# Rethinking the role of sleep dysfunction in psychosis

Sarah Reeve

Balliol College

University of Oxford

Submitted for the degree of DPhil in Psychiatry, Michaelmas Term 2017

Supervisors: Professor Daniel Freeman & Dr Bryony Sheaves

# Rethinking the role of sleep dysfunction in psychosis

Sarah Reeve, Balliol College

Submitted for the degree of DPhil in Psychiatry, Michaelmas Term 2017

## Abstract

Sleep dysfunction – including sleep disorder symptoms, dissatisfaction with sleep, and other sleep abnormalities - has long been linked with psychosis, but the traditional view has been that sleep dysfunction is a consequence of psychosis. This thesis reconceptualises this relationship by testing a causal role of sleep dysfunction in psychosis. The first step was a systematic review (Chapter 1), in which correlational, but no causal, evidence is found for an association between sleep dysfunction and psychosis. This was addressed in Chapter 2 with a non-clinical manipulation study (n=68) which found that sleep loss caused increases in psychotic experiences, mediated by increases in negative affect. Chapter 3 explored the longitudinal relationship between short sleep duration and psychotic experiences in an at-risk group (n=160), finding that short sleep duration predicted later severity of psychotic experiences (although this prediction was not robust against conservative controls). In Chapter 4 the first detailed assessment of sleep disorders in a clinical group of individuals with psychosis (n=60) was reported, finding that sleep disorders were common, untreated, and often complex. A subgroup (n=29) were assessed twice more over the subsequent three months, allowing statistical modelling of the influence of insomnia on psychotic experiences over time (Chapter 5). The results again supported a significant predictive role of insomnia on psychotic experiences in this clinical group, mediated by negative affect. Finally, a novel exploratory study into hypersomnia in psychosis (n=26; Chapter 6) was carried out. The results suggested that hypersomnia is not associated with sedation or longer sleep duration, but is associated with increased fatigue, sedentary behaviour and depression. Overall, this thesis demonstrates that sleep dysfunction is not just a consequence of psychosis, but appears to have a causal role in the onset and maintenance of psychosis. The clinical implications are that sleep might be a novel therapeutic target in treating psychosis.

# Declaration

The work described in this thesis was carried out between October 2014 and November 2017 under the supervision of Professor Daniel Freeman and Dr Bryony Sheaves. The work in this thesis is my own, with only the exceptions listed below:

- The statistical analysis in Chapter 2 was carried out by Professor Richard Emsley.
- The statistical approaches in Chapter 3 and Chapter 5 were advised on by Alecia Nickless, although I conducted the analysis itself.
- The Early Detection and Intervention Evaluation trial data (Chapter 3) was collected by a large team of researchers led by Professor Tony Morrison.

I declare that the work presented in this thesis has not been submitted for any other degree, in this or in any other university or institute of learning.

# Acknowledgements

Firstly, I'd like to thank my supervisors, Daniel and Bryony. Daniel may regret having met me back in 2011, as without that he would have back all the time and encouragement that he has so generously given me since. I can only hope that the progress I've made from being a clueless undergraduate, to a slightly more competent graduate student, to whatever comes next, might make that sacrifice worthwhile. Bryony managed to get off comparatively lightly, only meeting me at the start of my DPhil, but she still had her work cut out. Even so, she showed unending patience with all of my questions and problems – and even better, she would often have an inspired solution. Together they provided me with all the support, advice, and enthusiasm needed to survive – and even enjoy – carrying out a DPhil. All I can say is how much I appreciate what they've both done for me.

Thanks also to go the whole O-CAP team, who collectively made this DPhil far more fun than it should have been. Special thanks go to Josie and George for being there for the highs, the lows, and all the boring admin in-between. I'd also like to thank Felicity for her laughs, her brilliance as a conference buddy, and her encouragement in my first steps of clinical work. Louise, as my work wife, deserves a big thank you for always having time for me, and for her energy and enthusiasm for everything. Thank you also to Eleanor for all of the recruitment wine (and advice) she shared with me, and for her tolerance of my 'DPhil mornings' the day following. Extra thanks go to Jess and Emma for their help with proof-reading this thesis (in addition to their general excellence of course). I could easily keep going for so many O-CAPers past and present (Nicola, Rowan, Mar, Jon, Steph, Dimitri, Emilie, Natalie, Saša, the list goes on) – but there are just too many, so I will have to do my best to thank them in person instead.

