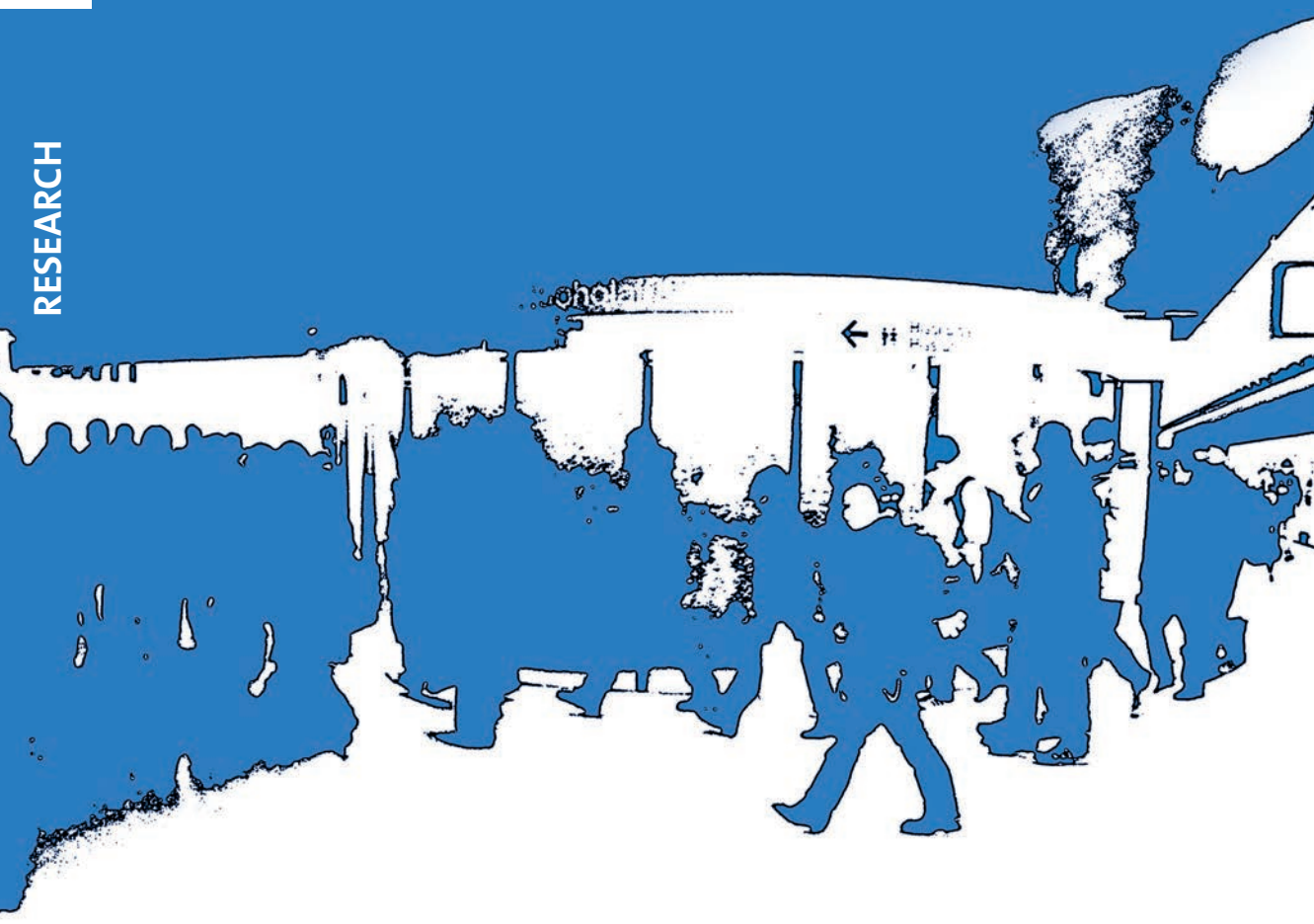
NATIONAL INSTITUTE FOR HEALTH AND WELFARE

Sebastian Therman

Mapping the uncanny

Assessing dimensions of psychotic-like experiences for clinical utility

RESEARCH



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RESEARCH 139 • 2014

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ACADEMIC DISSERTATION

To be publicly discussed, by due permission
of the Faculty of Behavioural Sciences
at the University of Helsinki in Auditorium 1
of Psychologicum, Siltavuorenpenger 1 A,
on the 14th of November, 2014, at 12 o'clock.

National Institute for Health and Welfare
Department of Mental Health and Substance Abuse Services
and
University of Helsinki
Institute of Behavioural Sciences

Helsinki 2014

NATIONAL INSTITUTE
FOR HEALTH AND WELFARE

Cover photo: Kirsikka Hynönen

ISBN 978-952-302-322-2 (printed)
ISSN 1798-0054 (printed)
ISBN 978-952-302-323-9 (online publication)
ISSN 1798-0062 (online publication)
http://urn.fi/URN:ISBN:978-952-302-323-9

Juvenes Print – Finnish University Print Ltd
Tampere, Finland 2014

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Stages of exacerbation and remission, with their varieties, may likewise be distinguished in psychopathies. In particular, the so-called precursory stage is for the most part clearly indicated, partly by a general, more or less striking, change in the personality of the individual […], and partly by the above-mentioned states of transition […]. Disturbed sleep, terrifying dreams, prolonged sleeplessness, confusion in the head, headache, sometimes alone, sometimes together with the above-mentioned states of transition; that is with diminutions of the cœnæsthesis, and of the perceptions of the senses (illusions, hallucinations, &c.), in manifold alternations or combinations, characterise this stage. Where it is totally wanting, this is owing to the rapidity and violence with which causes of insanity act. The supposition of Guislain, and of that excellent observer and close thinker Zeller, that every disorder of the mind is preceded by a stage of despondency, more or less decided, contains an *aperçu*, but needs a more accurate and restricted confirmation.

Ernst von Feuchtersleben:
Lehrbuch der ärztlichen Seelenkunde (1845).

English translation by H. Evans Lloyd:
The Principles of Medical Psychology (1847).

Abstract

Sebastian Therman, Mapping the uncanny: Assessing dimensions of psychotic-like experiences for clinical utility. National Institute for Health and Welfare. Research 139. 89 pages. Helsinki, Finland 2014.
ISBN 978-952-302-322-2 (printed); ISBN 978-952-302-323-9 (online publication)

Psychotic diseases are a great burden to both the affected individuals and society at large. Though psychoses are severe mental disorders, similar phenomena appear outside of the diagnosable disorders as psychotic or psychotic-like experiences (PLEs). The PLEs are on a continuum of liability and symptom expression in the population, from the healthy to the pathological, and the diagnosed disorders constitute the extreme of the distribution, rather than a clearly delineated class. Studying the psychosis continuum offers a way of understanding the underlying causes shared across the entire range. The frequent presence of PLEs before the first psychotic episode also helps in identifying a trajectory towards disease. However, the specific PLEs associated with increased psychosis risk or incipient disease require further elucidation. Though experiences similar to the "positive" symptoms of psychosis – primarily hallucinations and delusions – have been nominated as the most predictive of psychosis, these are broad categories that may contain subdivisions of varying levels of shared aetiology with psychotic disease, and varying predictive value.

In this thesis, the latent dimensions of self-reported PLEs were explored in one sample of 6,611 adolescents and one sample of 31,822 adults from the general population (Studies I & II), as well as in one sample of 71 and one sample of 731 adolescents in psychiatric care (Studies III & IV). Three different PLE questionnaires were employed in the separate studies: the PROD-screen, the 92-item version of the Prodromal Questionnaire, and the positive items of the Community Assessment of Psychic Experiences. The clinical significance of the identified dimensions was studied via their associations with general mental health, cognitive performance, and their predictive value with respect to psychiatric hospitalization in general or for psychosis specifically.

Overall, the results showed a general PLE structure of positive, negative, and disorganized dimensions similar to that of symptoms in non-affective psychotic disorders. The positive dimension further subdivided into dimensions of persecutory ideation, other delusions, and hallucinations – and, in one study, depersonalization experiences. These dimensions were correlated with general psychiatric health, as assessed by lifetime depression and anxiety. In contrast, questionnaire items intended to address hypomanic, grandiose, or magical thinking appeared unrelated to psychiatric health. In a smaller sample of adolescents in psychiatric care, the

positive, disorganized, and negative dimensions were not associated with cognitive performance, contrary to expectation. However, in a larger sample, especially functional disorganization, that is, impaired role functioning, was associated with later psychiatric hospitalization in general, while the depersonalization experiences dimension was the best predictor of hospitalization with a diagnosis of psychosis.

The identified latent dimensions of psychotic-like experiences demonstrate the structural validity of the PLE questionnaires, while the concurrent clinical correlates and predictive value establish criterion validity. In particular, the finding of the empirically derived depersonalization dimension being specifically predictive of psychosis merits attempts at replication. Modern psychometric methods used in the present thesis improve the utility of PLE related rating scales. In future studies a more fine-grained approach to assessing PLEs is recommended, in order to improve the accuracy of psychosis prediction and our understanding of the psychosis continuum.

Keywords: psychosis, psychotic-like, schizotypy, psychosis-proneness, questionnaire, psychometrics, latent model, factor analysis

Tiivistelmä

Sebastian Therman, Mapping the uncanny: Assessing dimensions of psychotic-like experiences for clinical utility [Käsittämätöntä kartoittamassa: psykoottisenkaltaisten kokemusten ulottuvuudet ja niiden kliininen hyöty]. Terveyden ja hyvinvoinnin laitos. Tutkimus 139. 89 sivua. Helsinki 2014.
ISBN 978-952-302-322-2 (painettu); ISBN 978-952-302-323-9 (verkkojulkaisu)

Psykoottiset häiriöt ovat merkittävä ongelma niin yksilölle kuin yhteiskunnalle. Vaikka psykoosit ovat vakavia mielenterveysongelmia, vastaavia kokemuksia ja oireita ilmenee myös diagnosoitavien häiriöiden ulkopuolella psykoottisina tai psykoottisenkaltaisina kokemuksina. Nämä kokemukset muodostavat väestössä jatkumon, jossa diagnosoidut häiriöt ovat jakauman toinen ääripää pikemminkin kuin selvästi rajattavissa oleva ilmiöluokka. Psykoosijatkumoa tutkimalla voidaan selvittää koko jatkumolle yhteisiä selittäviä tekijöitä. Lisäksi psykoottisenkaltaiset kokemukset edeltävät usein ensimmäistä psykoottista sairastumista, joten niiden tutkiminen auttaa tunnistamaan sairauteen johtavia kehityskaaria. Vielä on kuitenkin epäselvää, mitkä tietyt psykoottisenkaltaiset kokemukset ovat yhteydessä kohonneeseen psykoosiriskiin tai alkavaan sairauteen. Aikaisempien tutkimusten perusteella psykoosien ”positiivisia” oireita eli lähinnä harha-aistimuksia ja harhaluuloja muistuttavat kokemukset ennustavat parhaiten psykoosiin sairastumista. Positiivisten oireiden kaltaiset kokemukset on kuitenkin laaja ilmiöluokka, johon kuuluu useita alaluokkia. Niillä kaikilla ei välttämättä ole yhteyttä psykoottisiin häiriöihin eikä niistä ole hyötyä psykoosiin sairastumisen ennustamisessa.

Tässä väitöskirjassa tutkittiin itsearviointikyselyillä psykoottisenkaltaisia kokemuksia ja niiden ulottuvuuksia 6611 nuoren ja 31822 aikuisen aineistoissa (osatutkimukset I & II) sekä 71 ja 731 psykiatrisessa hoidossa olevan nuoren aineistoissa (osatutkimukset III & IV). Osatutkimuksissa käytettiin kolmea eri kyselymenetelmää: PROD-screen, Prodromal Questionnaire (92 kysymyksen versio), sekä Community Assessment of Psychic Experiences (vain positiiviset oireet). Eri ulottuvuuksien kliinistä merkitystä arvioitiin selvittämällä niiden yhteyttä yleiseen psyykkiseen hyvinvointiin, kognitiiviseen suoriutumiseen sekä myöhempään psykiatriseen sairaalahoitoon psykoosin vuoksi tai yleensä.

Kaiken kaikkiaan tulokset osoittivat, että psykoottisenkaltaiset kokemukset käsittävät samat kolme ulottuvuutta kuin ei-affektiivisten psykoosien oireet: positiivinen, negatiivinen ja hajanaisuusulottuvuus. Positiivinen ulottuvuus jakautui edelleen alaluokkiin vainoamisajatukset, muut harhaluulot ja hallusinaatiot – sekä yhdessä tutkimuksessa depersonalisaatiokokemukset. Nämä ulottuvuudet olivat yhteydessä masennukseen ja yleistyneeseen ahdistuneisuuteen. Sen sijaan

kysymykset, joilla arvioitiin hypomaanista, grandioottista tai maagista ajattelua eivät olleet yhteydessä mielenterveyteen. Vastoin oletuksia, psykiatrisessa hoidossa olevien nuorten suppeammassa aineistossa ulottuvuudet positiiviset, negatiiviset tai hajanaiset psykoottisenkaltaiset kokemukset eivät olleet yhteydessä kognitiiviseen suoriutumiseen. Sen sijaan laajemmassa aineistossa varsinkin toiminnallinen hajanaisuus ennusti myöhempää psykiatrista sairaalahoitoa yleensä, kun taas depersonalisaatioulottuvuus oli paras ennustaja kun sairaalahoitoon liittyi psykoosidiagnoosi.

Tutkimus tuo esiin, että psykoottisenkaltaisten kokemusten taustalla on useita eri ulottuvuuksia ja käytetyillä kyselylomakkeilla on sekä hyvä rakennevaliditeetti että hyvä kriteerivaliditeetti ennustettaessa myöhempää sairaalahoitoa. Erityisen kiinnostava ja toistotutkimuksen ansaitseva tulos oli uusi löydös, jonka mukaan depersonalisaatioulottuvuus ennustaa psykoosiin sairastumista. Tässä väitöskirjassa käytetyt modernit psykometriset menetelmät parantavat siis kyselylomakkeiden käyttöarvoa kun tutkitaan psykoottisenkaltaisia kokemuksia. Myös tulevissa tutkimuksissa psykoottisenkaltaisia kokemuksia tulisi tarkastella tällaisella hienojakoisemmalla lähestymistavalla, jotta saisimme tarkempaa tietoa psykoosijatkumon luonteesta ja psykoosiin sairastumisen ennustamistarkkuus paranisi.

Avainsanat: psykoosi, psykoottisenkaltainen, skitsotypia, psykoosialttius, kysely, psykometriikka, latentti malli, faktorianalyysi

Sammandrag

Sebastian Therman, Mapping the uncanny: Assessing dimensions of psychotic-like experiences for clinical utility [Att kartlägga det kusliga: dimensioner av psykoslikande upplevelser och deras kliniska nytta]. Institutet för hälsa och välfärd. Forskning 139. 89 sidor. Helsingfors, Finland 2014.
ISBN 978-952-302-322-2 (tryckt); ISBN 978-952-302-323-9 (nätpublikation)

Psykossjukdomar medför en stor belastning både för individen och för samhället. Trots att de är allvarliga mentala störningar, påträffas liknande fenomen utanför de diagnoserbara störningarna i form av psykotiska eller psykosliknande upplevelser. Dessa upplevelser bildar ett kontinuum av utsatthet och symtom, från det friska till det patologiska, istället för en klart avgränsad kategori. Forskning kring psykoskontinuet ger en bättre förståelse av de underliggande orsakerna som är gemensamma över hela skalan. Eftersom psykosliknande upplevelser ofta föregår den första psykotiska episoden är det också möjligt att identifiera sjukdomen innan den är fullt utvecklad. Det är dock fortfarande oklart vilka specifika psykosliknande upplevelser som har samband med förhöjd psykosrisk eller en begynnande psykossjukdom. De upplevelser som främst liknar de ”positiva” psykossymtomen, dvs. hallucinationer och vanföreställningar, anses bäst förebåda ett insjuknande i psykos. Dessa positiva symtom utgör dock breda kategorier som kan innehålla undergrupper av upplevelser med varierande etiologisk koppling till psykossjukdomar.

I denna avhandling undersöktes de latenta dimensionerna av självrapporterade psykosliknande upplevelser i en grupp på 6611 ungdomar och en grupp på 31822 vuxna ur den allmänna befolkningen (delstudier I & II), och i grupper på 71 och 731 ungdomar som vårdas inom psykiatrisk vård (delstudier III & IV). Tre olika frågeformulär för psykosliknande upplevelser utnyttjades i de olika studierna: PROD-screen, Prodromal Questionnaire med 92 frågor och Community Assessment of Psychic Experiences (endast de positiva symtomen). De identifierade dimensionernas kliniska betydelse undersöktes via deras samband med allmän psykisk hälsa, kognitiv prestanda och deras prediktiva värde med avseende på psykiatrisk sjukhusvård i allmänhet eller med psykosdiagnos.

Resultatet visar att de psykoslikande upplevelserna har en struktur med positiva, negativa och desorganiserade dimensioner i likhet med symtomen på icke-affektiva psykoser. Den positiva dimensionen indelades ytterligare i relaterade dimensioner av förföljelsetankar, andra vanföreställningar och hallucinationer – och i en delstudie även i depersonalisationsupplevelser. Dessa dimensioner uppvisade samband med depression och generaliserat ångestsyndrom. De frågor som gällde hypomani, grandiositet och magiskt tänkande hade ingen koppling till psykisk hälsa. I motsats till förväntningarna hade varken den positiva, negativa eller desorganiserade

dimensionen samband med kognitiv prestanda i den mindre gruppen unga som vårdats inom psykiatrisk vård. Däremot hade framför allt funktionell desorganisation, dvs. sänkt prestationsförmåga i vardagliga roller, samband med senare psykiatrisk sjukhusvård i allmänhet, medan dimensionen depersonalisationsupplevelser bäst förutspådde sjukhusvård för psykos.

