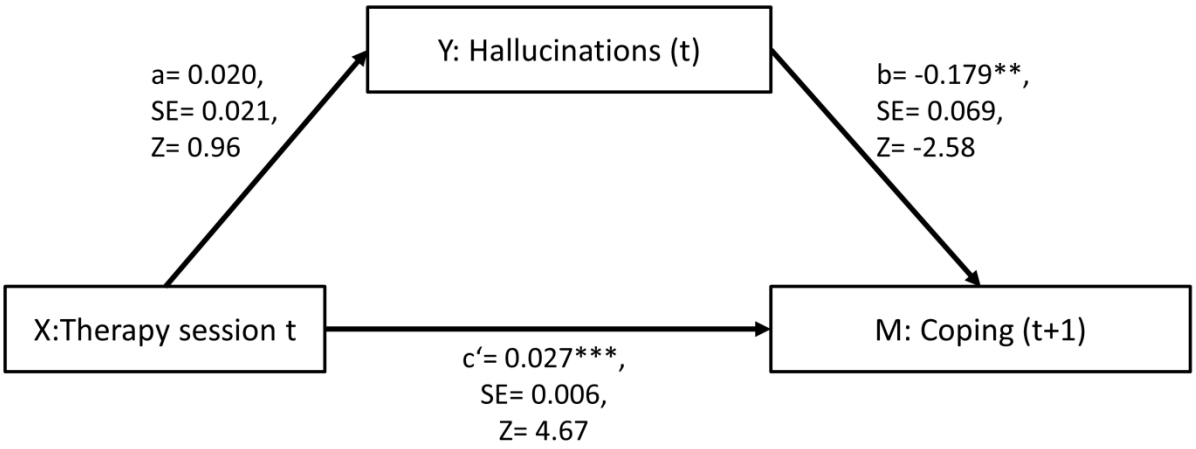
1.3 - Positive symptoms: Hallucinations

Mediation model:



Indirect effect ab= -0.009*, SE= 0.005, Z= -1.99

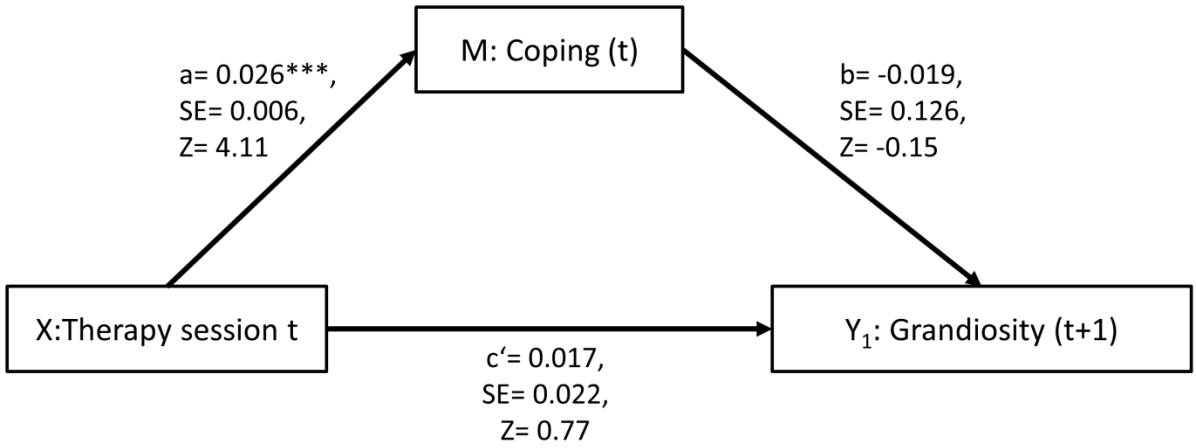
Reverse Mediation model:



Indirect effect ab= -0.004, SE= 0.005, Z= -0.76

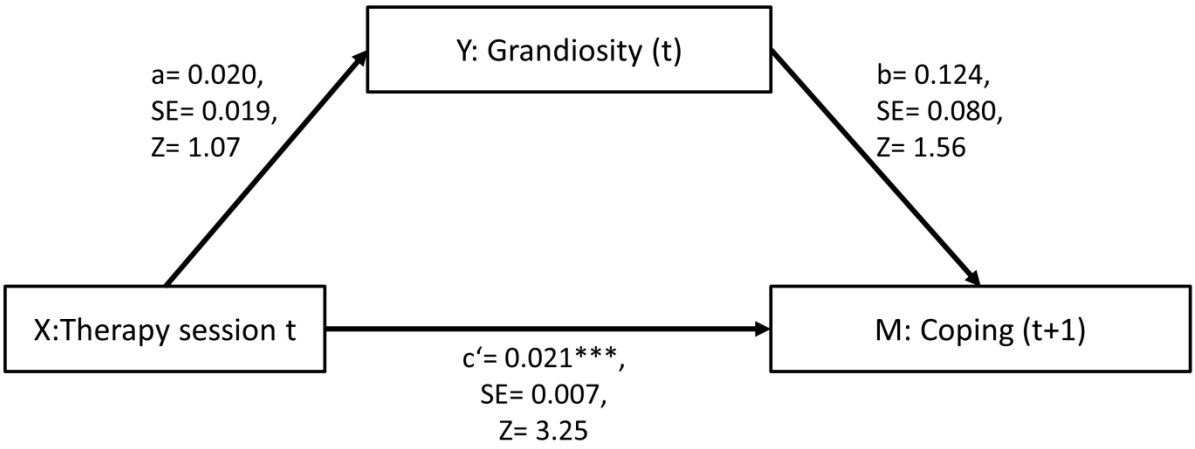
1.4 - Positive symptoms: Grandiosity

Mediation model:



Indirect effect ab= -0.000, SE= 0.003, Z= -0.15

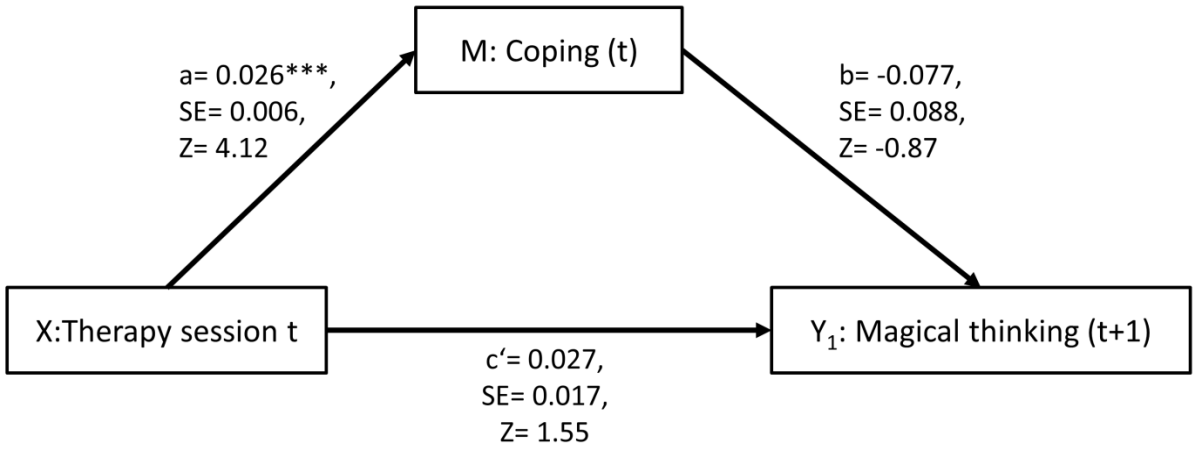
Reverse Mediation model:



Indirect effect ab= -0.003, SE= 0.002, Z= 1.36

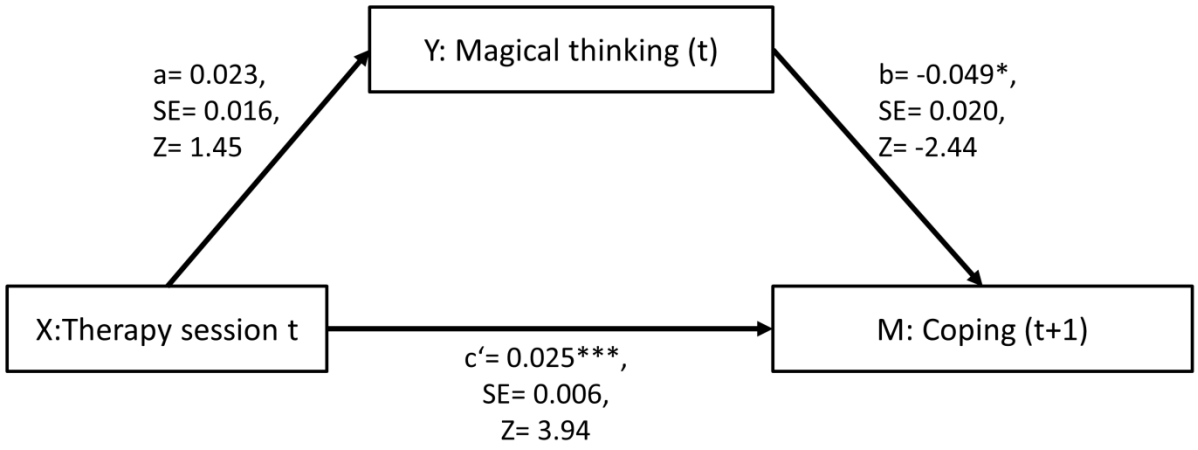
1.5 - Positive symptoms: Magical Thinking

Mediation model:



Indirect effect ab= -0.002, SE= 0.002, Z= -0.96

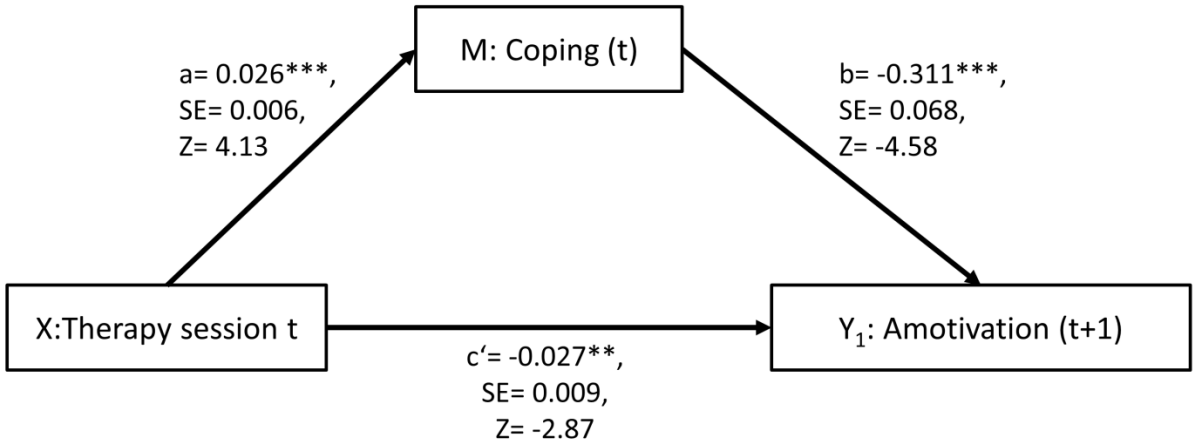
Reverse Mediation model:



Indirect effect ab= -0.001**, SE= <0.001, Z= -2.62

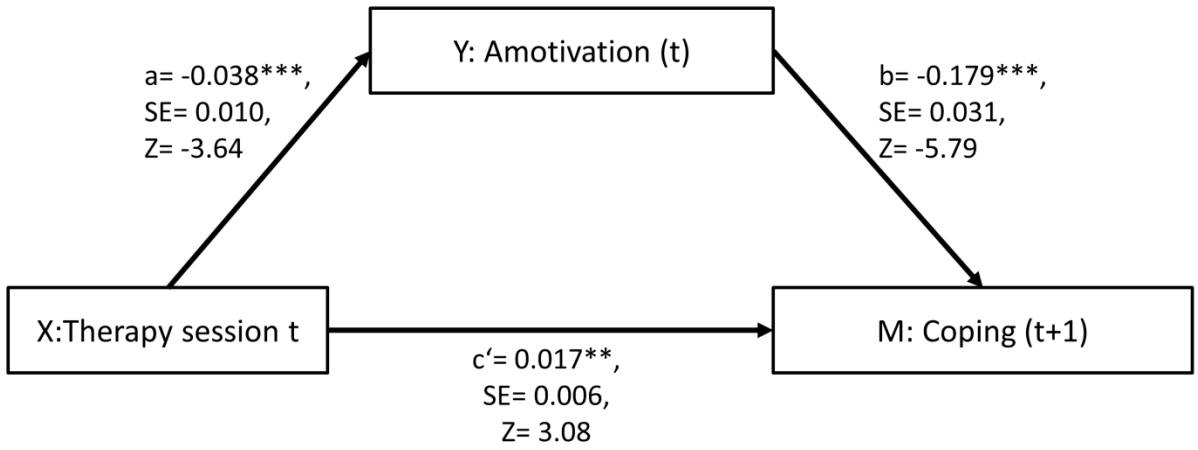
2.1 – Negative symptoms: Amotivation

Mediation model:



Indirect effect ab= -0.008***, SE= 0.002, Z= -3.50

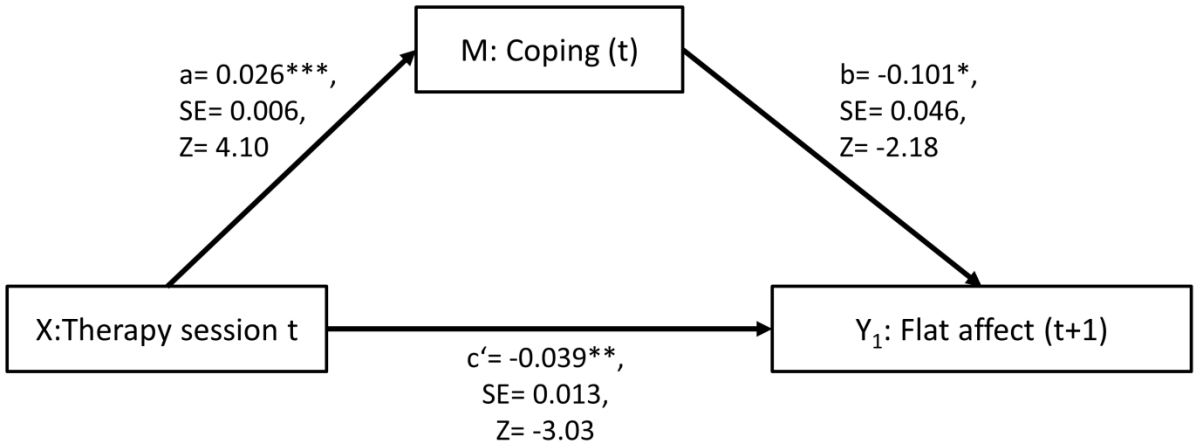
Reverse Mediation model:



Indirect effect ab= 0.007**, SE= 0.002, Z= 3.01

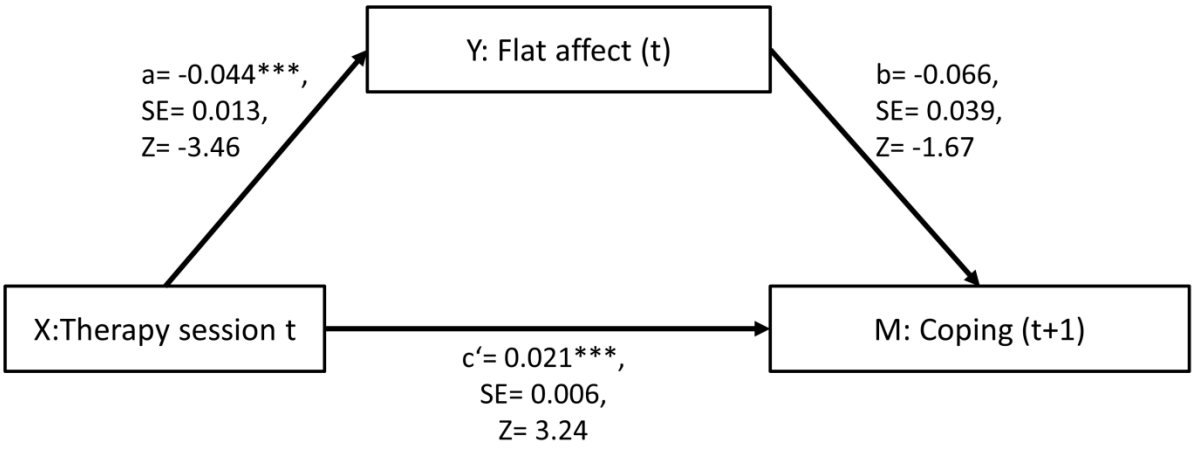
2.2 - Negative symptoms: Flat affect

Mediation model:



Indirect effect ab= -0.003, SE= 0.001, Z= -1.93

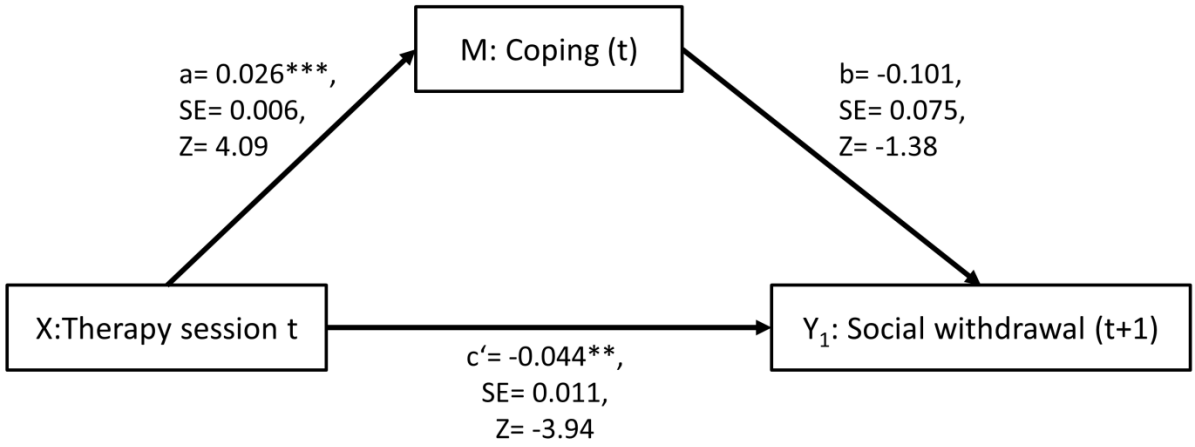
Reverse Mediation model:



Indirect effect ab= 0.003, SE= 0.002, Z= 1.54

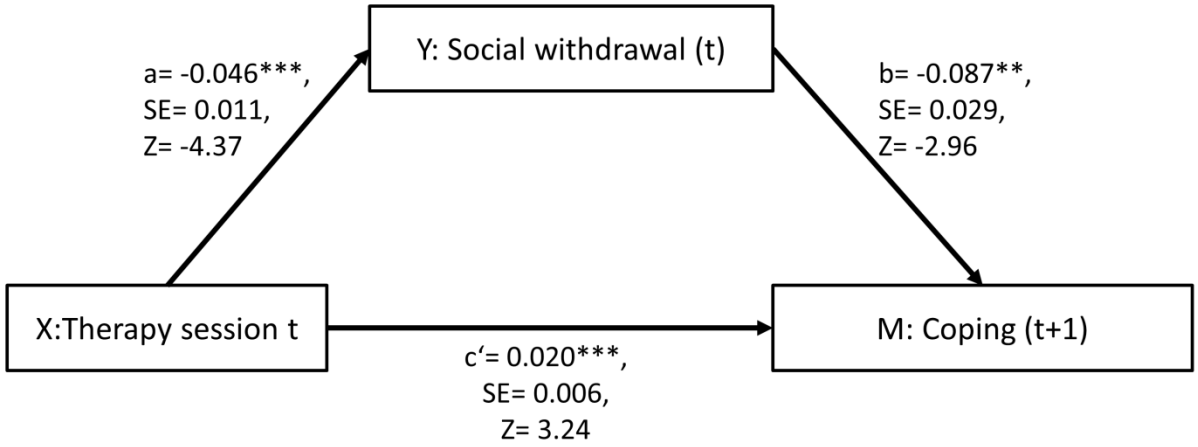
2.3 - Negative symptoms: Social withdrawal

Mediation model:



Indirect effect ab= -0.003, SE= 0.002, Z= -1.32

Reverse Mediation model:



Indirect effect ab= 0.004*, SE= 0.002, Z= 2.33