Of course, this DPhil is not just the result of the O-CAP team. Thank you to Richard Emsley and Alecia Nickless who both provided invaluable help with the statistics in this thesis. Thank you also to all the participants in my studies for their time and effort. I'd also like to thank the NHS and CRN staff who put so much work in to supporting my clinical studies, in particular: Matthew Broome, Bradley Mullins, Emma Donaldson, Carey Lewis, Emmie Williamson, and Antoinette McNulty. Thank you also to my funders (Department of Psychiatry, Medical Research Council, and Balliol College) without whom the DPhil wouldn't have been possible.

It is probably also a good time to thank the bizarre collection of people who chose to spend time with me over the last few years: Josh, Duncan, Ben, Elspeth, Gillian, Mirela, Jess, Kat, Charli, Fran, Sophie, and other friends. I'll pretend that their continual insistence that I have fun in both Oxford and London was helpful for this thesis, so that I get to thank them for hanging out with me and being interested in what I was doing.

Then to family. The reactions of my family to this DPhil can be characterised as 50% pride, and 50% a mixture of confusion, exasperation, and mockery. Yet, apparently this is the environment I thrive in – so thank you to them for providing it, and for being there before, during, and (hopefully) after this thesis. Thanks also to my parents for buying me a bed and a fridge, which were essential ingredients for surviving round two of student accommodation.

Lastly, thank you to Dave for putting up with three years of the X90 bus and Sunday sadness, and for always being there even when he was 40 miles away.

# Glossary

| Term | Description |
|---|---|
| Sleep dysfunction | A broad term comprising sleep disorder symptoms, objectively recorded sleep disturbance, or self-reported sleep disruption |
| Sleep disturbance | This term is used to refer to objectively recorded sleep issues (via polysomnography or actigraphy), unless otherwise specified. |
| Sleep disruption | This term is used to refer to subjectively reported sleep issues (that are non-specific to a particular sleep disorder), unless otherwise specified. |
| Psychosis | A collection of symptoms including delusions, hallucinations, and cognitive disorganisation. Most commonly associated with schizophrenia, but can occur in other mental health problems (e.g. bipolar disorder). |
| Delusions | An unfounded, often unusual belief, differing from normal beliefs in their distress or emotional charge, and in the extreme conviction with which they are held |
| Paranoia | An unfounded belief that others are deliberately intending to cause harm |
| Grandiosity | An unfounded belief relating to your superiority (in terms of skills, importance, fame, or some other dimension)e |
| Hallucinations | A sensory perception occurring in the absence of an external stimulus |
| Cognitive disorganisation | A tendency for thoughts and speech to become derailed, disorganised, or tangential |
| Negative affect | Negatively toned emotional states, used to collectively refer to depression and anxiety in this thesis |
| Depression | A collection of symptoms including low mood, hopelessness, lack of interest or motivation. |
| Anxiety | A collection of symptoms including feelings of fear or nervousness, autonomic hyperarousal, and tension. |

# Table of Contents

**1 Chapter 1 - The role of sleep dysfunction in delusions and hallucinations: a systematic review 1**

1.1 Introduction 1

1.2 Method 8

1.3 Results 9

1.4 Discussion 20

1.5 Aims for the thesis 25

1.6 Figures 27

1.7 Tables 28

**2 Chapter 2 - Disrupting sleep: the effects of sleep loss on psychotic experiences tested in an experimental study with mediation analysis 51**

2.1 Chapter abstract 51

2.2 Introduction 52

2.3 Method 55

2.4 Results 60

2.5 Discussion 62

2.6 Tables 66

**3 Chapter 3 - Sleep duration and psychotic experiences over time in patients at risk of psychosis: a secondary analysis of the EDIE-2 trial 71**