De identifierade latenta dimensionerna av psykosliknande upplevelser påvisar frågeformulärens strukturella validitet, och de samtida kliniska korrelaten bekräftar deras kriterievaliditet. Framför allt är den nya observationen om att den empiriskt härledda depersonalisationsdimensionen förutsäger psykossjukdomar ett resultat som är värt att undersöka vidare. De moderna psykometriska metoder som använts i avhandlingen förbättrar användbarheten av frågeformulären för psykosliknande upplevelser. En mer detaljerad metodologi är också att rekommendera i framtida studier om psykosliknande upplevelser, både för att öka precisionen i att förutsäga insjuknande i psykos och för att få ny kunskap om psykoskontinuet.

Nyckelord: psykos, psykosliknande, schizotypi, psykosbenägenhet, frågeformulär, psykometrik, latenta modeller, faktoranalys

Contents

List of original papers

I Therman S, Heinimaa M, Miettunen J, Joukamaa M, Moilanen I, Mäki P, Veijola J (2011). Symptoms associated with psychosis risk in an adolescent birth cohort: improving questionnaire utility with a multidimensional approach. *Early Intervention in Psychiatry* 5(4):343-8. doi: 10.1111/j.1751-7893.2011.00290.x

II Therman S, Suvisaari J, Hultman CM. (2014). Dimensions of psychotic experiences among women in the general population. *International Journal of Methods in Psychiatry Research* 23(1):62–68. doi: 10.1002/mpr.1427

III Therman S, Suvisaari J, Kalska H, Huttunen MO, Manninen M, Cannon TD (2009). Lack of association between neuropsychological performance and level of psychosis-proneness in an adolescent psychiatric sample. *The Journal of Nervous and Mental Disease* 197(9):669-74. doi: 10.1097/NMD.0b013e3181b3b152

IV Therman S, Lindgren M, Manninen M, Loewy RL, Huttunen MO, Cannon TD, Suvisaari J (2014). Predicting psychosis and psychiatric hospital care among adolescent psychiatric patients with the Prodromal Questionnaire. *Schizophrenia Research* 158(1-3):7-10. doi: 10.1016/j.schres.2014.06.031

Abbreviations

AIC	Akaike information criterion
APS	Attenuated psychotic symptoms [syndrome]
BIC	Bayesian information criterion, a.k.a. Schwarz criterion
CAPE	Community Assessment of Psychic Experiences; questionnaire for screening of psychotic-like experiences
CFA	Confirmatory factor analysis
CFI	Comparative fit index
CHR	Clinical high risk [for psychosis]
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, 5th Ed.
FIFA	Full-information factor analysis
GAD	Generalized Anxiety Disorder
HPS	Helsinki Prodromal Study
ICD-10	International Classification of Diseases, 10th revision
IRT	Item response theory
MDE	Major Depressive Episode
MIRT	Multivariate item response theory
NFBC86	Northern Finland 1986 Birth Cohort Study
PLE	Psychotic-like experience
PQ	Prodromal Questionnaire
RMSEA	Root mean square error of approximation
SPQ	Schizotypal Personality Questionnaire
WLH	Women's Lifestyle and Health Study
WRMR	Weighted root mean square residual

1 Introduction

Psychotic disorders, such as schizophrenia and bipolar disorder, are, due to their distressing nature and severe effects, among the most taxing diseases, causing suffering both among those afflicted and their kin. Affecting as many a 3.5% of the population over the lifetime (Perälä et al., 2007), psychotic disorders also cause great expenses for society (Olesen et al., 2012). However, neither the nature nor the aetiology of these disorders is very well understood (e.g., Broome et al., 2005; Holtzman et al., 2013; Howes & Murray, 2014), and standard treatments show on average only moderate advantage over placebo (for one recent meta-analysis, see Fusar-Poli, Kempton, & Rosenheck, 2013).

In recent years, much empirical data has been collected on the initial phase of psychotic illness, showing that the first acute episode is usually preceded by fluctuating, gradually worsening symptoms, in the "prodromal" phase (Fusar-Poli et al., 2013; Häfner, Löffler, Maurer, Hambrecht, & an der Heiden, 1999; Klosterkötter, Hellmich, Steinmeyer, & Schultze-Lutter, 2001; Yung & McGorry, 1996). In order to better understand the underlying disease process it is vital to study these early symptoms and associated features, as the prodromal phase may be the when the greatest changes happen in the brain (Fusar-Poli et al., 2011), and especially the structural brain deterioration characteristic of schizophrenia is largely present already during the first episode (Shepherd, Laurens, Matheson, Carr, & Green, 2012). Refining our picture of the early, attenuated symptomatology will not only help such causal elucidation, but also improve prevention.

Another avenue for understanding psychotic disorders is the range of similar experiences among the healthy general population or among non-psychotic psychiatric patients. Thoughts, perceptions, and behaviours similar to the symptoms of psychotic disorders, in the following called psychotic-like experiences (PLEs), have been found to be surprisingly common even in the general populace (Kaymaz et al., 2012), and provide a way of learning about their causes and correlates without the confounding elements present in clinical settings.

Improved measurement precision of these subthreshold phenomena and accurate characterization of their structure will help us understand the entire psychosis continuum from everyday uncanny feelings to the suprathreshold variety of psychotic disorders. Furthermore, careful psychometric analysis can improve the value of PLEs in predicting the development of full-blown disease.

1.1 Psychotic disorders

The word psychosis is derived from the Greek *psyche* ("mind, soul") and the suffix for a process or (abnormal) condition. Already when the term was used by Canstatt in 1841 and popularized within psychiatry by von Feuchtersleben it had a use similar to the modern concept: a severely disordered state, equivalent to "insanity" in the everyday language, with intertwined neurological and mental aspects (Beer, 1995; Bürgy, 2012). Psychoses were a subclass of "neuroses", which at that time meant any disorders of the nervous system, but without clear somatic causes. Interestingly, though von Feuchtersleben (1847) used the tentative categories idiocy (diminished activity), mania, fixed delusion, and folly/fatuity, he emphasized that they were "a representation of the phenomena which in reality occur in combination."

A consensus definition of psychosis does not, unfortunately, exist to this day. In the Diagnostic and Statistical Manual for Mental Disorders (DSM), 5th edition (American Psychiatric Association, 2013), widely used by both clinicians and researchers, psychosis is not even specifically defined, and it emerges as an implicit concept via the grouping of certain diagnoses as psychotic or having psychotic features, and then defining their specific symptoms. The key features are listed, however, being delusions (fixed, sometimes bizarre beliefs not susceptible to conflicting evidence), hallucinations (involuntary perceptions not based in external stimuli), disorganized thinking (derailed or incoherent speech), grossly disorganized behaviour (including catatonia), and negative symptoms (withdrawal and diminished emotional expression). Although the latest DSM versions have been intentionally agnostic about the correspondence of its classifications with any underlying phenomena (Heckers et al., 2013), the system's popularity has made its diagnoses a focal point of research, and its classifications will be presented briefly.

The principal psychoses are schizophrenia and schizophreniform disorder, the severest forms of affective disorders (some forms of severe unipolar depression, as well as some forms of depression or mania in bipolar disorder), and schizoaffective disorder (which is between the two former categories). Some other diagnoses are brief psychotic disorder, delusional disorder, and the catch-all headings "specified/unspecified schizophrenia spectrum and other psychotic disorder." All psychotic disorders in the DSM include either hallucinations or delusions as symptoms, but they are not required: most notably, the criteria for schizophrenia can be met without hallucinations or delusions, if the person's speech is disorganized, that is, frequently derailed or incoherent. Psychoses due to medical conditions or substance use offer a tantalizing glimpse into the mechanisms of psychotic symptoms via their known aetiology, but will be considered outside the definition of psychotic disorders for the purposes of this thesis.

These pragmatic attempts at creating objective criteria resulted from the overinclusiveness of previous definitions, which referred to gross impairments in everyday functioning or "reality testing" (American Psychiatric Association, 2000). In the absence of known biological causes, however, such phenomenological descriptions are inescapable, as the disturbances are in the very subjective domains of perception, thinking, and behaviour. At the relativist extreme, Heinimaa (2008) proposes the concept of psychosis to be wholly situational, as it depends on the lack of comprehension between the assessor and the assessed.

A striking feature of psychotic disorders is that the borders between the diagnoses are blurred: differential diagnoses can be hard, the individual's diagnoses may change over the disease course, and correlates such as familial (Mortensen, Pedersen, & Pedersen, 2010) and genetic risk (GROUP Consortium, 2013) seem to be at least partially shared. A contributing factor to the confusion is that diagnostic systems attempt to achieve diagnostic utility rather than nosologic validity (First et al., 2004), when both symptom expressions and underlying biological causes are to a large extent shared between diagnoses. In fact, the U.S. National Institute of Mental Health, a major funding source, created their own fully dimensional proposal in their Research Domain Criteria (Cuthbert & Kozak, 2013), and will only fund work based on this model, in an effort to have research based on the available evidence rather than convenient categories. The DSM-5 has adapted by introducing dimensional descriptors, so that diagnoses are paralleled by ratings on eight scales.

The aetiologies of psychotic disorders are still quite unclear, but many lines of research, related to obstetric complications, developmental problems, and brain structure, indicate that low-level changes in the brain are involved in psychotic disorders, especially schizophrenia (Howes & Murray, 2014). The dopamine system has been implicated as a proximal cause, especially as it seems to be the system though which antipsychotic medications have an effect. The step from neurotransmitter to experience is challenging, however. One possibility of bridging the gap was proposed by Kapur (2003): psychotic symptoms – specifically, hallucinations and delusions – are caused by the distorted salience (emotional importance) of perceptions and thoughts, which is caused by excessive, context-independent release of dopamine. Though the merits of the many aetiological theories of psychosis are outside the scope of this review, one observation relevant to our current concern needs to be mentioned: Linscott and van Os (2010) conclude that the vast majority of current theories about the causes of schizophrenia would lead to a continuous expression in the phenotype, and in its population structure.

1.2 The psychosis continuum

Due to empirical difficulties in assigning boundaries, a "psychosis continuum" has been proposed (e.g., Strauss, 1969; van Os, Linscott, Myin-Germeys, Delespaul, & Krabbendam, 2009), ranging from peculiar, but ordinary and fleeting thoughts and

perceptions among the psychologically healthy to crippling delusions and hallucinations in psychotic disorders. Similarly, speech and behaviour may vary from the slightly odd to the outright bizarre or incomprehensible, and disinterest in activities or social contact from temporary passivity to total indifference. This scale of experiences has become evident in population studies, where psychosis symptoms are inquired about also among healthy participants: no clear demarcation between the healthy and the pathological can be made (Binbay 2012). The continuum is roughly visualized in Figure 1.

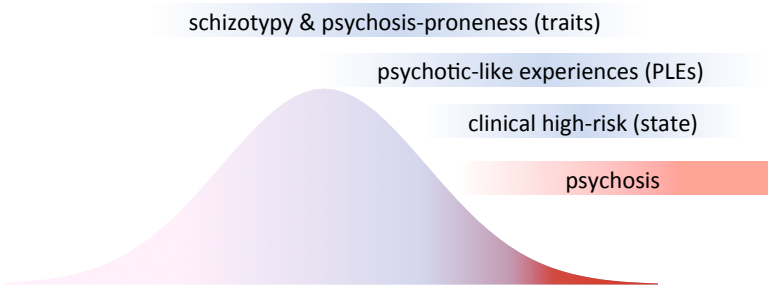

Figure 1. Schematic visualization of the psychosis continuum, with the intensity ranges covered by four central concepts indicated. The population is here presented as being normally distributed along a latent dimension, from non-pathological (left) to pathological (right). The distribution may actually be half-normal, with no appreciable distribution among the asymptomatic population (such that the left half of the graph doesn't exist), but results are highly dependent on the measures employed (Johns & van Os, 2001).

Exploring the psychosis continuum outside established psychotic disease has many advantages. For instance, data collection may be more reliable, as the participants are not affected by antipsychotic medication, disease-associated difficulties in self-expression, or fears of involuntary hospitalization (B. Nelson, Fusar-Poli, & Yung, 2012; van Os, Hanssen, Bijl, & Ravelli, 2000).

The middle levels of the psychosis continuum can be thought of as an intermediate phenotype (Lenzenweger, 2013), a related but less severe expression of the same causes that produce psychotic disorders. Studying the neural and genetic correlates of experiences across the whole continuum can thus help us understand the causes of both. In addition, understanding the less-severe forms of these experiences can disentangle our understanding of the more severe forms as, for instance, Berkson's (1946) paradox is avoided (a.k.a. hospitalization bias: flawed

ascertainment due to greater likelihood of inclusion in a clinical study when more than one condition is present), a phenomenon which previously seems to have influenced our understanding of psychotic disorders (Maric et al., 2004).

One of the strongest motivations for adapting the psychosis continuum concept has been immediate clinical utility: if signs of risk or impending disease could be identified, overt psychotic episodes could perhaps be ameliorated and even prevented (Yung & McGorry, 1996). In general population studies, mostly concerning young people, having subthreshold psychotic experiences has indeed been shown to be associated with a 3.5 times higher (0.6%) yearly risk for psychosis (Kaymaz et al., 2012). It has also become evident that, even when they do not progress to psychotic disorders, many psychotic-like experiences are distressing in themselves, and thus in need of treatment (van Os & Murray, 2013).

1.2.1 Psychosis-proneness and schizotypy

The idea of a continuum of psychotic-like experience, perhaps linked to "psychic vulnerability" to severe mental disorder, is as old as the concept of psychosis (Bürgy, 2012). Concrete hypotheses tested by empirical research have nevertheless been slow to emerge. From the 1960s, Meehl (1962) championed the concept of schizotypy, which was originally conceived as an inherited trait predisposing to schizophrenia. Schizotypy was thus defined as a taxon, a taxonomic unit, sharply delineated in nature – you either have it or you don't. The concept proved influential, and due to its descriptive value was included as a personality disorder in the major diagnostic systems in 1978 (ICD-9) and 1980 (DSM-III), with a prevalence of up to 4% (Coid, Yang, Tyrer, Roberts, & Ullrich, 2006; Pulay et al., 2009). Schizotypal personality disorder is robustly associated with psychotic disorder with respect to genetics, neuroanatomy, cognition, and environmental correlates (M. T. Nelson, Seal, Pantelis, & Phillips, 2013), and the sparse existing evidence for its utility in predicting psychosis among selected clinical populations indicates rates of transition to psychosis of up to 40% over a decade (Raine, 2006). The underlying premise of a simple genetic aetiology of schizophrenia and schizotypy was not borne out, however, as the polygenic background of schizophrenia has been established in genome-wide association studies (Sullivan, Daly, & O'Donovan, 2012).

The existence of a separate group of people subject to psychosis-proneness, schizotypy, or psychotic experiences is, as a simple dichotomy, attractive in being the simplest characterisation possible. However, this position has proved untenable. When the concept was operationalized in instruments such as the Schizotypal Personality Questionnaire (SPQ, Raine, 1991), it turned out that score distributions did not have a clear peak with distinct groupings of individuals (Figure 2a), and some studies now conceptualized the underlying schizotypy as a trait you could have more or less of, as a matter of degree. Nevertheless, the mere fact that attempts to

quantify schizotypy leads to continuous distributions doesn't prove that the underlying trait is continuous. A relatively rare dichotomous trait such as a schizotypy taxon could produce a skewed distribution if the indicators (questionnaire items) used to quantify the trait are imperfectly correlated with the taxon and each other: the noise would smooth out the "bump" representing the smaller peak related to the taxon (Figure 2b).

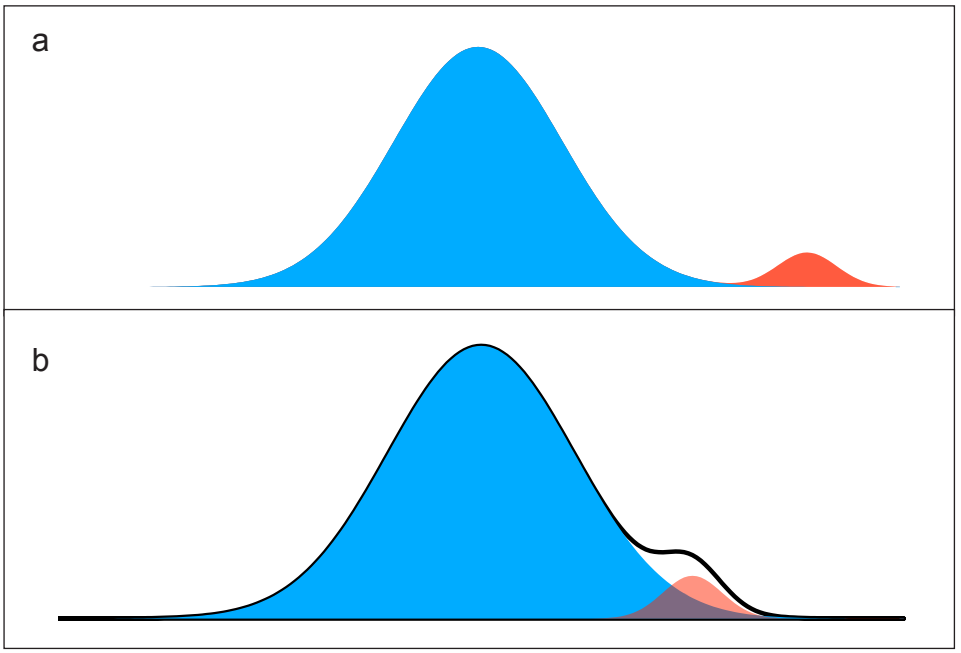

Figure 2. a) Idealized distribution of schizotypy scores reflecting a true taxon. In this non-existent scenario with a superior measurement, a cut-off can be established that almost perfectly separates schizotypal (right) and non-schizotypal (left) individuals.
b) Distribution of schizotypy scores as envisioned in the quasidimensional approach: the total distribution of the trait (black line), though almost normal, shows a bump at the upper end which reflects the underlying subpopulation of "true" schizotypic individuals.