3.1 Chapter abstract **Error! Bookmark not defined.**

3.2 Introduction **Error! Bookmark not defined.**

3.3 Methods **Error! Bookmark not defined.**

3.4 Results **Error! Bookmark not defined.**

3.5 Discussion **Error! Bookmark not defined.**

3.6 Figures **Error! Bookmark not defined.**

3.7 Tables **Error! Bookmark not defined.**

**4 Chapter 4 - Sleep disorders in early psychosis 98**

4.1 Chapter abstract **Error! Bookmark not defined.**

4.2 Introduction **Error! Bookmark not defined.**

4.3 Method **Error! Bookmark not defined.**

4.4 Results **Error! Bookmark not defined.**

4.5 Discussion **Error! Bookmark not defined.**

4.6 Figures **Error! Bookmark not defined.**

4.7 Tables **Error! Bookmark not defined.**

**5 Chapter 5 - Insomnia, negative affect, and psychotic experiences over time: modelling relationships in patients with early psychosis 120**

5.1 Chapter Abstract **Error! Bookmark not defined.**

5.2 Introduction **Error! Bookmark not defined.**

5.3 Method **Error! Bookmark not defined.**

5.4 Results **Error! Bookmark not defined.**

5.5 Discussion **Error! Bookmark not defined.**

5.6 Figures **Error! Bookmark not defined.**

5.7 Tables **Error! Bookmark not defined.**

**6 Chapter 6 - Hypersomnia in psychosis: an initial investigation 147**

6.1 Chapter abstract **Error! Bookmark not defined.**

6.2 Introduction 147

6.3 Method **Error! Bookmark not defined.**

6.4 Results **Error! Bookmark not defined.**

6.5 Discussion **Error! Bookmark not defined.**

6.6 Figures **Error! Bookmark not defined.**

6.7 Tables **Error! Bookmark not defined.**

**7 Chapter 7 - Conclusions 167**

7.1 Summary of the thesis 167

7.2 Limitations 169

7.3 Recent results 171

7.4 Future directions 173

7.5 Figures 178

**8 References 179**

8.1 Chapter 1 References 180

8.2 Chapter 2 References 201

8.3 Chapter 3 References 207

8.4 Chapter 4 References 212

8.5 Chapter 5 References 217

8.6 Chapter 6 References 221

8.7 Chapter 7 References 226

# Chapter 1

# The role of sleep dysfunction in delusions and hallucinations: a systematic review

*This chapter has been adapted from the following paper, attached in Appendix 1.1*

*Reeve, S., Sheaves, B., & Freeman, D. (2015). The Role of Sleep Dysfunction in the Occurrence of Delusions and Hallucinations: A Systematic Review. Clinical Psychology Review, 42, 96–115.*

## 1.1 Introduction

Psychotic disorders have long been associated with sleep dysfunction. In case study descriptions of schizophrenia Kraepelin (1919) frequently refers to disturbed sleep and suggests that in treatment "*Rest in bed, supervision, care for sleep and food, are here the most important requisites"* (p.279). Bleuler (1950) also noted that sleep disturbances were common in psychosis: "*Sleep is habitually disturbed...Many patients do not want to sleep because they want to know what goes on during the night, or because they fear some violence to themselves while asleep"* (p.59). Patient accounts similarly show awareness of an interaction between their psychotic experiences and their sleep: *"They [the voices] keep me from going to sleep"*; *"the more tired I am the worse they get"* (Waite, Evans, et al., 2016). However, it is only in the last few years that a research agenda has emerged concerning sleep dysfunction as a putative contributory causal factor and therapeutic target in the occurrence of psychotic experiences (Harvey & Murray, 2011).

Outside of the clinical realm a literature exists showing the effects of sleep deprivation on individuals in the general population. Small studies carried out in the 1950s and 1960s reported that sleep deprivation in otherwise healthy individuals leads to emergence of psychotic-like experiences, such as hallucinations, with the frequency and severity of these experiences increasing with time spent awake (Bliss, Clark, & West, 1959; Brauchi & West, 1959; Katz & Landis, 1935; Luby, Frohman, Grisell, Lenzo, & Gottlieb, 1960; Pasnau, Naitoh, Stier, & Kollar, 1968; J. J. Ross, 1965; West & Janszen, 1962). Illustrative descriptions from these studies include: "*He saw a fine smoke begin to rise from the floor….as he stared at the floor more closely, fine jets of water appeared to be rising"* (Bliss et al., 1959)

and: "*During the course of the vigil Z [attributed] persecutory intent to one of the experimenters. He became more and more certain that this experimenter was personally interested in making life disagreeable for him*" (Katz & Landis, 1935). Intriguingly, one experimental study found that 100 hours of wakefulness was associated with a resurgence or exaggeration of psychotic symptoms in a small sample (n=6) of inpatients with schizophrenia (Koranyi & Lehmann, 1960).