Especially Lenzenweger (2006) has championed the view of the "true" schizotypy taxon being hidden in the upper-end "tail" of the population's distribution, employing the MAXCOV statistical technique to estimate taxon size based on questionnaire responses. Such taxonicity studies usually define about 10% of the population as schizotypal. More recently, other lines of evidence have marginalized this position, and supporting results may be artefacts of skewness and

atypical populations (M. T. Nelson et al., 2013). A recent systematic review did, however, find that methodologically appropriate newer studies showed a preponderance of evidence for a category underlying the phenotypic continuity, though it is unclear whether it could be due to nonlinear effects of a causal continuum (Linscott & van Os, 2010). Correlative evidence, such as quasi-continuous associations between positive and negative symptoms across the entire phenotypic continuum, can be explained by interactions between multiple aetiological factors (Binbay et al., 2012).

Another early approach to defining a psychosis risk syndrome was psychosis proneness, which was advanced by the Chapmans starting in the 1970s (Chapman & Chapman, 1987). Psychosis proneness was also envisioned as a stable trait, but was defined psychometrically. To probe putative psychosis risk indicators, the Chapmans created several questionnaires known as the Wisconsin scales, most notably the social anhedonia, perceptual aberration, and magical ideation scales. High psychosis risk was usually defined *ad hoc* as being in the top 5% of a scale. However, their approach was more agnostic regarding the possibility of a taxon, in that this method is equally applicable when the underlying trait is continuous, as it increases statistical power when comparing groups. Both extremes in positive and negative psychosis-proneness were associated with 1.5-fold higher odds for psychosis over the next 10 years (Kwapil, Gross, Silvia, & Barrantes-Vidal, 2013), which is insufficient for using these instruments for screening. Similarly, in a population sample that returned these questionnaires at age 31, those who were hospitalized with a psychotic disorder during the following 11 years had only moderately higher scores than those who weren't (Miettunen et al., 2011). The Chapmans (1980) also created a structured interview for probing hallucinations and delusions as continua. Their interview studies, however, didn't lead to very good predictive rates (Kwapil, Chapman, & Chapman, 1999); one reason was that their samples were drawn from college students with very low psychosis incidence within the next 10 next years.

1.2.2 Psychotic-like experiences (PLEs)

Psychosis-proneness and schizotypy inventories didn't quite perform as well as hoped in detecting individuals on a trajectory towards psychosis. The Wisconsin scales had been constructed with classical test theory in mind, where a normal distribution of scores is ideal, and thus contain many items that are not very pathological. Also measures such as the SPQ have a fairly normal distribution in the general population, and thus may not be ideal for screening psychosis risk. The conceptualization of these schizotypy and psychosis-proneness scales as measuring a stable trait also conflicts with the finding of psychotic-like experiences fluctuating over time, and gradually intensifying before psychosis.

Also the growing recognition that psychotic-like or even psychotic experiences are fairly common (McGorry et al., 1995) led to a need for new measures with better measurement properties. The Peters et al. (1999) Delusions Inventory is a case in point: it was explicitly designed to measure degrees of symptom expression, a wide range of delusions short of full-blown psychosis but retaining content validity, and incorporating degrees of conviction and distress. This can be called the psychotic-like experiences (PLE) paradigm. Another overlapping research tradition has been assessing symptoms drawn from psychotic disorder definitions – frank hallucinations and delusions – usually designated as (subclinical) psychotic symptoms, and often using structured interviews (e.g., Bak et al., 2005). As several large population studies have included some psychosis symptoms in their questionnaires and structured interviews, there is now a fairly good consensus of their prevalence at about 7%, with about 20% of these being persistent; the method of assessment has a great impact as self-report, even with metaphorical item phrasings left out, triples observed rates (Linscott & van Os, 2013). Among adolescents, a meta-analysis summarized that psychotic symptoms are reported by 7.5% (Kelleher, Connor et al., 2012), though there may here likewise be a difference between questionnaire and interview responses; the best congruence has been demonstrated for verbal hallucination items (Kelleher, Harley, Murtagh, & Cannon, 2011). However, a perennial problem in compiling the available research is the very wide range of item content, which is compounded in those studies where allowed responses are dichotomously "yes" or "no" (Linscott & van Os, 2010).

Being so common and transient, psychotic-like experiences in the general population seem fairly benign, but are naturally more pathological when more severe (Werbeloff et al., 2012; Zammit et al., 2013), persistent (Dominguez, Wichers, Lieb, Wittchen, & van Os, 2011), or associated with symptom-specific distress, affective dysregulation, or poor interpersonal functioning (Collip et al., 2013; Hanssen, Bak, Bijl, Vollebergh, & van Os, 2005; van Rossum, Dominguez, Lieb, Wittchen, & van Os, 2011; Wigman, van Winkel et al., 2011; Wigman, van Nierop et al., 2012); in depression and anxiety disorders they seem to be twice as common as among people without affective disorders. Psychotic symptoms in non-clinical populations also share, to a degree, many predisposing features with psychotic disorders, such as obstetric complications, social risk factors, trauma history, and brain abnormalities (Kelleher & Cannon, 2011). There is even emerging evidence that genetic variations previously linked with psychotic disorders have interacting effects with detrimental environmental conditions on the intensity of psychotic symptomatology (Alemany et al., 2011; Ramsay et al.,2013; Vinkers et al., 2013) .

1.2.3 Attenuated psychotic symptoms as a sign of high risk

Both retrospective and prospective research into the psychosis prodrome, the symptomatic period preceding the first psychotic episode, has uncovered a number of psychotic-like symptoms that are common in the year or years just before transition to psychosis (e.g., Klosterkötter et al., 2001; Yung & McGorry, 1996). These symptoms have been used to define various Clinical High-Risk (CHR) syndromes (also known as Ultra-High Risk or At-Risk Mental States), operationalized as a number of interview and questionnaire instruments (Daneault, Stip, & Refer-O-Scope Group, 2013). The at-risk designation typically requires worsening positive symptoms, or disorganization symptoms such as subjective thought disturbances (in the German "basic symptoms" tradition), but also negative symptoms (Cornblatt, 2002) and poor social functioning (Thompson, Nelson, & Yung, 2011) have been included in some formulations. Structural and functional brain imaging of CHR, with some of it comparing patients transitioning to psychosis to those who don't, has shown impairment consistent with this clinical picture (Smieskova et al., 2013). There has been much cause for optimism regarding the UHR strategy, as intervention studies show less transition to psychosis especially among patients treated with cognitive-behavioural therapy (Stafford, Jackson, Mayo-Wilson, Morrison, & Kendall, 2013; van der Gaag et al., 2013); at least a certain segment of patients can be identified and helped with preventive measures.

Nevertheless, the extension of CHR research to clinical practice is not straightforward. The existing research has shown acceptable predictive accuracy in the highly risk-enriched settings where it has been conducted (Fusar-Poli et al., 2013), and there is hope that it will be complemented with genetic (Bousman et al., 2013), epigenetic (Guidotti et al., 2014), cognitive (Fusar-Poli et al., 2012) and biomarker (Koutsouleris et al., 2014) indicators in the future. In light of these findings, a diagnosis of attenuated psychosis syndrome (APS) was included as a research diagnosis the DSM-5; the lack of evidence for its reliability and predictive utility in clinical practice precluded its inclusion in the main section (Tsuang et al., 2013). Though originally intended to be a prodromal and progressive syndrome, it was in the end redefined as a condition in its own right. One reason was that the APS syndrome can cause great distress, and long-term disability, regardless of any transition to psychosis. The main reason, however, was the lack of research into its prognostic value in wider use; it is clear that a large part of the predictive success of the risk criteria is attributable to sampling strategies in CHR studies, rather than the criteria themselves (Fusar-Poli, Yung, McGorry, & van Os, 2014). In fact, when assessed in the general population in the age at greatest risk for psychosis (van der Werf et al., 2014), the APS criteria were met by as many as 13% of participants, with most reporting no associated distress, and none reporting help-seeking related to these experiences (Schultze-Lutter, Michel, Ruhrmann, & Schimmelmann, 2013).

From the above, it can be seen that the identification of patients for indicated psychosis prevention is still a hard problem. CHR studies arguably lose specificity in the common practise grouping all psychoses together when defining criteria for transition from a prodromal state to psychosis, and it remains unclear to which extent certain symptoms predict specific psychotic disorders. On the other hand, first-episode psychosis diagnoses – the principal prevention target of psychosis prodrome research – are liable to change, especially among younger patients and towards the ambiguous schizoaffective diagnosis (Salvatore et al., 2009). This is not surprising, in that diagnoses may contain a minimum duration, as in schizophrenia, and data are more limited at the initial stage. Another, more pragmatic reason for not distinguishing between outcome groups by diagnosis is the small number of outcome events in the expensive prospective studies, which forces merging for adequate statistical power. To ameliorate this relatively costly rate of effort per observed outcome, the prodromal research tradition has produced a number of self-report questionnaires designed for initial screening. These questionnaires may even help identifying patients at risk directly, but their utility outside specialized clinics is still unclear, and reported effect sizes for predicting conversion have been modest (Gale, Glue, & Gallagher, 2013).

1.3 Dimensions of psychotic-like experiences

From the earliest days of naming psychotic disorders, the varying symptoms have been treated as groups; thus hallucinations are one entity, be they visual, tactile, or auditory. This implied structure and co-dependence of symptoms can be empirically studied by examining the patterns of variation within and across individuals. For cross-sectional research, this has meant, in practice, factor analysis and cluster or latent class analysis (Linscott & van Os, 2010; Potuzak, Ravichandran, Lewandowski, Ongur, & Cohen, 2012). The former strives to group symptoms, while the latter identifies natural subgroups of people. Cluster or latent class analysis corresponds to the long-standing division of schizophrenic disorders into certain subgroups, such as paranoid or catatonic schizophrenia, but the evidence for their validity has been so weak that they have been dropped from the DSM classification in its latest version. In contrast, it has been argued that further advancement in etiological research requires addressing individual symptoms or symptom dimensions, such as hallucinations or persecutory ideation (Bentall & Fernyhough, 2008), and there is even some evidence for better clinical utility of a dimensional model (Esterberg & Compton, 2009).

Within schizophrenia research, there is a long tradition of factor analysis of patients' anomalous experiences and behaviour. The earliest distinction gaining universal acceptance was between *positive* and *negative* symptoms: the former implying something added to the norm and the latter something being missing (Andreasen & Olsen, 1982; Crow, 1980). Positive symptoms include hallucinations

and delusions, as well as incoherent actions, while negative symptoms comprise flattened affect, poverty of speech, and reduced volition. Later studies found that a third factor of disorganized symptoms could be separated, with components previously assigned mainly to the positive symptom axis: disorganized speech and action (Liddle, 1987), and other cognitive difficulties. When items measuring affect among other symptoms of schizophrenia are included, they are also separable (McGrath et al., 2004), and a five-factor model with excitement and emotional distress added to the three-factor model seems fairly stable (Lindenmayer, Bernstein-Hyman, & Grochowski, 1994; van der Gaag et al., 2006). It has been argued, however, that the number of found dimensions extracted is greatly dependent on assumptions, sample size, and methodology, and one study therefore proposed as many as 11 correlated but separable dimensions to account for the non-affective symptoms of schizophrenia alone (Stuart, Pantelis, Klimidis, & Minas, 1999). Similar subdivisions of positive symptoms in psychotic disorders have been found by other groups as well (e.g., Ryu et al., 2013).

When repeated factor-analytic studies with the SPQ and other methods found evidence for a stable three-factor solution (e.g., Claridge et al., 1996; Lin et al., 2013; Raine et al., 1994; Reynolds, Raine, Mellingen, Venables, & Mednick, 2000), these separate but related factors became accepted as the most common description of the instruments' internal structure, and by extension, the phenomenon of schizotypy itself. This Positive-Negative-Disorganized structure, found in many different samples, paralleled the typical description of non-affective schizophrenia symptoms described above (Potuzak et al., 2012), and the most widely replicated further modification was also the same: a subfactor of paranoid ideation being separable from the other positive symptoms (Compton, Goulding, Bakeman, & McClure-Tone, 2009). Broadly similar structures have also been found in interview-based ratings of CHR symptoms (Comparelli et al., 2011; Demjaha, Valmaggia, Stahl, Byrne, & McGuire, 2012; Hawkins et al., 2004). However, when examining the SPQ at item level rather than using the nine given subscale scores, it appears that at least five dimensions are discernible (Chmielewski 2008). Similarly, the Peters et al Delusions Inventory shows a multifactorial structure within delusions (Peters 1999, Jones & Fernyhough 2007). The unclear number of empirical factors of PLEs and schizotypy – as measured with varying methods – clearly requires further research.

1.4 Cognitive deficits across the psychosis continuum

Of the psychotic disorders, especially patients with schizophrenia has consistently shown large average impairments (Cohen's $d \approx -1$, Probability of Superiority 25%) on a wide variety of cognitive tasks such as short-term memory, attention, and executive functioning, with the differences perhaps largest in verbal long-term memory (Fioravanti, Bianchi, & Cinti, 2012). It is unclear how much of these

differences can be attributed to treatment (medication or an impoverished environment), but most of the changes seem to be present already during the first episode (Mesholam-Gately, Giuliano, Goff, Faraone, & Seidman, 2009). Language development and IQ are also moderately impaired already in the premorbid phase (M. Cannon et al., 2002; Khandaker, Barnett, White, & Jones, 2011), and a relative drop in verbal ability during adolescence appears to predict adult schizophrenia (MacCabe et al., 2013), indicating that some cognitive deterioration is part of the early disease or precedes it. Though less studied, affective psychoses exhibit similar, but slightly weaker results (Bora, Yucel, & Pantelis, 2010), and euthymic (currently emotionally balanced) bipolar patients perform slightly better again, but are still clearly impaired as a group in many task domains (Cohen's $d \approx -0.7$, Probability of Superiority 30%). Clinical high-risk patients and relatives of schizophrenia patients seem to be intermediate between schizophrenia patients and controls (Bora et al., 2014; Valli, Tognin, Fusar-Poli, & Mechelli, 2012), while relatives of bipolar patients showed mostly small impairments (Bora et al., 2010). The added impairment in clinical high-risk patients actually developing a psychosis appears slight (Bora & Murray, 2014; De Herdt et al., 2013), and also schizotypy has been associated with a wide array of mild cognitive disturbances (Ettinger, Meyhofer, Steffens, Wagner, & Koutsouleris, 2014), which implies that these performance impairments precede full-blown psychosis and are present across the psychosis spectrum.

It would thus seem likely that psychotic-like experiences, when they are indicative of a shared underlying continuum, would be accompanied by performance deficits in cognitive tasks, especially in clinical contexts. There is little research so far pertaining specifically to PLEs. Among general population adults, Ziermans (2013) found weak associations between questionnaire-based positive symptoms and working memory performance. In a large population sample of children, PLEs were associated with a slightly poorer attention and processing speed at an earlier age (Niarchou et al., 2013), similar to the subtle processing speed and verbal fluency impairments in adults (Krabbendam, Myin-Germeys, Hanssen, & van Os, 2005; Simons, Jacobs, Jolles, van Os, & Krabbendam, 2007). There is a dearth of evidence regarding clinical non-UHR samples, which is unfortunate considering the potentially biasing effects of highly enriched sampling.

1.5 What are the latent dimensions of psychotic-like experiences, and what is their clinical utility?

Psychotic-like experiences are known to be on a continuum with and to be predictive of later psychosis to a certain degree, especially in clinical settings, and thus have the potential be used for primary screening of risk or even risk prediction. However, currently both positive and negative predictive values are low, and fully exploiting the potential of PLEs as predictors will require careful development of

both individual measures and the underlying concepts, in order to refine and increase predictive specificity. Specifically, the latent symptom dimensions of PLEs need to be identified and replicated across age groups, gender, and patient status. These latent structures also need to be validated against theoretically plausible associated features such as psychiatric health, cognitive performance, as well as against prospective psychosis-related outcomes.

2 Aims of the study

The study concerned the factorial structure of psychotic-like experiences in four samples, and the found factors' clinical correlates and predictive value.

The specific research questions of the study were:

1 Is there a dimensional structure to psychotic-like experiences (PLEs) comparable to that of psychotic symptoms, psychosis-proneness, and schizotypy? Do the empiric latent dimensions of PLEs match the *a priori* assumptions of questionnaire construction, also in different age groups?

2 Studies II & III: Do the latent dimensions of PLEs have the expected clinical correlates in symptoms and cognitive performance?

3 Study IV: Are the dimensions of PLEs clinically useful, especially for predicting psychotic disorders?

3 Methods

The materials and methods are here presented in summarized form; for detail at the level of full replicability, the reader is urged to consult the original articles. As all but one of the present studies employed latent factor analysis of PLEs, the psychometric reasoning for its use is first presented in greater detail.

3.1 Latent factor analysis

> It can scarcely be denied that the supreme goal of all theory is to make the irreducible basic elements as simple and as few as possible without having to surrender the adequate representation of a single datum of experience.
>
> *Albert Einstein: On the Method of Theoretical Physics [the Herbert Spencer Lecture], 1933.*
>
> Everything should be made as simple as possible, but not simpler.
>
> *Common paraphrase of the above.*

All psychological measurements are done under some implicit or explicit model of how the measured phenomena and its quantified operationalizations are related. As psychological constructs such as PLEs cannot be directly observed, it is called unobservable or *latent*, and has to be estimated from *manifest* variables, such as questionnaire responses. Each latent construct requires many manifest variables as indicators, which is why latent factor analysis is a form of data reduction.