In this chapter existing research on the link between disrupted sleep and individual psychotic experiences will be reviewed, with the aim of exploring whether psychotic experiences and sleep dysfunction are related, and if so, how. After reviewing the existing research addressing these questions the findings will be integrated into the theoretical literature of psychosis and sleep, thereby highlighting research questions for the rest of the thesis.

### 1.1.1 Psychotic experiences

This review is intended to cover the relationship between sleep dysfunction and the main positive psychotic experiences– hallucinations and delusions. Empirical research indicates that within non-affective psychotic diagnoses such as schizophrenia are actually multiple independent experiences, including paranoia, grandiosity, cognitive disorganisation, and hallucinations (Peralta & Cuesta, 1999; Ronald et al., 2014; Vazquez-Barquero, Lastra, Nu, Castanedo, & Dunn, 1996; Wigman et al., 2011). The heritability of each type of psychotic experience has been found to vary (Zavos et al, 2014).

Whilst psychotic experiences are typically associated with psychotic disorders such as schizophrenia, they are also common in the general population, with the prevalence of hallucinations and delusions estimated from epidemiological studies to be in the region of 7 – 11% (Linscott & van Os, 2013). In clinical groups the association of individual psychotic experiences is inflated due to Berkson's bias, whereby individuals with multiple problems are more likely to come into contact with clinical services (Bak, Drukker, van Os, & Delespaul, 2005; Maric et al., 2004). The individual psychotic experiences are now known exist on spectra of severity in the general population. In other words, like emotional disorders (Plomin, Haworth, & Davis, 2009), they exist as quantitative traits in the general population, with clinical populations experiencing the severe end of the continua.

The evidence supporting the idea that non-clinical and clinical psychotic experiences exist on the same continuum is threefold: in both groups they are associated with similar environmental (e.g. trauma, cannabis use) and psychological factors (e.g. anomalous experiences, worry) (Freeman, Pugh,

Vorontsova, Antley, & Slater, 2010; Johns & van Os, 2001); milder psychotic experiences are more common in families of individuals with psychotic disorders than families without such a history (e.g. van Os, Linscott, Myin-Germeys, Delespaul, & Krabbendam, 2009); and adolescents who report psychotic experiences are at greater risk of developing psychotic disorders in adulthood (e.g. Fisher, Caspi, & Poulton, 2013).

A focus on individual psychotic experiences has led to the development of detailed theoretical models, most notably for paranoia and hallucinations. Paranoia, defined as unfounded ideas of deliberate harm from others, is a key component of psychotic experience. Persecutory delusions as seen in clinical settings represent the severe end of a spectrum of persecutory ideation in the general population (Bebbington et al., 2013). One model for persecutory delusions (Freeman, Garety, Kuipers, Fowler, & Bebbington, 2002) conceptualises them as threat beliefs arising from a search for meaning of experiences that are unusual or emotionally significant for the individual. Factors such as negative emotional context, anomalous experiences, and cognitive biases contribute to the formation and selection of the threat belief. This and related models have led to the development of several highly targeted therapeutic interventions (Foster, Startup, Potts, & Freeman, 2010; Freeman et al., 2014; Freeman, Dunn, Startup, et al., 2015; Garety et al., 2014; K. Ross, Freeman, Dunn, & Garety, 2011) with demonstrable clinical success.

Cognitive models of hallucinations, defined as a sensory perception occurring in the absence of an external stimulus, are currently less comprehensive than those for delusions. Furthermore, the models that exist focus almost exclusively on auditory verbal hallucinations, neglecting hallucinations occurring in other forms or sensory modalities. One common feature in cognitive models for auditory verbal hallucinations is a dysfunction in 'source monitoring' such that internal experiences are misattributed externally (e.g. own thoughts being perceived as external voices). Some models of hallucinations also incorporate a direct role for emotion in symptom formation, which would predict that the content of the hallucination reflects emotional concerns (Garety, Kuipers, Fowler, Freeman, & Bebbington, 2001). More recently, models of auditory verbal hallucinations have sought to illuminate shared and differential mechanisms supporting hallucinations in clinical and non-clinical populations (J. M. Ford et al., 2014; Waters, Allen, et al., 2012). It is hoped that this will lead to improvement in theoretical models for hallucinations. To date these models have been affected by a reduced consensus

in empirical findings, evidenced by the relatively few instances of translation from model to therapeutic intervention compared to persecutory delusions.