Whereas the single-parameter latent factor model allows items to vary in severity (a.k.a. difficulty or threshold, corresponding to the regression intercept), the two-parameter model also assigns items varying discriminability (a.k.a. loading, corresponding to regression slope; see Figure 3). In multidimensional models, there is a separate loading parameter for each dimension. It has been further been suggested that psychopathology data should have two additional parameters per dichotomous item, allowing both a floor and ceiling level (Waller & Reise, 2010), as even the most extreme anxiety, for instance, doesn't include all the possible symptoms. In practice, however, this discrepancy is expressed in the two-parameter model as lower loading instead. There are also both one-dimensional and multidimensional extensions of the two-parameter model for polytomous Likert-type responses, where the thresholds between successive response alternatives can be modelled separately for each item (Figure 4).

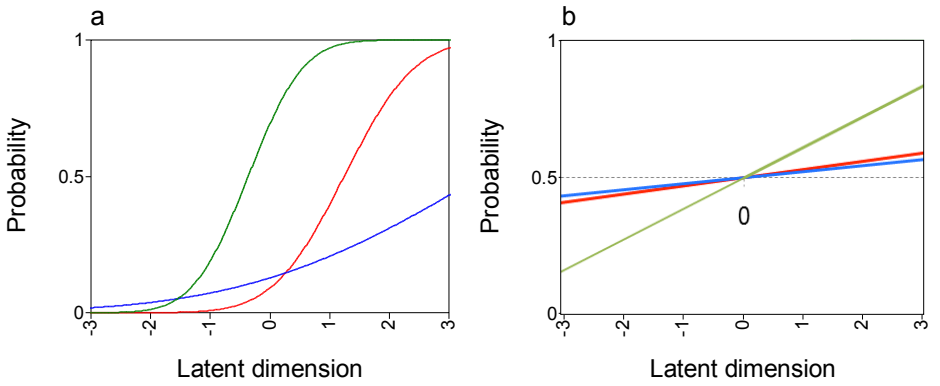

Figure 3. Current psychometric theory considers modern measurement models better for assessing latent phenomena than those based on classical test theory (Embretson & Reise, 2000). The best measurement properties (interval scale measurement) are obtained in single-parameter Item Response Theory (IRT) models, also known as Rasch models, but they have the troublesome requirement of equal item loading. In psychiatric settings, where items are chosen for their content rather than their measurement properties, a more pragmatic choice is the two-parameter IRT model and its multidimensional extensions (Wirth & Edwards, 2007).
a) Item response functions under latent trait models for three dichotomous items. The two equally discriminating items differ in severity (location on the latent dimension). The third item has poor discriminability (flat slope).
b) The corresponding item regression lines for traditional factor analysis. Note that the more severe of the discriminating items is assigned a regression line almost as poor as that of the third item.

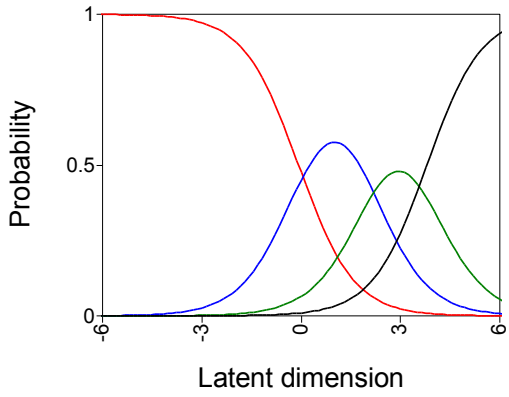

Figure 4. Item response functions of four ordered categorical response alternatives to a single item, showing response probability for each as a function of position on the normalized latent trait. Here an average person (latent trait level 0) would have approximately equal probability of selecting either of the first two alternatives, and a small probability of endorsing the third or fourth.

IRT-type models have several attractive properties in clinical research compared to classical test theory (Thomas, 2011). A clear advantage when assessing psychopathological content such as PLEs is that the severity of response alternatives is modelled, whereas psychometrically aware researchers using traditional factor analysis have explicitly avoided "strong" items (e.g., Claridge et al., 1996); it has long been known that spurious "difficulty factors" are otherwise obtained (Ferguson, 1941). Furthermore, latent trait estimates for individuals are inherently distributions, which can be used as such in research to retain the full information therein, or abstracted to point estimates (corresponding to standardized z-scores) and error terms. In any case, person estimates are more accurate, especially at the extremes, than under classical test theory (Dumenci & Achenbach, 2008). Another advantage of IRT is that items and persons can also be visualized on the same continuum. Items also have properties that can be directly compared across populations, rather than being dependent on sample characteristics (Embretson & Reise, 2000).

For the purpose of questionnaire or test construction, IRT-based models allow an item's added information value over the range of the latent factor can be assessed: this allows the researcher to explicitly choose which a combination of items that optimizes precision at the point where it is needed, at the cut-off point in screening (Figure 5). If the purpose of the questionnaire is screening, the most effective solution is to include only items of a severity corresponding to the cut-off point; items of significantly lesser or greater severity will not provide much additional information, unless they have superior discriminability. This property naturally also allows examination of existing scales. (Reeve & Fayers, 2005).

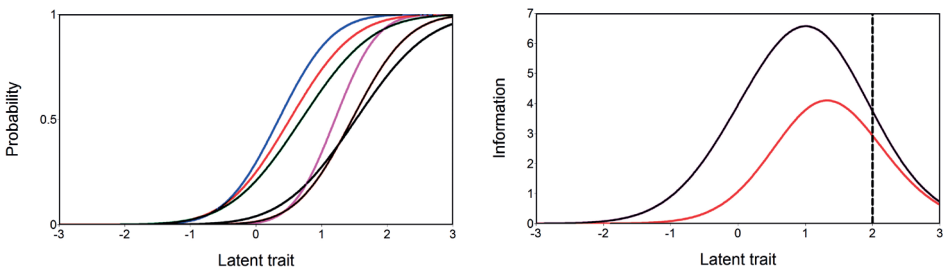

Figure 5. The relationship between item severity and cut-offs in a screening instrument. On the left are the item characteristic curves of six items with approximately equal discriminability: three with severity around 0.5, and three with severity around 1.5. On the right are the information curves for all items together and for the three more severe items only. At the indicated cut-off, selecting 2.5% of the population, the added information provided by the three less severe items is minor.

Last, but not least, the IRT models fit real-life responses to questionnaires better than sum scores or traditional factor analysis. Factor analysis assumes normally distributed continuous variables, which is a false assumption for both dichotomous and ordered categorical Likert-type data (Wirth & Edwards, 2007). The main drawback with having more detailed and realistic models with more parameters is that they require large datasets for estimation, often with 1000 respondents or more (de Ayala, 2009).

3.1.1 Dependence on assessed content domains

> On two occasions I have been asked, —" Pray, Mr. Babbage, if you put into the machine wrong figures, will the right answers come out?" […] I am not able rightly to apprehend the kind of confusion of ideas that could provoke such a question.
>
> *Charles Babbage: Passages from the Life of a Philosopher (1864).*

A vital issue in factor analysis of psychological constructs – as in any data analysis – is that we can only sensibly analyse what we have measured correctly. The engineering disciplines succinctly express this with the term GIGO; "garbage in, garbage out" (or even more provocatively, "garbage in, gospel out"). Reliability and noise can fortunately be quantified, but what if we haven't measured the necessary thing at all? If we haven't thought to ask about a specific domain of experiences, it will not exist. This concern is especially valid for PLEs, in that more specific inquiries lead to more reliable results: asking about specific experiences ("do you see dead people") leads not only to less false positives than general inquiries ("do you see things others don't see"), but seemingly paradoxically also – with enough items – to more true positives. In other words, numerous concrete inquiries may lead, in aggregate, to a larger number of endorsements by the respondents than more abstract wordings, and with less false positives (responses with trivial explanations).

Naturally, the very nature of the PLEs, being elusive and relatively rare, makes them hard to probe for: especially youngsters don't know what is asked about, if they don't have personal experience. In addition, the type of experience may seem at odds with getting reliable responses. Some questionnaires, for instance, are constructed with the assumption that one cannot rely on self-reported paranoid ideation or thoughts of reference, and leave such items out. The obvious result is that such questionnaires cannot inform us on the interplay between paranoid thoughts and other positive symptoms. This is unfortunate, as assessments of paranoid ideation have been demonstrably reliable (Kelleher et al., 2011); at less than fully psychotic intensity, self-reflection and sharing are quite possible, as the thoughts often are situational.

3.1.2 Determining the number of factors and testing model fit

In exploratory factor analysis, there is not any single way to determine the number of dimensions to assign to a particular data set. Any model is an abstraction, and researchers have to compromise between the parsimony of the model and its fit with the data – and the underlying reality itself. This suggests that we should minimize the number of components: use as few as are necessary. Models with fewer dimensions are also more stable and replicable across data sets. Furthermore, in constructing factor models of psychological constructs, sample size is vitally important. Conservative rules of thumb have called for up to 20 observations for each item in the model (Hair, Black, Babin, Anderson, & Tatham, 2006). Though stable models are achieved in practice with less than that, required samples are often in the hundreds or thousands, especially with a larger number of parameters.

Time-honoured ways of selecting the appropriate number of dimensions are the Kaiser eigenvalue criterion and the scree test (Cattell, 1966). The eigenvalue criterion calls for accepting the factors that have an eigenvalue greater than one, which means that they explain more than a single item's worth of variance. The reasoning is that such factors actually condense information – factors with an eigenvalue under one arguably have less explanatory power than individual items. The scree test is also based on eigenvalues, and examines their relative distribution. After the first few factors, the eigenvalues of the remaining factors usually decreases linearly, and this "scree" under the steep "cliff" of the first few factors is discarded, though the factor at the bend may be included. Both the Kaiser criterion and the scree tests have, despite their popularity, proved unsatisfactory (Zwick & Velicer, 1986). Theoretical assumptions also necessarily play a part in selecting a certain model, and ultimately, content analysis on part of the researcher decide – the retained factors have to make sense (Worthington & Whittaker, 2006). Factor models are naturally easiest to interpret when they exhibit a structure with every item loading on a single factor; note that this is not the same as Thurstone's (1947) "simple structure". Such parsimony of representation is desirable in exploratory analyses. However, care must be taken, as this model is not necessarily the best representation of the data; for example, item uniqueness may be hidden in artificially inflated factor correlations (D. A. Sass & Schmitt, 2010).

The generated factor model is not determinate, in that there is any number of possible item loadings that are mathematically equally good. Choosing between these is known as rotating the model. In psychological use, the unrotated model generated by a particular factor algorithm is usually not as easily interpretable as a rotated one. As in the actual factor estimation, there are several different algorithms for rotation, which optimize different criteria. The most relevant choice is, however, between orthogonal and oblique methods, where the latter allow factors to be correlated (Browne, 2001); already Thurstone (1947), the pioneer of factor rotation, advocated oblique methods as more appropriate to psychology.

3.1.3 Latent factor models used in the included studies

In Studies I & II latent factors were identified with full-information factor analysis (FIFA, Bock, Gibbons, & Muraki, 1988) as implemented in TESTFACT 4.0 (Wood et al., 2003) and Mplus 6 (Muthén & Muthén 2011), which estimates the parameters of the factor model by fitting with numerical integration (Maximum Likelihood) to the raw data. FIFA uses the full data rather than correlation matrices, thus providing a better representation of the data than methods assuming uni- or multivariate normality. FIFA also shares has an attractive property common to all Maximum Likelihood –based numerical methods, which is that a number of numeric model selection criteria based on the likelihood function are available, notably the Bayesian Information Criterion (BIC, Schwarz, 1978) and the Akaike Information Criterion (AIC, Akaike, 1973). The former compensates goodness-of-fit somewhat more for added model complexity, thus being more conservative in selecting the number of factors, and was used in the present studies. The method requires exponential computational resources with increasing numbers of items, and despite improvements such as adaptive integration, it is currently unfeasible for datasets with items in the magnitude of a hundred (Wirth & Edwards, 2007).

Depending on the number of parameters (the complexity of the model), FIFA may requires large datasets for reliable convergence. As complex FIFA models achieve adequate stability at 500 response sets (Forero & Maydeu-Olivares, 2009), factor analysis of the tetrachoric or polychoric correlation matrix may be preferable in smaller samples. This approach was employed in Study IV, where the number of items was exceptionally large. In even smaller data sets, where the number of parameters in the model is too large compared to the number of response sets, subscales can be used for initial data reduction. The latter method was used in Study III, which also allowed the use of a linear model without intercepts.

As the measured aspects of psychopathology can be related, perhaps expressing common underlying causes, the latent factors were allowed to correlate in all studies except Study III, where the small sample size forced the use of the interpretationally simpler orthogonal Varimax solution. The preferred rotation algorithm was Oblimin (with the k weighting parameter set to 0), also known as Direct Quartimin (Jennrich & Sampson, 1966), which minimizes row (item loading) complexity and is the optimal way of uncovering an existing simple structure (Browne, 2001; D. A. Sass & Schmitt, 2010). In Study I, the Promax rotation criterion was employed, as it was the only oblique rotation method available in the TESTFACT program. Promax derives its rotation target from the Varimax solution.

Before further analyses, all PLE indices (items or subscales) were checked for sufficient shared variance with other indices. As latent factors are measured with multiple indicators, any one that is not related to other indicators or the overall construct is unlikely to address what was intended.

3.2 Participants

One clinical and two population-based data sets were utilized in this thesis. A comparison of the four study samples is presented in Table 1.

Table 1. Comparison of study populations.

	Study I	Study II	Study III	Study IV
Name abbreviation	NFBC86	WLH	HPS pilot	HPS
Sampling	General population	General population	Clinical	Clinical
N in analyses	6611	31822	71	731
Age range	15-16	41-61	12-19	15-19
Age mean	16	51	16	16
Proportion females	51%	100%	66%	68%

3.2.1 Study I: Northern Finland 1986 Birth Cohort

The Northern Finland 1986 Birth Cohort Study (NFBC) is a longitudinal study in the two northernmost provinces of Finland (Järvelin 1993, Järvelin 1997). Originally it comprised 9 479 children with expected dates of birth between July 1st, 1985 and June 30th, 1986, representing 99% of all births in the area at that time (Järvelin 1997). In the follow-up at age 16, a total of 9 215 adolescents were alive and reachable at a known address; 7 344 of them responded to a postal questionnaire, yielding a comparatively high response rate of 80%.

3.2.2 Study II: Women's Lifestyle and Health

The Women's Lifestyle and Health study was started in 1991, when a health questionnaire was mailed to a representative population sample of 96 000 Swedish women aged 30-49 years in the Uppsala region (Ekman 2006). In 2003 and 2004 a follow-up questionnaire was sent to 47 859 respondents, who were at that time aged 41-61 years. The follow-up questionnaire, which was returned by 34 415 women (72%, representing 36% of the original sample) included items on psychiatric health, which are the focus of Study II.

3.2.3 Studies III & IV: Helsinki Prodromal Study

The Helsinki Prodromal Study (HPS) was a collaborative project initiated in 2001 by Kansanterveyslaitos (Finnish National Health Institute, since 2009 part of the Institute for Health and Welfare) and the University of California, Los Angeles (UCLA). The main aim of the study was to test psychosis prodrome detection methods in an unselected adolescent psychiatric sample. Participants were therefore required to have no present or previous diagnosis of psychosis, and to be without organic brain disorders, but otherwise there were no diagnostic group limitations. For methodological purposes, all were required to speak Finnish at a native language level.

The methods of the Helsinki Prodromal Study were based on those used at the Center for the Assessment and Prevention of Prodromal States (CAPPS) at UCLA. CAPPS data have been reported primarily as part of the North American Prodrome Longitudinal Study (T. D. Cannon et al., 2008).

A pilot sample of 71 patients (66% females) aged 12-19 were recruited in 2001 and 2002 from the local adolescent mental health wards (n = 27) and one of the outpatient adolescent psychiatric clinics (n = 44). In addition, a control group of 72 volunteers (78% females) aged 14-19 was recruited from a local public school, representing 80% of approached students. They only took part in cognitive testing, establishing a reference for the clinical studies. Data from the pilot was used in Study III.

The main part of the study was conducted in two parts, in 2003-2004 and in 2007-2008, with participation extended to all adolescent psychiatric clinics in Helsinki. As the intent of the study was to study new patients only, inclusion criteria were further restricted in that all patients were recruited upon the start of their treatment episode, and had received no systematic psychiatric care apart from the contact leading to referral during the previous 2 years. Due to the large number of eligible patients, invitations were sent based on an initial questionnaire screening. Data from the screening and a register follow-up was used in Study IV.

3.3 Questionnaires

When studying very subjective phenomena such as psychotic-like experiences and psychiatric symptoms, data are always mediated by the participants' subjective interpretations and comprehension. Interviews allow an iterative process of determining the quality and significance of experiences, in that respondents can verify their understanding of what is asked about, and the interviewer can pose follow-up questions in unclear situations. Questionnaires, on the other hand, offer an opportunity to reach a far larger number of people, and may thus lead to more effective time use in clinical practice, especially as first-stage screening.

3.3.1 PROD-screen (Study I)

The PROD-screen (Heinimaa et al., 2003) is designed to be a brief screen for psychosis risk symptoms, and refers to experiences during the past 12 months. It has 21 yes/no items, covering both putative specific risk symptoms (PLEs) and more general psychiatric complaints (e.g., anxiety, decision-making difficulties). Item selection was influenced by both the German tradition of examining the prodromal manifestations of "basic symptoms" of psychosis (Klosterkötter, Schultze-Lutter, Gross, Huber, & Steinmeyer, 1997) and the Australian view of combining attenuated psychotic symptoms with general symptoms and deteriorating levels of functioning (Yung & McGorry, 1996). Positive, negative, disorganized, and affective symptom dimensions were explicitly included, and sensitivity was emphasized over specificity.

Classical psychometric properties such as internal consistency, item-total correlations, and test-retest reliability of PROD-screen have not been reported. The factorial structure of the PROD-screen has likewise not been previously empirically investigated, but the creators of the scale have designated 12 items as specific to psychosis risk (mild forms of hallucinations, delusions, and subjective cognitive disturbances). Based on their comparison with interview-based assessments in a clinical setting, the authors suggest a tentative cut-off of two "specific" symptoms to maintain an acceptable sensitivity. This division has been shown to identify a group of help-seekers with somewhat poorer functioning (Granö et al., 2011), providing initial external validation. In Study I the PROD-screen was filled in by the adolescents recruited from the NFBC86 birth cohort, with the time range inquired about shortened to 6 months.

3.3.2 CAPE (Study II)

The Community Assessment of Psychic Experiences (Hanssen et al., 2003; Stefanis et al., 2002) is a questionnaire intended to assess clinically relevant PLEs. In fact, the CAPE is an explicit attempt to address psychotic experiences (PEs), identical to those seen in psychotic disorders, in non-clinical populations (Konings, Bak, Hanssen, van Os, & Krabbendam, 2006). The items are divided into positive, negative, and depression symptoms; disorganization and mania have intentionally been left out due to concerns about the possibility to measure them with questionnaires. Only the 20 positive symptom items of the CAPE were included in the questionnaire used in Study II. The positive symptom items of the CAPE are based on the Peters et al. Delusions Inventory (Peters et al., 1999), which in turn is derived from the ninth edition of the Present State Examination (Wing, Cooper, & Sartorius, 1974).

Most items have a "Do you ever…" preface, making the probed time span indeterminate, but in all likelihood weighted towards more recent experiences. There are two four-point response scales to each item: a frequency scale ("never", "sometimes", "often", and "almost always") and a distress scale. Many studies

employing the CAPE, including Study II, present only the frequency scale, due to respondent difficulties with double scales and interpretation difficulties when both are used, such as the unclear meaning of reported distress when the participant also reports never having had an experience. However, frequency and distress on the CAPE are strongly correlated (Stefanis et al., 2002).

In terms of classical psychometrics, the frequency ratings of the CAPE have shown fairly good internal consistency, with Cronbach's α values reported at around .8 for the three hypothesized dimension sum scores (Brenner et al., 2007), and .96 for the total scale (Wigman et al., 2011). The dimensional sum scores have also shown good test-retest reliability, with correlations over an interval of several months being around .7 (Konings et al., 2006). Criterion validity has been moderate, with correlations over .4 for associations with interview-assessed schizotypy dimensions (Konings et al., 2006).

3.3.3 Affective questionnaire items (Study II)

The follow-up questionnaire of the Women's Lifestyle and Health used in Study II included a number of hierarchical items corresponding to the symptom criteria for a major depressive episode (MDE) and generalized anxiety disorder (GAD) in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV, American Psychiatric Association, 2000). These items allowed approximate research diagnoses of lifetime and current MDE and GAD, though the questionnaire format precluded the use of bereavement and mixed state exclusions, as well as some criteria and subcriteria, namely change in appetite as an alternative to weight change, hypersomnia, psychomotor agitation or retardation, indecisiveness, lack of energy, frequency of fatigue and worthlessness, and suicidal ideation/attempt. In addition, MDE here required both the mood and anhedonia criteria rather than just one of these.

3.3.4 Prodromal Questionnaire (Studies III & IV)

The Prodromal Questionnaire (PQ; Loewy, Bearden, Johnson, Raine, & Cannon, 2005) is a 92-item list of potentially disturbing experiences, focusing on recent changes to the worse. As in the PROD-screen, responses are either yes or no, with yes always being symptomatic. The content is based on items of the SPQ and probe questions from the Structured Interview for Prodromal Syndromes (SIPS), with some original items. The PQ covers positive, negative, disorganized, and general psychotic-like symptoms – all thought to be more frequent in the psychosis prodrome. The scale is further subdivided into 26 subscales, with one to seven items each. The PQ has been explicitly designed for use as an initial screen to select patients for interview with the SIPS or similar specialized psychosis risk assessment methods (Loewy et al., 2005). Initially reported classical psychometric indices among help-seeking individuals were Cronbach's α = .96 for the whole scale and .79

to .92 for the four main dimensions, while dimension sum score correlations with corresponding interview-based scores were .49 to .60, except for disorganization, where the value was .27. Especially the positive subscale has been reported to distinguish between healthy controls, non-psychotic first-visit psychiatric outpatients, and psychotic first-visit patients (Chiu, Hwu, Shiau, Yao, & Hsieh, 2010). The PQ was used in the pilot and main phases of the Helsinki Prodromal Study (HPS).

3.4 Cognitive assessment (Study III)

In the pilot phase of the Helsinki Prodromal Study, a standardized battery of cognitive assessment was used to assess both general performance and functions that could be markers for impending psychosis. The total duration was approximately 100 minutes, and was completed in a single session with almost all participants. The included tests were selected to address cognitive functions known at the time to be impaired in psychotic disorders (Green, Kern, Braff, & Mintz, 2000) and, for some, to have to be affected both by manifest disease and hereditary liability (T. D. Cannon et al., 2000), thus providing good coverage of the cognitive domains suspected to be associated with near-future transition to psychosis. In Study III, they were used for correlative validation of the clinical relevance of PLEs. The test battery is described in detail in Table 2.

3.5 Register follow-up of psychiatric hospitalization (Study IV)

In the main part of the Helsinki Prodromal Study, there was a register-based follow-up of the participants. All hospital care episodes in Finland are registered in the national Finnish hospital discharge database, as part of the Care Register for Health Care (Hoitoilmoitusrekisteri, or HILMO, in Finnish). Psychiatric admission and discharge diagnoses (under the ICD-10 system) from birth to the end of the year 2011 were retrieved for the 819 participants of the questionnaire screening of the Helsinki Prodromal Study, excluding the 61 who had refused register follow-up. The follow-up time was 3-9 years, the mean being 6 years.

The primary outcome of interest, a psychosis diagnosis, was defined as comprising both non-affective psychotic disorders and affective disorders with psychotic features (F20, F22, F29, F30.2, F31.2, F31.5, F32.3, and F33.3). The 27 patients who were assigned such a diagnosis of psychosis during the stay they participated in screening, or had received one previously, were excluded from the study. The final sample size was thus 731.

The secondary outcome of interest, psychiatric hospitalization for any reason, included any treatment at a psychiatric hospital ward, as well as stays at other hospitals with a psychiatric diagnosis (F00-F99, X60-X85, or Y87.0). This outcome was included as a general indicator of psychiatric illness severity. The 77 patients with a previous or current psychiatric hospitalization were excluded from the follow-ups analyses of this outcome, which thus concerned 654 individuals.

Table 2. Description of cognitive variables
(Table 2 from Study III, reproduced with permission)

Type of task	Specific test
Digit Span	Digit Span subtest of Wechsler Memory Scale – Revised (WMS R; Wechsler, 1987)
Visual Span	Visual Span subtest of Wechsler Memory Scale, version III (Wechsler, 1997b)
Verbal Episodic Memory	First story from Prose Learning subtest of WMS-R
Visual Episodic Memory	Visual Reproduction subtest of WMS-R
General Verbal Ability	Abbreviation of the Vocabulary subtest of the Wechsler Adult Intelligence Scale – Revised (Wechsler, 1981)
Nonverbal Reasoning	Matrix Reasoning subtest of Wechsler Adult Intelligence Scale – Third Edition (Wechsler, 1997a)
Simple Reaction Time	Novel computerized task; responding to randomly timed visual stimulus
Choice Response Delay	Novel computerized task; response time increase compared to Simple Reaction Time
Dual Task Performance	Bourdon-Wiersma line cancellation Dual Task (Vilkki et al., 1996)
Visuomotor Speed	Trails A subtest of Halstead-Reitan Battery (Reitan and Wolfson, 1985)
Task Switching	Trails B subtest of Halstead-Reitan Battery (Reitan and Wolfson, 1985)
Verbal Learning	Words correctly recalled on five initial trials of California Verbal Learning Test (Delis et al., 1987)
Verbal Recognition Discriminability	Discriminability (*d'*) in Recognition condition of California Verbal Learning Test (Delis et al., 1987)
Verbal Fluency	Items generated, Verbal Fluency subtest of the Multilingual Aphasia Examination (Benton and Hamsher, 1976)

3.6 Statistical analysis

Used factor models have been detailed in section 3.1.3. In study IV, the association between predictors and outcomes was examined with Cox regression, a proportional hazards model where the predictors multiplicatively determine the hazard, which is assumed equal over the timespan. All regressions were stratified by gender because of their unequal baseline risk.

In Study III, *post-hoc* power analyses to examine the sufficiency of the sample size for answering the research questions were performed with G*Power version 3.0.10 (Faul, Erdfelder, Lang, & Buchner, 2007).

In study II, group difference are expressed as Glass's Δ effect sizes, which is the difference in means between a particular symptomatic group and the non-symptomatic group, with the latter's standard deviation as unit. The closely related index known as Cohen's *d* (Cohen, 1988), which uses a pooled standard deviation, was used to compare patients and controls in Study III. Cohen's *d* is related to Hedges' *g** (Hedges & Olkin, 1985), popular in meta-analyses, differing by a small correction factor.

4 Results

The summary of the main results are presented by study. More detailed results are available in the original articles.

4.1 Study I: Dimensions of psychotic-like experiences

The structure of the PROD-screen was examined with exploratory full-information factor analysis (FIFA) in the NFBC86 birth cohort at age 16.

Out of the 21 items of the PROD-screen, one item ("Feeling euphoric or especially competent and important") showed insufficient shared variance with the other variables, with the standardized loading on the latent factor in the one-dimensional model being only .22 (all others were .43 or higher). As this item also had the highest endorsement rate at 44%, it was judged to assess only everyday feelings of achievement rather than the intended manic tendencies, and was excluded from further analyses.

An exploratory FIFA of the remaining 20 items was estimated with 1 to 5 factors, the number of indicators being too few for a more detailed model (Fabrigar, Wegener, MacCallum, & Strahan, 1999). The three-dimensional solution had the best Bayesian Information Criterion (BIC) score. The eigenvalue criterion would have selected the same number of dimensions, while the scree plot (Figure 6) would perhaps have indicated the presence of a fourth factor.

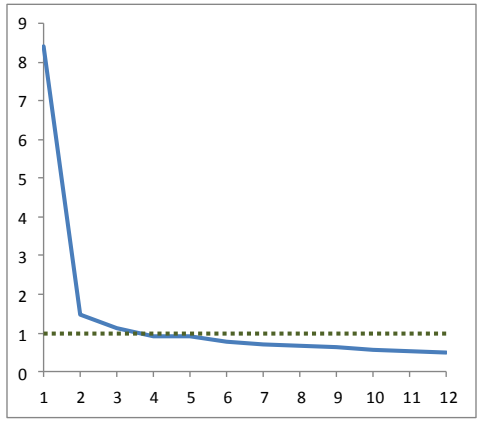

Figure 6. Scree plot of the first 12 eigenvalues of the PROD-screen sample tetrachoric correlation matrix.

The Promax-rotated model is presented in Table 3. The Positive factor included the subjective thought disorders termed "basic symptoms", thoughts of reference, and hallucinatory experiences. The Negative factor addressed difficulties in social and role functioning, while the General factor consisted primarily of the anxiety, depression, stress, and sleep/appetite items. The decision-making item and the akathisia item each had very equal loadings on two factors. The three factors were highly correlated, with correlation coefficients from .64 to .78.

Table 3. Endorsement rates and standardized factor loadings of the Promax-rotated 20 PROD-Screen items included in the three-dimensional Full-information item factor analysis (FIFA)

Item	Yes (%)	Positive	Negative	General
Weird Thoughts or Behaviours*	14.6	**0.91**	-0.18	-0.04
Something Inexplicable Going On*	7.1	**0.78**	-0.15	0.17
Speed of Thoughts*	20.3	**0.69**	-0.08	-0.01
Being Followed or Influenced*	5.9	**0.65**	0.01	0.04
Hearing Disorders*	8.1	**0.64**	-0.03	0.01
Difficulties Thinking Clearly*	35.3	**0.56**	0.10	0.07
Visual Disorders*	14.0	**0.53**	-0.05	0.00
Thoughts of Reference*	18.8	**0.51**	0.12	0.02
Self-Control While Communicating*	8.1	**0.46**	0.35	-0.15
Understanding Text or Speech*	17.0	**0.43**	0.26	-0.10
Making Decisions	26.0	0.36	0.29	-0.03
Making Contact With Others	10.1	-0.19	**0.90**	0.02
Initiative and Task Completion	12.8	-0.04	**0.65**	0.10
Social Withdrawal	11.3	-0.12	**0.60**	0.18
Difficulties with Routines*	2.2	0.12	**0.48**	-0.08
Anxiety	30.4	0.09	-0.02	**0.78**
Depression	24.5	-0.02	0.08	**0.78**
Stress Tolerance	18.3	-0.01	0.10	**0.67**
Sleep or Appetite	15.9	0.12	-0.02	**0.58**
Akathisia	9.1	0.30	0.06	0.33

* Items designated by the PROD-screen authors as specific to psychosis risk

4.2 Study II: Subdimensions of psychotic-like experiences and their clinical correlates

In Study II, the positive PLEs reported in a general population sample were examined for multifactoriality, and the levels of the resulting latent dimensions were compared between groups with lifetime depression, generalized anxiety, both, or neither.

Table 4. Response frequencies as percentages for the 20 CAPE positive symptom items in the Women's Health and Lifestyle Study

Item	Never	Some-times	Often	Almost always
Conspiracy	91.9	7.6	0.35	0.10
Double meaning	56.7	41.1	1.93	0.28
Being persecuted	95.7	4.0	0.25	0.10
False appearance	31.1	63.3	5.42	0.20
Odd looks	84.8	13.9	1.01	0.28
Messages from TV	86.8	12.6	0.35	0.17
Being important	70.6	24.7	3.92	0.77
Being special	60.4	34.5	4.16	0.87
Voodoo	78.4	18.2	2.13	1.23
Telepathy	47.2	45.9	5.78	1.15
Thought withdrawal	93.6	6.0	0.43	0.06
Thought insertion	94.1	5.5	0.29	0.11
Thought echo	94.2	5.5	0.30	0.05
Thought broadcasting	95.4	4.3	0.25	0.04
External control	95.2	4.2	0.42	0.18
Influenced by devices	94.9	4.6	0.45	0.11
Visual hallucinations	95.8	3.7	0.35	0.12
Verbal hallucinations	97.7	2.2	0.12	0.03
Voices conversing	99.5	0.5	0.05	0.02
Capgras syndrome	98.6	1.3	0.07	0.03

Note: Cells are colour coded to indicate relative frequency.

4.2.1 Factor analysis of CAPE positive symptoms

The positive symptoms of the CAPE included in the Women's Lifestyle and Health Study follow-up questionnaire were analyzed with full-information factor analysis.

Table 5. OBLIMIN-rotated factor loadings of the 20 CAPE positive symptom items probed in the Women's Health and Lifestyle Study.

	5 factors					6 factors					
Item	**F1**	**F2**	**F3**	**F4**	**F5**	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
Conspiracy	**.79**	.03	-.04	-.02	.13	**.76**	.03	-.04	-.01	.16	-.02
Double meaning	**.74**	-.03	.05	.12	-.16	**.77**	-.01	.08	.04	-.14	.09
Being persecuted	**.73**	.01	-.02	-.04	.25	**.70**	.05	-.04	.02	.24	-.07
False appearance	**.51**	.20	.16	.13	-.21	**.44**	.14	.17	.05	-.05	.28
Odd looks	**.48**	-.10	.08	.17	.02	**.50**	-.07	.07	.27	-.08	-.10
Messages from TV	**.37**	.17	.11	.07	-.07	.27	.16	.04	.06	-.03	**.39**
Being important	-.04	**.91**	-.07	.02	.01	-.04	**.87**	-.08	-.02	.05	.06
Being special	.07	**.71**	.14	-.04	.02	.07	**.77**	.11	.04	-.07	-.08
Voodoo	.03	-.06	**.83**	-.04	.04	.04	-.05	**.81**	-.02	.04	-.05
Telepathy	.02	.11	**.75**	.06	-.06	.00	.11	**.74**	.06	-.03	.08
Visual hallucinations	-.02	.04	**.50**	.02	**.40**	-.02	.04	**.49**	.01	**.42**	-.04
Thought withdrawal	.09	.01	-.10	**.83**	-.05	.08	.00	-.10	**.64**	.11	.25
Thought insertion	-.03	-.02	.01	**.83**	.05	-.02	-.02	-.01	**.72**	.12	.13
Thought echo	.01	.02	.06	**.67**	.13	.01	.04	.03	**.81**	-.01	-.09
Thought broadcasting	.06	.03	.05	**.62**	.11	.06	.04	.03	**.76**	-.04	-.07
External control	.04	.10	.21	**.45**	.20	.05	.12	.19	**.50**	.14	-.09
Influenced by devices	-.01	.13	.32	**.39**	-.02	-.05	.10	.33	.23	.13	.29
Verbal hallucinations	.09	.01	.08	.14	**.72**	.08	-.01	.08	.09	**.77**	.00
Voices conversing	.07	.06	.01	.09	**.87**	.05	.04	.00	.05	**.91**	.01
Capgras syndrome	.03	.07	.15	.32	**.38**	.03	.07	.13	.34	**.36**	-.05

Response frequencies, from which three thresholds were calculated for each item, are reported in Table 4. Factor models of increasing dimensionality were estimated. The single-dimensional model already provided a moderately good fit to the data, as it explained over 44% of the variance. All items had loadings above .5 in the one-dimensional model, indicating sufficient shared variance, and all items were retained for further analyses. The BIC index increased monotonously with added dimensions. The six-dimensional model was, however, not interpretable, in that the last rotated factor loaded only weakly on all items, and the five-dimensional model was therefore chosen for further analyses. Table 5 presents both the final five-dimensional and the six-dimensional models.