In contrast with existing reviews linking sleep and schizophrenia (Benson, 2006, 2008; Cohrs, 2008; Lunsford-Avery & Mittal, 2013; Monti & Monti, 2004; Pritchett et al., 2012; Waters & Manoach, 2012; M. Zanini et al., 2013), this chapter will particularly focus on research that investigates the association of sleep dysfunction with individual psychotic experiences, with attention also paid to studies that jointly assess delusions and hallucinations as positive symptoms. Schizotypy studies are excluded, due to the mixing of positive psychotic experiences and other factors (e.g. dissociation) within the concept of schizotypy, unless the studies separate out individual psychotic experiences.

### 1.1.2 Sleep and sleep dysfunction

The regulation of sleep can be conceptualised in a two process model (Borbély, 1982) comprising a circadian component (intrinsic synchronisation of body functions to the light-dark cycle) and a homeostatic component, commonly referred to as 'sleep pressure' or need for sleep, which accumulates during wakefulness and is dissipated by sleep. Sleep itself can be divided into rapid eye movement (REM) and non-rapid eye movement (NREM) sleep stages. NREM sleep can further be divided into stages 1, 2, 3, and 4 in order of increasingly deeper sleep. Stages 3 and 4 are characterised by the presence of slow, high amplitude waves of neural activity and are often referred to jointly as slow wave sleep (SWS) or delta sleep. A typical sleep phase passes through NREM stages 1 to 4 before moving to a REM sleep stage. This cycle takes around 90 minutes, and repeats throughout the night, with an increasing predominance of REM sleep in the latter half of the night (Brown, Basheer, McKenna, Strecker, & McCarley, 2012).

These stages can be identified using polysomnography (PSG - see Table 1a), providing several objective measures of sleep. Another objective measure of sleep can be gained from actigraphy. This technique requires participants to wear a wrist watch style device which monitors movement and light exposure, usually over several weeks. This can then allow the interpolation of sleep-wake and circadian function (especially when combined with melatonin sequencing). Key sleep parameters relevant to this review are listed in Table 1b.

Sleep disorders comprise a broad range of disturbances (see Table 2). All of these disorders are associated with a subjective complaint of dissatisfaction in quality, timing, or amount of sleep, with

diagnosis requiring daytime distress and/or impairment. Definitive diagnosis of several sleep disorders (for example sleep apnoea) requires polysomnographic assessment, although this is not time or cost-efficient to carry out on a large scale. Therefore, many studies investigating sleep dysfunction rely on self-report of dissatisfaction with sleep quality, timing, or amount of sleep. These measures may then be considered as indexing symptoms of a sleep disorder such as insomnia (or other sleep disorders with appropriate additional symptom reports, e.g. nightmares) or simply be taken as a measure of low satisfaction with sleep.

In this thesis, unless otherwise specified, sleep dysfunction will be used as a broad term to encompass abnormalities in objective sleep variables (Table 1b), sleep disorders or symptoms (Table 2), and also subjective dissatisfaction with sleep in the absence of a sleep disorder diagnosis.

### 1.1.3 Sleep dysfunction in schizophrenia

Schizophrenia is the most common non-affective psychotic disorder, and a diagnosis long anecdotally linked with sleep dysfunction. Therefore when reviewing the link between sleep dysfunction and psychotic experiences, it is worthwhile to first consider what has been learned about the relationship between sleep dysfunction and schizophrenia. However, there is a great deal of variability reported in the literature. In part this can be explained by the heterogeneity of groups studied, for example, in symptoms, age, medication status, and also by the small sample sizes imposed by the demands of PSG. For example, most of the sleep variables listed in Table 1 have been reported to be altered in patients with schizophrenia (Monti & Monti, 2004). Yet a meta-analysis by Chouinard and colleagues (2004) found that medication-free patients with schizophrenia only exhibited increased sleep latency, decreased total sleep time, and decreased sleep efficiency. Furthermore, treatment naïve patients were found to exhibit a different set of sleep characteristics in comparison to the previously treated patients. This highlights the complex interaction of sleep dysfunction with symptom and medication status. Various circadian rhythm alterations such as melatonin phase and sleep/wake pattern irregularity have also been widely reported among patients with schizophrenia, and have previously been proposed to have etiological and therefore therapeutic relevance to the disorder (Anderson & Maes, 2012; Monti et al., 2013). Yet again, the interaction of circadian processes with antipsychotic medication and the wide range of dysfunction recorded prevent more detailed conclusions. Overall, it is clear that many aspects of sleep architecture are altered in individuals with schizophrenia. However, the interpretation of particular differences is often challenging due to the lack of consensus linking