Table 6. Correlations between OBLIMIN-rotated CAPE factors.

	5 factors					6 factors					
	F1	**F2**	**F3**	**F4**	**F5**	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
F1 Paranoia	1					1					
F2 Grandiosity	.33	1				.32	1				
F3 Magical Thinking	.34	.39	1			.32	.41	1			
F4 Delusions	.61	.42	.43	1		.57	.42	.44	1		
F5 Hallucinations	.41	.23	.40	.57	1	.42	.29	.40	.63	1	
F6 (Uninterpreted)						.19	.23	.03	.25	.04	1

In the two-dimensional model the two "grandiosity" items formed a factor separate from the others, and remained separate all the way to the six-dimensional model. In three dimensions, items addressing magical thinking formed their own factor, in four, paranoia split from hallucinations and other delusions. In five dimensions, finally, hallucinations and delusions had their own factors, with the total explained variance rising to almost 63%. Factors were fairly strongly correlated, as expected from the single-dimensional results. For example, paranoia and other delusions were correlated at .6 in the final 5-factor model (Table 6).

Two items had significant cross-loadings with the magical thinking factor, namely the item intended to probe visual hallucinations ("Do you ever see objects, people or animals that other people cannot see?") and the one concerning devices ("Do you ever feel as if electrical devices such as computers can influence the way you think?"). It is likely that some responders interpreted these items metaphorically rather than literally.

Table 7. Factor score means and standard deviations by lifetime diagnosis group, standardized on the non-disordered group's distribution.

	MDE n = 6343 (19.9%)	GAD n = 375 (1.2%)	Both MDE and GAD n = 929 (2.9%)
	M (SD)	M (SD)	M (SD)
1. Paranoia	0.49 (1.17)	0.72 (1.18)	0.94 (1.24)
2. Grandiosity	0.08 (0.99)	0.25 (1.04)	0.14 (0.97)
3. Magical Thinking	0.24 (1.08)	0.34 (1.15)	0.39 (1.08)
4. Delusions	0.40 (1.15)	0.70 (1.31)	0.86 (1.34)
5. Hallucinations	0.38 (1.23)	0.56 (1.31)	0.75 (1.46)

4.2.2 Levels of psychotic-like experience subdimensions by affective disorder group

The factor score levels of the three diagnostic groups MDE, GAD, and MDE+GAD differed markedly across the five identified subdimensions of positive PLEs (Table 7). Scores on all five dimensions were higher in the GAD group than in the MDE group. Furthermore, with the exception of the "grandiosity" factor, scores were highest in the most afflicted MDE+GAD group.

Table 8. Odds ratios for top 5% scorers on dimension having lifetime MDE or GAD, compared to all those scoring lower.

	Factor	Odds Ratio (OR)	95% Confidence Interval (CI)
F1	Paranoia	4.1	3.7-4.6
F2	Grandiosity	1.2	1.1-1.3
F3	Magical Thinking	2.0	1.8-2.2
F4	Delusions	2.8	2.5-3.1
F5	Hallucinations	2.4	2.1-2.6

The factor effect sizes compared to the non-disordered population (Glass's Δ) were large (0.70 to 0.94) for paranoia, delusions, and hallucinations in all groups with lifetime GAD, MDE or both. In contrast, effect sizes were negligible in all groups for "grandiosity" (0.08 to 0.25), and small for magical thinking (0.24 to 0.39). Expressed in the reverse, odds ratios for a person scoring in the top 5% on a factor having lifetime MDE or GAD ranged from 4.1 for paranoia to 1.2 for "grandiosity" (Table 8).

4.3 Study III: Cognitive correlates of psychotic-like experiences

The cognitive correlates of psychotic-like experiences were examined by correlating factor scores of Prodromal Questionnaire (PQ) responses and task scores on cognitive test battery.

4.3.1 Factor analysis of Prodromal Questionnaire subscales

The Prodromal Questionnaire consists of 26 subscales. Due to the small sample, the number of variables in the factor analyses was reduced by using postulated subscales instead of individual items; each subscale score was the sum of its endorsed items. To further reduce the number of variables, the general symptom subscales (Sleep Problem, Dysphoric Mood, Role Functioning, and Stress Symptoms) – not assessing PLEs *per se* – were excluded from the factor analysis, and a General Symptoms Index was instead derived by simply adding their scores. The General Symptoms Index proved to have a fairly high reliability in this sample, with Cronbach's α calculated from subscale sums at 0.69.

Of the remaining 22 subscales, the single-item scales were added to the scale they correlated with the strongest, and somatic and olfactory hallucinations were combined. The resulting 18 subscales were transformed to approximate normality, and analysed with common factor analysis (Principal Axis Factoring algorithm, Varimax rotation). Though the number of observations per variable was still small, an easily interpretable three-factor solution was found (determined by both scree test and eigenvalue criteria), explaining 53% of the total variance; the factor solution is presented in Table 9. The three factors were named the Positive, Interpersonal, and Disorganized symptom dimensions, with the Interpersonal factor being composed mostly of items thought of as negative symptoms, such as social withdrawal. The Disorganized factor was fairly strongly (r = .7) correlated with the General Symptoms Index.

4.3.2 Cognitive performance dimensions

In order to decrease the number of statistical tests, and to decrease the impact of test-specific variance and measurement error, the 20 scores of the cognitive testing was also subjected to a factor analysis identical to that of the PQ. The identified factors,

which accounted for 38% of the variance, were named Memory, Visuospatial ability, and Attention. The factor solution is presented in Table 10.

Table 9. Varimax-rotated Principal Axis Factoring of PQ subscales

Subscale	Positive	Inter-personal	Disor-ganized
Auditory Hallucinations	**.85**	.24	.15
General Hallucinations	**.84**	.18	.16
Visual Hallucinations	**.76**	.11	.14
Magical Thinking	**.63**	-.19	.19
Somatic & Olfactory Hallucinations	**.62**	.04	.27
Ideas of Reference	**.51**	.20	.33
Perplexity	**.47**	.38	**.44**
Hygiene & Social Attentiveness	**.46**	**.42**	.19
Telepathy	**.44**	.20	**.43**
Conceptual Disorganization	**.51**	.12	**.66**
Avolition	.07	.30	**.64**
Experiencing Emotions	**.55**	.27	**.56**
Attention Problem	.19	.20	**.55**
Odd Behaviour	**.47**	.03	**.54**
Paranoia	.18	.14	**.50**
Social Isolation	.15	**.78**	.07
Expressing Emotions	.04	**.63**	.35
Social Anxiety	.01	**.53**	.36

4.3.3 Associations between symptom and cognitive factors

All correlations between symptom and cognitive factors were small and statistically nonsignificant (absolute linear r < .11); controlling for the General Symptoms Index did not change results. The patients were on average moderately impaired in Visuospatial ability (Cohen's $d = 0.6$), and slightly impaired in Memory ($d = 0.2$), but the latter was not a statistically significant difference. Among the patients, inpatients had worse Memory performance than outpatients ($d = 0.6$).

As the sample was small, *post hoc* power analyses were performed to determine whether there were enough observations to detect meaningful associations between factor score variables. With the Type I error level (α) set at 5%, a sample size of 71 achieves in a two-sided t-test an acceptable power (1 - β) of 73% in detecting a bivariate normal correlation of .3 or greater, which is the lower limit for a moderate magnitude in Cohen's (1988) terminology.

Table 10. Varimax-rotated Principal Axis Factoring of cognitive test scores

Task	Memory	Visuospatial Ability	Attention
Prose Recall, Delayed	**.90**	-.08	.06
Prose Recall, Immediate	**.88**	-.03	.12
CVLT Learning	**.56**	.13	.20
Visual Reproduction, Immediate	**.49**	**.44**	.09
Vocabulary	.39	.20	.29
CVLT Recognition Discriminability	.37	.04	.06
Choice Response Delay	.27	.23	-.08
Trail Making Task A	.02	**.61**	.09
Dot Cancellation	.01	**.61**	.17
Matrix Reasoning	.20	**.60**	.22
Trail Making Task B	.22	**.57**	.29
Visual Span, Forward	.03	**.54**	.18
Visual Span, Backward	.00	**.54**	.18
Visual Reproduction, Delayed	**.51**	**.51**	.08
Digit Span, Forward	.12	.16	**.76**
Counting Backwards	.16	.39	**.47**
Digit Span, Backward	.18	.20	**.44**
Simple Reaction Time	-.10	.21	**.43**
Verbal Fluency (Animal Naming)	.21	.23	.28
Dual Task Performance	.18	.00	.21

4.4 Study IV: Psychotic-like experiences as predictors of psychosis

4.4.1 Latent dimensions of the Prodromal Questionnaire

The size of the questionnaire sample in the Helsinki Prodromal Study proper allowed testing the *a priori* dimensional model of the Prodromal Questionnaire (PQ) with Confirmatory Factor Analysis (CFA). In the CFA of the 4-dimensional model (positive, negative, disorganization, and general symptoms) each item was assigned to one latent factor, with factors allowed to correlate and loadings estimated freely on the assigned factor. In this model, the root mean square error of approximation (RMSEA) was an acceptable 0.04 but the comparative fit index (CFI) was under .90, a commonly held limit for good fit (Hair et al., 2006), thus indicating a need for exploratory analysis.

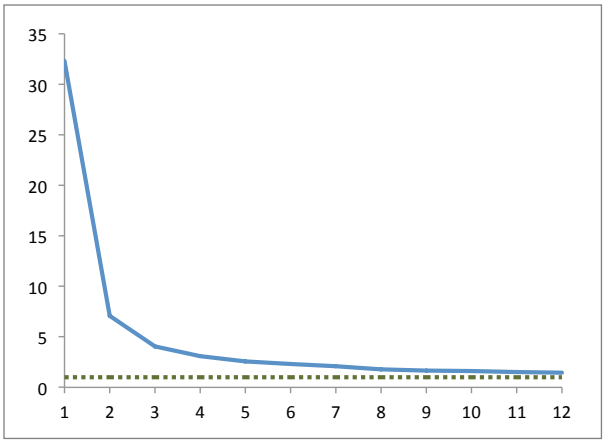

Figure 7. Scree plot of the first 12 eigenvalues of the Prodromal Questionnaire sample tetrachoric correlation matrix in Study IV.

Exploratory latent factor models with dimensions from one to ten were estimated from the tetrachoric correlation matrix with the WLSMV algorithm and Oblimin-rotated. The scree plot is shown in Figure 7, and demonstrates the unclear dimensionality of the data: several dimensions are clearly present, but there is no sharp "elbow" in the curve. With this number of items, the eigenvalue test is clearly too liberal, including 20 factors. Fit indices (CFI, RMSEA, and WRMR) improved with each added dimension, but the ten-dimensional model did not produce an interpretable last factor, and the nine-dimensional model was retained. The used indices showed excellent fit (CFI .99, RMSEA 0.014, WRMR 0.74), as the recommended values for models with more than 250 observations and binary outcomes are CFI > 0.95 (or 0.96), RMSEA < 0.05 and WRMR < 1.0 (Yu, 2002).

The identified nine factors were named Role Functioning, Delusional Ideation, Hallucinations, Oddness, Social Avoidance, Magical Thinking, Dysphoria, Depersonalization, and Anhedonia.

4.4.2 PLEs as predictors of psychosis-related or other psychiatric hospitalization

Survival curves, with patients grouped by gender, are presented separately for psychosis and hospitalization outcomes in Figure 8. Though psychiatric hospitalization rates were very similar over the next nine years, males were 2.5 times more likely to be hospitalized with psychosis.

All nine latent dimensions were entered singly in Cox regressions, as well as the Total PQ Sum Score and Positive Subscale Sum Score, which were the *a priori* predictors (Table 11). Four of these were statistically significantly better than chance in predicting psychosis, namely Depersonalization, Role Functioning, Dysphoria, and Total PQ Sum Score. With the strongest predictor Depersonalization in the model, none of the others offered improvement. For the psychiatric hospitalization outcome, five variables were statistically significant predictors when considered separately: Role Functioning, Social Avoidance, Depersonalization, Total PQ Sum Score, and Positive Subscale Sum Score. When the best predictor Role Functioning had been entered, the other variables did not improve significantly on the model.

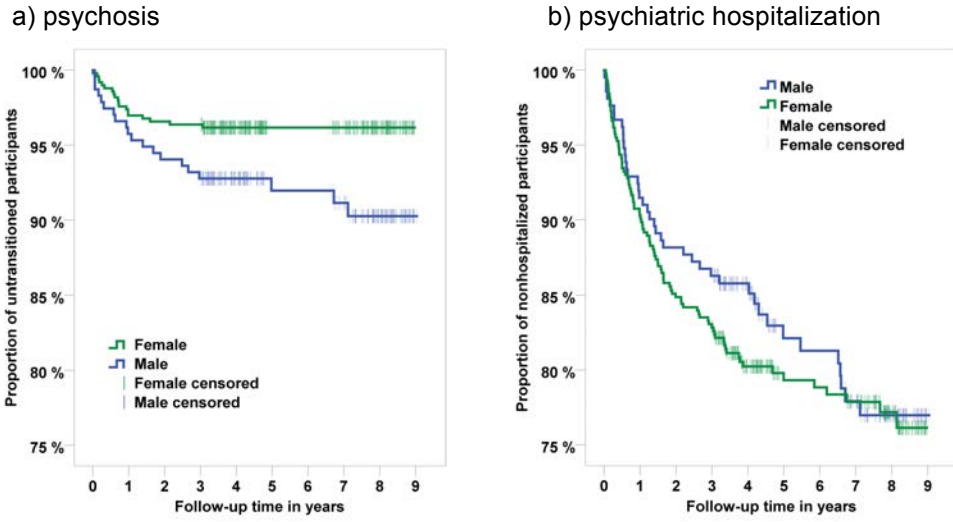

Figure 8. Kaplan-Maier survival curves by gender.

Table 11. Cox proportional hazards models predicting psychosis and hospitalization with individual PQ factors and sum scores.

a) Psychosis, n = 731

	Hazard	95% CI for HR		
Normalized PQ factor	**Ratio (HR)***	**Lower**	**Upper**	**p**
PQ Total Score	**1.45**	**1.04**	**2.02**	**0.027**
PQ Positive Symptoms	1.28	0.93	1.75	0.130
F1 Role Functioning	**1.49**	**1.08**	**2.07**	**0.017**
F2 Delusional Ideation	1.23	0.89	1.70	0.206
F3 Hallucinations	0.97	0.70	1.34	0.864
F4 Odd	1.26	0.92	1.73	0.156
F5 Social Avoidance	1.24	0.91	1.68	0.174
F6 Magical Thinking	1.04	0.75	1.43	0.821
F7 Dysphoria	**1.41**	**1.00**	**1.99**	**0.047**
F8 Depersonalization	**1.60**	**1.16**	**2.23**	**0.005**
F9 Anhedonia	1.37	0.99	1.89	0.056

b) Hospitalization, n = 654

	Hazard	95% CI for HR		
Normalized PQ factor	**Ratio (HR)***	**Lower**	**Upper**	**p**
PQ Total Score	**1.28**	**1.07**	**1.53**	**0.007**
PQ Positive Symptoms	**1.20**	**1.01**	**1.43**	**0.035**
F1 Role Functioning	**1.32**	**1.11**	**1.58**	**0.002**
F2 Delusional Ideation	1.16	0.97	1.37	0.097
F3 Hallucinations	1.18	0.99	1.39	0.059
F4 Odd	1.08	0.91	1.29	0.355
F5 Social Avoidance	**1.24**	**1.05**	**1.47**	**0.013**
F6 Magical Thinking	1.17	1.00	1.38	0.057
F7 Dysphoria	1.18	0.98	1.43	0.080
F8 Depersonalization	**1.23**	**1.03**	**1.47**	**0.024**
F9 Anhedonia	1.17	0.98	1.39	0.085

* HR is per standard deviation increase of the predictor.
Note: statistically significant predictors at α = .05 are in bold.

5 Discussion

The psychotic-like experiences in general and clinical populations showed a structure similar to that found in studies of schizotypy, psychosis proneness, and the symptoms of psychotic disorders. The questionnaires thus demonstrated structural validity, a *sine qua non* for their use in screening. In line with previous findings, several subdimensions of positive PLEs were found to be associated with affective psychiatric symptoms, while functional disorganization (role functioning) predicted psychiatric hospitalization in general, and depersonalization predicted hospitalization for psychosis.

5.1 Study I: Structure of PLEs in a general adolescent population

In Study I it was shown that PLEs of the type evident in prodromal phases of psychotic disorders were quite commonly reported by adolescents in the general population, with reported endorsement frequencies of up to 35% for the items labelled specific to psychosis risk. Clearly invalidating the specificity hypothesis, such high rates are similar to what has been found among other general-population adolescents of the same age (Kline et al., 2012; Ronald et al., 2014). However, the highly variable endorsement rates, with the lowest at 2%, can be interpreted as evidence of thoughtful and non-random responding, making the problem primarily one of item selection. Self-reported PROD-screen symptoms among mildly symptomatic help-seeking adolescents have also been found to have moderate to substantial agreement rates with clinician-interview validations (Granö et al., 2014), with the exception of the "euphoria" item, which was also left out in Study I. The present finding that this item is also unrelated to the others makes it a clear candidate for removal, to improve screening accuracy. To be viable, the PROD-screen requires improvement: in a comparison with two other psychosis-risk screening questionnaires, the PROD-screen fared slightly worse than the others (Kline et al., 2012). However, as the authors of that study note, this difference may be due to the PROD-screen including also other than positive psychosis items, in contrast with the other questionnaires. Therefore the weaker performance of the PROD-screen was not surprising, as the criterion outcome in that study was based on positive psychosis items in a structured interview. The screening instruments should ideally be validated against the relevant clinical outcome, such as transition to psychosis or level of general functioning.

The positive/negative/disorganized/affective factor structure implied by the categorization in the SOPS item source was nearly replicated, though the positive and disorganized symptoms mainly loaded on a single factor. The disorganization items may have been too few to allow detecting this separable dimension, and both

the "weird thoughts and behaviours" and "difficulties thinking clearly" had actually been adapted as combinations of positive and disorganized symptom description in the sources. Interestingly, the "understanding text and speech", "self-control while communicating", and "making decisions" items, all of which could be considered symptoms of disorganization, showed significant cross-loading, a sign of misfit. The BIC criterion for selecting the number of dimensions may have led to a somewhat conservative result, but with no previous factor analyses of the PROD-screen available, caution is warranted. In practice, the small number of items precludes more than four exploratory factors, regardless of the underlying structure. In fact, when analysing PLEs among adolescents in a smaller population sample with the 20-item positive symptom scale of the CAPE, a four factor-structure of bizarre experiences (thought control delusions), persecutory ideation, hallucinations, and magical thinking emerged (Yung et al., 2009). Of these, the PROD-screen doesn't address outright delusions or magical thinking at all.

A spurious single dimension could be produced by simple response tendency, but the meaningful structure of the data supports the supposition that the majority of the responses are "true", in that they actually reflect the intended phenomena. PLEs of the type found in the psychosis prodrome can thus be measured in the general adolescent population. However, even though at least some PLEs can be meaningfully assessed even among children around 10 years of age (Kelleher et al., 2012; Laurens, Hobbs, Sunderland, Green, & Mould, 2012), and are somewhat predictive of psychosis (Poulton et al., 2000), only about a third persist into later adolescence (Dominguez et al., 2011; Downs, Cullen, Barragan, & Laurens, 2013; Thapar et al., 2012). The large endorsement rates in this study do show that much of the responses are a product of normal variation rather than pathology, and the strategy of moving beyond dichotomous responses to frequency and distress scales (Peters et al., 1999) appears justified. Even with such improvements however, self-rated hallucinations and delusions among young adults seeking help at an early psychosis clinic were weak predictors of the corresponding clinician-rated symptoms (Schultze-Lutter et al., 2014). Nevertheless, in a prospective study of adolescent questionnaire-assessed PLEs, especially the continuous persistence of symptoms led to as high as tenfold odds of psychosis some 8 years later (Dominguez et al., 2011). Apparently PLEs in later adolescence are significantly more pathological than earlier, underscoring the need for their routine assessment in clinical practice (Kelleher, Keeley et al., 2012).

Investigating the differential utility of the identified PLE dimensions for predicting psychosis – while taking into account item severity – would be an interesting further line of research. In a prospective analysis of the same PROD-screen data in the NFBC86, endorsing at least two of four specific items (difficulty making contact with others; social withdrawal; thoughts of reference; being followed or influenced) chosen based on previous research (Salokangas et al., 2009) was associated with a three- to fourfold risk for psychosis (Mäki et al., 2014).

Unfortunately, even a manifold risk is not sufficient for effective screening considering the low incidence of psychosis in the general population (Kline & Schiffman, 2014), but such research builds on our understanding of the psychosis continuum, and the combined use of other variables, such as help-seeking, may improve results.

5.2 Study II: Structure of positive PLEs and their clinical correlates among adult women in the general population

In Study II, a five-dimensional structure of positive symptoms was found, and two of the latent factors appeared mostly nonpathological in the general population. There is little previous research of this age group, and in light of the present findings the structure of positive symptoms appears stable over a wide age range.

The data set had extreme differences in item endorsement: for instance, only 0.5% responded that they heard "voices conversing" sometimes or more often, while almost 70% felt at least sometimes that "people are not what they appear to be" – which is, of course, a realistic appraisal. On the other hand, less than 6% responded "often" to the latter item, which may reflect the true level of inconveniencing persecutory psychotic-like experiences (Linscott & van Os, 2013). Similarly, though over 40% sometimes felt that "people speak with a double meaning", only some 2% reported having this experience often or almost always. Also for many other items, there was a great divide between "sometimes" and "often". In contrast, the most severe "delusional thinking" items probing persecutory ideation, experiences of thought interference, and external control had partial endorsement ("sometimes" or more often) at about 5%. The response scale thus seems to work well, but taking into account the relative severities of the various responses is essential. The FIFA method, similarly to most factor analytic methods, is not able to disentangle the various response alternatives, as the item is associated as a whole with the latent factors: in future studies it may be more appropriate to associate individual response alternatives with the factors, in order to dissociate the most common responses from the more severe ones, since the former may not be addressing the psychosis continuum.

The structure of positive psychotic-like experiences among adult women appears to be the same as in younger age groups. The exploratory five-dimensional structure very nearly reproduced a model based on young adolescent samples (Wigman, Vollebergh et al., 2011), which has previously been showed excellent fit among young women with confirmatory factor analysis (Wigman, Vollebergh et al., 2012). The original adolescent study was conducted with dichotomized data (experience present or not), which may explain the minor differences. A very similar result was also found in a another study of general-population adolescents, which reported a four-factor structure – essentially the same as the present one, but with the two non-pathological factors combined (Yung et al., 2009); here the inability to distinguish

between those factors can be attributable to their use of linear factor analysis. Another study using the CAPE found no correlation between overall positive symptom level and age in the range 18 to 65 years (Nitzburg, Malhotra, & Derosse, 2014), which indirectly also supports the stability of the latent structure across different age groups. The present latent structure results are probably also generalizable to men at this age, as gender-specific effects on the structure of the schizotypy trait have been shown to be virtually non-existent (Bora & Baysan Arabaci, 2009; Reynolds et al., 2000). Furthermore, a recent meta-analysis found that rates of positive psychosis-proneness, as measured with the Wisconsin scales, are almost the same among women and men (Miettunen & Jääskeläinen, 2010), and similar results have been found for methods probing subclinical psychotic experiences (Maric, Krabbendam, Vollebergh, de Graaf, & van Os, 2003; Rössler, Hengartner, Ajdacic-Gross, Haker, & Angst, 2012), including some specifically using the CAPE (Armando et al., 2010; Nitzburg et al., 2014).

Paranoia, other delusions, and hallucinations (but not grandiosity or magical thinking beyond a marginal degree) were somewhat more frequent among those with a history of depression or generalized anxiety, which corresponds on the part of depression exactly to previous findings with the CAPE among young help-seekers (Yung et al., 2006). That study did not, however, find corresponding associations with anxiety disorders, which may be partly due to their combining of all the heterogeneous DSM-IV anxiety diagnoses into one category. As in Study I, items addressing "grandiosity" appeared unrelated to the other items, and were in this Study II not associated with affective disorders. This corresponds to previous findings of this factor not being associated with current depression (Armando et al., 2010; van Os et al., 1999). Also Wigman and colleagues (2011) concluded from weaker associations with distress ratings and general psychopathology that the grandiosity and magical thinking dimensions may be unrelated to the extended psychosis phenotype. This reasoning is supported by a study showing that magical thinking did not decrease in contrast to other positive PLEs in conjunction with improving depression level and mood disorder remission. Similarly, the items loading on the latent factors here unassociated with psychiatric problems – with the exception of the "being special or unusual" item – have previously been found not to distinguish between patients with a history of psychosis from general-practitioner patients without a history of psychiatric disorder (Verdoux et al., 1998).

In CHR patients, defined primarily by their positive symptoms, anxiety (15%) and depression (40%) are quite common, but unevenly represented (Fusar-Poli, Nelson, Valmaggia, Yung, & McGuire, 2014), perhaps indicating a stronger link between the positive symptoms and depression. Conversely, in the general population findings of Study II, generalized anxiety disorder was associated with slightly stronger positive symptoms than depression. This discrepancy may be explained by only a single, severe diagnosis being assessed in Study II, or bias in the

clinical population; resolving the issue would benefit from systematic dimensional assessments of the affective aspects in future population studies of PLEs.

5.3 Study III: Cognitive correlates of PLEs among adolescents in psychiatric care

The associations between dimensions of schizotypy and cognitive performance were explored in a sample of adolescents in psychiatric care.

A three-dimensional latent factor model of the PQ showed adequate fit with the data, and closely paralleled the *a priori* structure. The one directly comparable study, an exploratory factor analysis of all 26 originally postulated PQ subscales together (Rietdijk et al., 2014) in a clinical adolescent sample, conservatively identified only a positive and a negative factor, though a third factor would have improved on their fit indices and extracted another 5% of the variance. Their choice not to extract a third factor was apparently driven by the noninterpretability of the third factor; the inclusion of the general symptoms in that study may have obscured the results.

As expected, the patients showed cognitive performance impairment, with some additional impairment in the inpatient group. However, all correlations between symptom factors and cognitive performance factors had absolute values of .11 or less, indicating no association. Previous research targeting CHR patients has found them to be slightly cognitively impaired compared to controls, and several domains of cognitive performance predict transition to psychosis (Fusar-Poli et al., 2012). Also, in another recent meta-analysis (De Herdt et al., 2013), it was concluded that working memory or visual learning may improve psychosis prediction algorithms for UHR groups, while another suggested verbal memory (Valli et al., 2012). In any case, effect sizes are small in all domains (Bora et al., 2014), approximately $d = 0.4$ (Probability of Superiority 39%). It is not clear, however, that this finding should extend across the psychosis continuum, and it may partially be an artefact of recruiting practices. In studies of the linear associations between various cognitive domains and psychotic-like experience subdimensions, absolute correlations have been only in the order of .1, as in the present study (Simons et al., 2007; Ziermans, 2013).

In the main part of the Helsinki Prodromal Study, however, results were directly comparable, as the association between interview-based PLE factors and cognitive performance was addressed in a larger sample with the same non-specific recruitment strategy (Lindgren et al., 2010). In that study, positive symptoms were associated with poorer visuospatial functioning (in comparing CHR and non-CHR groups, and within the non-CHR group), and negative symptoms were associated with weaker verbal task performance, with correlations between $r = -0.2$ and $r = -0.4$. A likely interpretation of these disparities – besides a Type II error due to sampling chance – is therefore that Study III was too small to detect the existing relatively weak associations, with the *post hoc* power analysis indicating that this

may be the case. Alternately, it is possible that the questionnaire assessment of PLEs was statistically noisier than a structured interview.

5.4 Study IV: PLEs as predictors of psychosis among adolescents in psychiatric care

The structure of the Prodromal Questionnaire was examined exploratively at an item level, and the resulting latent factors were used as predictors of psychosis and all-causes psychiatric hospitalization over several years.

In Study IV, using the Helsinki Prodromal Study screening sample, the screening instrument was found to have nine interpretable factors, representing an intermediate level of detail between the proposed main factors and subscales. Of these, the three factors Dysphoria and Anhedonia appear to indicate the two main aspects of depression, and are not specifically linked to the psychosis continuum, though they may be aggravating factors. Items indicating various degrees of disorganization loaded on a factor here named Role Functioning, while negative symptoms may be addressed by Social Avoidance; the latter may, however, be more indicative of social anxiety than lack of interest. Among the putative positive symptoms, magical ideation was clearly separable from delusions, and hallucinations and depersonalization were also distinct.

The best predictor of later hospitalization for a psychotic disorder was the latent depersonalization factor. Had the positive symptoms been treated as a single entity, this distinction would, of course, not have been made. The standardized hazard ratio of 1.6 for the depersonalization predictor of later psychosis was fairly low, but almost identical to the best predictor in a similar study using interview rating scales (Demjaha et al., 2012). Likelihood ratios for future psychosis among questionnaire test-positives in samples with about 50% UHR participants tend to be in the range of 2.5±1, with post-test probabilities of transition to psychosis ranging between 0.1 and 0.2 percent (Gale et al., 2013). In a direct comparison of three questionnaires (Prime Screen, Prodromal Questionnaire-Brief, and Youth Psychosis At-Risk Questionnaire-Brief) in a small sample of mainly UHR adolescents, the three performed the same as measured by area under the curve (AUC) on the sensitivity/specificity plot (Kline et al., 2012). In the EPOS study of help-seeking CHR patients, where the participants mostly were young adults, an *ad hoc* selection of SPQ items addressing ideas of reference and negative symptoms was associated with a doubled transition-to-psychosis rate (Salokangas et al., 2013), and a similar outcome was obtained in the NFBC86 study (Mäki et al., 2014). These results demonstrate that the dichotomous items, with a fairly high endorsement rates in the general population, are not very efficient for screening. To remedy this situation, the PQ has more recently been updated to employ a distress scale (Loewy, Pearson, Vinogradov, Bearden, & Cannon, 2011).

The main finding of depersonalization predicting psychosis is not altogether surprising, as self-reported positive schizotypy is fairly strongly associated with dissociation, even when similar item content and childhood trauma is accounted for, which may indicate shared aetiology (Moskowitz, Barker-Collo, & Ellson, 2005; Startup, 1999). In fact, questionnaire measures of positive schizotypy (or psychosis-proneness) and dissociation overlap in the detachment/depersonalization aspect (Pope & Kwapil, 2000; Watson, 2001). Dissociation has also been suggested to predispose to psychosis (Allen, Coyne, & Console, 1997; Allen & Coyne, 1995). Sass and Parnas (2003) have even proposed the theory that the core of schizophrenia is a disturbance in ipseity (self-experience), with twin aspects of exaggerated awareness of the self (as an object) and diminished sense of self-possession (being a subject). Their work builds on the phenomenological work of Jaspers, who recognized over 100 years ago the importance of self-consciousness to the formation of psychotic experiences (Bürgy, 2008). There are already some hypothesis-driven findings of self-disorder disturbances as prospective predictors of psychosis (B. Nelson, Thompson, & Yung, 2012; Parnas et al., 2011), and the present explorative result reinforces that dissociative experiences need to be specifically addressed in CHR research (Parnas, 2005).

5.5 Methodological considerations

The use of questionnaires is, of course, a problematic endeavour when elusive experiences are mediated through the necessarily brief item text and the respondent's recall, comprehension, and forced-choice response. The respondent's own understanding of the experience does not necessarily correspond to the language used in the items and response alternatives. These problems can, however, be ameliorated with using a larger and varied range of items, and subsequent data reduction, such as factor analysis.

In the present studies, the factor analytic approach appeared to fit the data well, within the limits of measurement noise and unique variance of items. Other alternatives exist, perhaps most prominently Latent Class Analysis (LCA), which attempts to find natural groupings of individuals based on the similarity of their response patterns. This method is the data-driven counterpart of the diagnostic systems of psychiatry, in that it allocates persons into categories. Its explanatory power for PLEs is somewhat doubtful, however; LCA and mixture analyses tend to produce profiles corresponding to categories of the total score (Rietdijk et al., 2014; Shevlin, Adamson, Vollebergh, de Graaf, & van Os, 2007).

In practice, the use of contemporary psychometric methods helped in the confident identification of superfluous items. No formal comparison with classical factor analysis was performed, however, so any gain in measurement precision was unfortunately not quantified. The number of dimensions extracted was also somewhat subjective, in that no numerical algorithms were used that would

unequivocally determine the number. Several such methodological avenues for exploratory analysis do exist, besides those based on the employed RMSEA and CFI when using ML extraction. Horn's Parallel Analysis, Velicer's Minimum Average Partial procedure, or more recently Comparison Data are at least to some extent applicable to multifactorial categorical data, but none guarantee perfect extraction of factors even in simulations (Ruscio & Roche, 2012), and extracting uninterpretable factors is pointless despite methodological sophistication.

There were also a number of limitations associated with the individual studies. In Study I, the PROD-screen showed fairly high endorsement rates on all items, making it very hard to determine how pathological a reported experience is – a "Yes" can range from tentative to very empathic and distressed. As response scales such as the frequency ratings of the CAPE appear to be quite easily understood and produce more information, a change in this direction would be recommended for improving the PROD-screen. The items are so few as to limit the level of detail required in the still-necessary exploratory work.

In the second study, the CAPE response distributions were plausible, and the extremely low endorsement rates for the two higher frequency categories of most hallucination and delusion items showed that responses were non-random. The study was, as is evident, hampered with respect to determining the factorial structure of PLEs in only including the "positive" items. Though the structure of the full scale has been addressed before in both exploratory and confirmatory analyses, the exceptionally large sample would have allowed a robust estimation of a MIRT model with four parameters (intercept and thresholds) for each item, even with a greater number of dimensions. The Women's Lifestyle and Health questionnaire was also suboptimal for testing clinical correlates; rather than using established scales for depression and anxiety, an *ad hoc* adaptation of hierarchical interview items was used. In addition to the wording being untested, some respondents had not fully understood the instructions for filling out these interrelated items on the form, which led to avoidable measurement noise. The relative magnitudes of the found associations are likely not affected by this, however.

In Study III, the main result was a negative finding, with no association between PLE and cognitive dimensions. Though power analyses indicated adequate sample size for detecting moderate associations, the study may still have been underpowered; especially when the sample isn't specifically selected for a type of PLEs as in most CHR studies, the true associations may be slightly smaller, as suggested by a the later study by our group (Lindgren et al., 2010). The use of self-reported PLEs may also attenuate the association, as part of the symptom endorsements are false positives.

In the fourth study, sample size and follow-up time were adequate for examining the research question. The explanatory power of the identified PLE dimensions still remained quite small. As with the PROD-screen, multiple response alternatives might improve on the information gained at very little added cost in respondent

effort – a change which has been applied in a more recent, shortened version (Loewy et al., 2011). Unfortunately, that shortening of the questionnaire was based on correlations with cross-sectional semi-structured interview-based scoring; though the PQ is intended for use with such an interview, data from the prospective studies of psychosis outcomes such as Study IV could better inform the selection of items for screening, as the validation data would be the final outcome of interest itself.

5.6 Conclusions and implications for future research

The exploratory analyses of PLEs revealed latent factors supporting a continuum from ordinary to psychotic experiences. Nevertheless, the subdivision of positive symptoms and the somewhat arbitrary selection criteria for the number of factors available in most situations indicate an underlying structure with very fluid demarcations. Many experiences do reliably occur together with a whole range of others, but common factors explain only a half of the total variance in reported symptoms. Though all the included studies used questionnaires, the same phenomenon is apparent when using structured interviews, and cannot be attributed to method-related assessment imprecision. This is partially unavoidable, despite future improvements in methods and items, as the individual PLEs are not necessarily common to all persons, and questionnaire measurement requires concrete and specific items, leaving much item-specific variance. The number of factors extracted is therefore somewhat arbitrary, and may need to balance accuracy in description against reliability in measurement. Ultimately, this choice will be made by predictive utility.

As all of the present studies used one PLE questionnaire each, the relationship between PLEs and the schizotypy/psychosis-proneness thought to be more permanent could not be examined. PLEs have previously shown moderate stability over the short term, but need to be studied together with other psychosis continuum measures in longitudinal settings to tease apart the state-trait aspects of these experiences.

In each of the examined instruments, some items were clearly not addressing PLEs or associated psychiatric problems. Healthy self-image and everyday fluctuations in well-being make it hard to assess hypomanic experiences and grandiosity by inquiring merely about relatively ordinary subjective affect. Moderate levels of magical thinking also appear to be a harmless phenomenon, as no association was found with psychiatric disorder. In order to incorporate these aspects of mania and possibly delusional ideation into questionnaires, it may be necessary to address more severe symptoms and refer to consequent behaviour rather than mere ideation.

Within the above-mentioned limits, the identified latent dimensions of psychotic-like experiences demonstrate the structural validity of the PLE questionnaires, while the concurrent clinical correlates and predictive value establish criterion validity.

Especially the finding of the empirically derived depersonalization dimension being specifically predictive of psychosis merits attempts at replication.

Finally, a conceptual conundrum will be is addressed: the extracted factors were correlated, but still separate; what is therefore their common relationship with the higher-order psychosis continuum concept? If the correlation was only detected in clinical studies, it could be argued the interrelatedness is a sampling artefact, but it is also found among general population samples, such as in Study I. If, on the other hand, this finding was an artefact of response tendency – a valid concern in self-report questionnaire studies – no meaningful dimensions would emerge. This theoretical gap can potentially be bridged by current theories of striatal dopamine dysfunction, as they can potentially account for positive symptoms through aberrant salience attribution, and for negative symptoms though reduced reward-dependent learning and heightened sensitivity to aversive stimuli (Heinz & Schlagenhauf, 2010). At least during acute schizophrenia, striatal dopamine synthesis is fairly elevated with Hedges' $g^* \approx 0.9$ (Fusar-Poli & Meyer-Lindenberg, 2013), lending empirical support. Striatal dopaminergic disturbance could perhaps even account for the cognitive and motor abnormalities present before the prefrontal cortical loss found in established psychotic disorder (Howes & Murray, 2014).

Despite the hope of finding the biological underpinnings of psychosis and creating definitive diagnostic tests, questionnaires are for the foreseeable future a cost-effective means of initial screening. The symptom- and deficit-focused approach deriving from psychiatry and neuropsychology could, however, be combined with other types of data. For instance, in an experience sampling study among patients with psychotic disorders, momentary level of psychotic symptoms varied with the current level of psychotic experiences, moderated by positive and negative affect, and with environmental stress (van Os, Lataster, Delespaul, Wichers, & Myin-Germeys, 2014). Similar methods could help identify clinically significant aberrant experiences within the entire psychosis spectrum, both on the aggregate and individual level. With such repeated measurements, which are onerous for the respondent, careful item analysis before inclusion is of course vital, underscoring the methodological arguments of this thesis.

In order to identify causal factors, it is also important to have a well-delineated phenotype. It has been proposed that individual symptom domains, such as paranoid delusions, should be addressed in order to progress in our understanding of underlying causes (Bentall & Fernyhough, 2008) of psychotic expression. In the present thesis, modern psychometric methods improved the conceptual separation and measurement precision of PLE-related rating scales. Such methods can thus be used to estimate the intensity of experience in the separate domains in non-psychotic populations, and provide clearer targets for aetiological research. In future studies a more fine-grained approach to assessing PLEs is recommended, in order not only to improve psychosis prediction accuracy but also our understanding of the psychosis continuum.

6 Acknowledgements

> Folly, as Töltenyi very justly observes, has a large circle of thought, a copiousness of ideas, but in the process of thought there are blanks and gaps, because the connexion between the ideas is wanting.
>
> *Ernst von Feuchtersleben: Principles of Medical Psychology (1847)*

This thesis has been long in the making, and there have been many people involved; too many to mention by name, but my gratitude is great towards you all.

I wish to thank to my superiors at KTL and THL for believing in me and my – perhaps foolish – foray into the milder expressions of the psychosis spectrum. I especially wish to express my vast esteem and gratitude towards my supervisor Jaana Suvisaari, a true scientist. Not only is she a patient, lucid, and inexhaustible fount of psychiatric research knowledge, which I have done my best to incorporate in this work, but also a considerate, compassionate, and skilled leader of her unit. I am thankful to Jouko Lönnqvist and Mauri Marttunen, successive heads of my department, who have both shown unflinching support for me in my development as a researcher. My supervisor and university teacher Hely Kalska has been my inspiration since my very first year of studies, demonstrating how psychological practice and research should be combined. Though I have not been able to follow her example, it reminds me of the importance of keeping clinical research grounded in hands-on experience and respect for subjective experience. She also introduced me early to both the questionnaire assessment of dimensional psychopathology and to the schizophrenia research team I joined, thus setting the path for this work.

The formative experience in my career was being recruited by Matti Huttunen as a research assistant. He has been a mentor and inspiration, in his continuous search for understanding of the twists of the human mind as an inimitable combination of therapist, author, and theorist. Our research coordinator Ulla Mustonen was for years and years the unifying force of our team, and I sorely miss the companionship of working together. Marko Manninen has been my closest co-worker for a dozen years, and we have shared many strange experiences and much fun doing psychosis research; his no-nonsense approach has kept my feet on the ground. Maija Lindgren has also long been a cherished co-worker and friend, inspirational in her ethical approach to work and science, and now in helping me understand the psychosis prodrome. Similarly, the other former team members Pirjo Käki, Tiia Pirkola, Antti Tanskanen, Annamari Tuulio-Henriksson, Taina Laajasalo, Mirka Torpo, and Liisa Varonen, have all made it a joy to be part of the group; thank you for your friendship.

My former employer Tyrone Cannon, the principal investigator and initiator of the Schizophrenia Twin and Helsinki Prodromal Studies, has been a central influence in his thinking on psychosis, and in his generous sharing of resources and

commentary, opening up for me the field of the psychosis risk research. Theo van Erp, David Glahn, and Rachel Loewy were great seniors in his group, in their exemplary scientific work and guidance, and in their friendly welcome.

Heartfelt thanks to Juha Veijola, Pirjo Mäki and Jouko Miettunen for inviting me into and working together on the NFBC86 study. Markus Heinimaa from Turku has also been a valuable source of collegial advice. I am likewise very happy that Christina Hultman and Elisabete Weiderpass graciously allowed me to work with and publish on the WLH data. All the involved personnel at the Helsinki adolescent psychiatric units receive heartfelt thanks for making the HPS data collection possible. I am, of course, in the greatest debt to all the participants in the studies, who shared their experiences, their time, and their trust; I hope we make it worthwhile. Furthermore, this work would not have been possible without the generosity of the following funding sources: the Päivikki and Sakari Sohlberg Foundation, the Ella and Georg Ehrnrooth Foundation, the Jalmari and Rauha Ahokas Foundation, the Emil Aaltonen Foundation, the Yrjö Jahnsson Foundation, and the Finnish Graduate School for Psychiatry.

Paolo Fusar-Poli, in agreeing to be my opponent, made me simultaneously humbled and grateful. Gratitude and humility was also induced by the thorough work of examiners Martti Tuomisto and Erika Jääskeläinen, who read this thesis with great attention, and offered valuable suggestions on changes, additions, and expanding context. Laura Hokkanen was very kind for taking on the role of *custos*, which I endeavor to make as easy as possible.

I wish to thank my friends for taking my mind off work every once in awhile – and also for discussing that work and forcing me to ponder its relevance to society. Finally I am grateful to all my extended family, Harriet, Heikki, Liisa, Samuli, Iikka, and Kirsikka, for being such unique individuals. My son Amos: thank you for sharing your joy of discovery! Virpi, the light of my life, without whom this work would not exist; I am fortunate beyond belief or merit in sharing with you not only a passion for science, but everything else.

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Note: for the sake of legibility, most DOI handles have been replaced by their corresponding shortDOI:s, which work equivalently on http://www.doi.org.

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8 Appendices

8.1 Community Assessment of Psychic Experiences (CAPE)

Positive items and frequency scale only, as used in Study II (Swedish version).
Source: http://cape42.homestead.com/. Retrieved on 2014-06-01.
Response alternatives are “Never, “Sometimes”, “Often“, and “Nearly always”.

Item
Do you ever feel as if people seem to drop hints about you or say things with a double meaning?
Do you ever feel as if things in magazines or on TV were written especially for you?
Do you ever feel as if some people are not what they seem to be?
Do you ever feel as if you are being persecuted in some way?
Do you ever feel as if there is a conspiracy against you?
Do you ever feel as if you are destined to be someone very important?
Do you ever feel that you are a very special or unusual person?
Do you ever think that people can communicate telepathically?
Do you ever feel as if electrical devices such as computers can influence the way you think?
Do you believe in the power of witchcraft, voodoo or the occult?
Do you ever feel that people look at you oddly because of your appearance?
Do you ever feel as if the thoughts in your head are being taken away from you?
Do you ever feel as if the thoughts in your head are not your own?
Have your thoughts ever been so vivid that you were worried other people would hear them?
Do you ever hear your own thoughts being echoed back to you?
Do you ever feel as if you are under the control of some force or power other than yourself?
Do you ever hear voices when you are alone?
Do you ever hear voices talking to each other when you are alone?
Do you ever feel as if a double has taken the place of a family member, friend or acquaintance?
Do you ever see objects, people or animals that other people cannot see?

8.2 PROD-screen (Heinimaa et al., 2003)

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Have you had any of following experiences during last six months?
Worrying, nervousness or anxiety (at least one week)
Trouble with sleep or loss of appetite (at least one week)
Bodily restlessness, e.g., pacing up and down, not being able to sit still (at least one week)
Difficulty in coping with stress related to ordinary daily life events (at least one week)
Difficulties thinking clearly or concentrating, interfering thoughts, or thoughts interrupted
Difficulties in considering alternatives or in making even minor decisions
Experience of thoughts running wild or difficulty in controlling the flood of thoughts
Difficulties in understanding written text or heard speech
Depression, apathy, loss of energy, or marked tiredness (at least one week)
Difficulty in controlling your speech, behaviour, of facial expression while communicating
Difficulty or uncertainty in making contact with other people (at least one week)
Lack of initiative or difficulty in completing tasks (at least one week)
Social withdrawal, e.g., avoidance of company, feeling best in solitude (at least one week)
Feeling that events in the environment or other people´s behaviour specifically concern yourself
Feeling unusually good or especially competent or important
Disorders in connection with vision, e.g., blurred vision, visual oversensitivity, or changing visual perceptions
Disorders in connection with hearing, e.g., oversensitivity, hearing odd sounds, or hearing sounds without a clear source
Difficulties in carrying out ordinary routine activities, e.g., washing, dressing, housework, shopping, cycling, driving, etc. (at least one week)
Feeling that something strange or inexplicable is taking place in yourself or in your environment
Feelings, thoughts, or behaviours that are weird or peculiar
Feelings that you are being followed or being influenced in some special way

8.3 Prodromal Questionnaire (Loewy et al., 2005)

The English language version of the 92-item version of the Prodromal Questionnaire (Loewy 2005) is reproduced here, with permission by the main author. Note that Studies III & IV used the Finnish-language version.
The response alternatives are “Yes” and “No”.

1 I am easily distracted by noises or other people talking.
2 The passage of time feels unnaturally faster or slower than usual.
3 I often have difficulty organizing my thoughts or finding the right words.
4 When I look at a person, or look at myself in a mirror, I have seen the face change right before my eyes.
5 I sometimes get strange feelings on or just beneath my skin, like bugs crawling.
6 I do not get along well with people at school or at work.
7 Familiar surroundings sometimes seem strange, confusing, threatening or unreal.
8 I often seem to live through events exactly as they happened before (déjà vu).
9 I sometimes smell or taste things that other people can’t smell or taste.
10 I have difficulty concentrating, listening or reading.
11 I have had troubles at school or work recently.
12 Sometimes I think that people can read my mind.
13 I have heard things other people can't hear like voices of people whispering or talking.
14 I can't express my feelings as well as I used to.
15 I have interests that other people find odd.
16 I have lost a sense of who I am.
17 I am less interested than I used to be in keeping clean or dressing well.
18 I often hear unusual sounds like banging, clicking, hissing, clapping, or ringing in my ears.
19 I often mistake shadows for people or noises for voices.
20 Things that I see appear different from the way they usually do (brighter, duller, larger, smaller, or changed in some other way).
21 I tend to be very quiet and keep in the background on social occasions.
22 People sometimes stare at me because of my odd appearance.
23 I wander off the topic or ramble on too much when I am speaking.
24 I believe in telepathy, psychic forces, or fortune-telling.
25 I often feel that others have it in for me.
26 My sense of smell sometimes becomes unusually strong.
27 Sometimes I have felt that I’m not in control of my own ideas or thoughts.
28 I have been feeling unhappy or depressed lately.
29 Everyday things affect me more than they used to.

30 I believe that I am especially important or have abilities that are out of the ordinary.
31 Other people think that I am a little strange.
32 Sometimes my thoughts seem to be broadcast out loud so that other people know what I am thinking.
33 I often feel that I have nothing to say or very little to say.
34 I am unusually sensitive to noise.
35 I am superstitious.
36 I have heard my own thoughts as if they were outside of my head.
37 I have trouble focusing on one thought at a time.
38 I often feel that other people are watching me or talking about me.
39 I get very nervous when I have to make polite conversation.
40 People comment on my unusual mannerisms and habits.
41 I am less interested in school or work lately.
42 I find it hard to be emotionally close to other people.
43 I tend to avoid social activities with other people.
44 I feel very guilty.
45 I am an odd, unusual person.
46 I sometimes feel that things I see on television or read in the newspaper have a special meaning for me.
47 My moods are highly changeable and unstable.
48 I have been unable to enjoy things that I used to enjoy.
49 My thinking feels confused, muddled, or disturbed in some way.
50 Sometimes I feel suddenly distracted by distant sounds that I am not normally aware of.
51 Recently, I have begun talking to myself.
52 I have had the sense that some person or force is around me, even though I could not see anyone.
53 I am in danger of failing out of school, or have been fired from my job.
54 I have some eccentric (odd) habits.
55 At times I worry that something may be wrong with my mind.
56 I have felt that I don't exist, the world does not exist, or that I am dead.
57 I have been confused at times whether something I experienced was real or imaginary.
58 People find me aloof and distant.
59 I tend to keep my feelings to myself.
60 I have experienced unusual bodily sensations (tingling, pulling, pressure, aches, burning, cold, numbness, shooting pains, vibrations or electricity).
61 I hold beliefs that other people would find unusual or bizarre.
62 People say that my ideas are strange or illogical.
63 I feel worthless.

64 I feel that parts of my body have changed in some way, or that parts of my body are working differently than before.

65 My thoughts are sometimes so strong that I can almost hear them.

66 I am not very good at returning social courtesies and gestures.

67 I sometimes see special meanings in advertisements, shop windows, or in the way things are arranged around me.

68 I often pick up hidden threats or put-downs directed at me in what people say or do.

69 I sometimes use words in unusual ways.

70 I am often angry, easily irritated or offended.

71 I have felt like I am looking at myself as in a movie, or that I am a spectator in my own life.

72 I am less able to do usual activities or tasks.

73 I have not been sleeping well lately.

74 At times I have felt that some person or force interferes with my thinking or puts thoughts into my head.

75 I have had experiences with the supernatural, astrology, seeing the future or UFOs.

76 Some people drop hints about me or say things with a double meaning.

77 I am often concerned that my closest friends, classmates, or co-workers are not really loyal or trustworthy.

78 I have little interest in getting to know other people.

79 I have seen unusual things like flashes, flames, blinding light, or geometric figures.

80 I get extremely anxious when meeting people for the first time.

81 I have felt like I am at a distance from myself, as if I am outside my own body or that a part of my body did not belong to me.

82 I find that when something sad happens, I am no longer able to feel sadness, or when something joyful happens, I can no longer feel happy.

83 I cry often.

84 I have seen things that other people apparently can't see.

85 I feel unable to carry out everyday tasks because of fatigue or lack of motivation.

86 Everyday things are more stressful than before, like school or work, social situations, deadlines or changes in a schedule.

87 I often avoid going to places where there will be many people because I will get anxious.

88 I have felt more nervous or anxious lately, and find it hard to relax.

89 I feel uninterested in the things I used to enjoy.

90 People often find it hard to understand what I am saying.

91 I have trouble remembering things.

92 People say that I seem “spacey” or “out of it”.