particular aspects of sleep architecture (e.g. decreased stage 2 sleep) to daytime functioning (Wilson & Argyropoulos, 2012).

Where data exist, they indicate that prevalence rates of sleep disorders are elevated in schizophrenia. The majority of research has focused on insomnia, with estimates for the prevalence of clinically significant insomnia among individuals with a diagnosis of schizophrenia varying from 36 - 80%, depending on study recruitment criteria and definition of insomnia used (Freeman, Pugh, Vorontsova, & Southgate, 2009; Palmese et al., 2011; Xiang et al., 2009). Regardless, even the lowest estimates support the conclusion that rates of insomnia are elevated among patients with schizophrenia as compared to the general population (see Table 2). Rates of sleep apnoea also appear elevated in individuals with schizophrenia - around 15% of patients have been found to exhibit clinically significant symptoms (Sharafkhaneh, Giray, Richardson, Young, & Hirshkowitz, 2005). The link between sleep apnoea and schizophrenia is likely to be partly caused by the increased BMI in patients with schizophrenia, which is itself contributed to by long term use of antipsychotics and lifestyle factors (Winkelman, 2001). However there is a possible direct contribution of particular antipsychotic medications via their effect on muscle tone in the upper airway (Kalucy, Grunstein, Lambert, & Glozier, 2013). Symptoms of hypersomnia such as excessive daytime sleepiness and extended nocturnal sleep period are also commonly observed in patients with schizophrenia, and are again likely to be partly influenced by medication (Hawley, 2006; Hawley et al., 2010). For instance, one initial empirical study suggested that daytime sleep propensity is lower in patients with schizophrenia than in the non-clinical population, yet the researchers also found that antipsychotic medication increased sleep propensity and subjective complaints of sleepiness (Kluge et al., 2012). No aggregated figure for parasomnia prevalence is available for patients with schizophrenia, although there is recent evidence for an increased rate of nightmares among individuals with psychotic disorders (Michels et al., 2014; Sheaves, Onwumere, Keen, Stahl, & Kuipers, 2014).

Despite the apparent high prevalence of sleep disorders in patients with schizophrenia, and improving sleep being among patients' highest priorities for treatment (Auslander & Jeste, 2002; Waite, Evans, et al., 2016), sleep disorders in schizophrenia are rarely addressed directly. Clinicians and researchers have traditionally described sleep difficulties in schizophrenia as a secondary symptom, or simply ascribed their frequent presentation to the effects of antipsychotic medication or social isolation (Wilson & Argyropoulos, 2012). Yet many sleep disorders have existing effective treatments, which

are beginning to be validated in psychiatric groups (Freeman, Waite, Startup, et al., 2015; Waite, Myers, et al., 2016). This new approach coincides with the recent change in conceptualisation of sleep disorders in diagnostic manuals, with guidelines now in place stating that clinically significant sleep disorders should be considered as comorbid diagnoses and receive independent clinical attention accordingly, regardless of the presence of other mental or medical conditions (AASS, 2014; APA, 2013).

### 1.1.4 The current review

This review will restrict itself to examining the association between sleep dysfunction and individual psychotic experiences, specifically focusing on delusions and hallucinations, across clinical and non-clinical populations. The review attempts to address the following questions:

1. Do sleep dysfunction and psychotic experiences co-occur?
2. Does sleep dysfunction predict the onset or persistence of individual psychotic experiences? (or vice versa)
3. Does a change in sleep influence psychotic experiences? (or vice versa)

Factors mediating the relationship between sleep and psychotic experiences will be identified in the course of this investigation where possible.

## 1.2 Method

A search was carried out on PubMed for English language papers published in peer-reviewed journals containing the following terms: (Sleep OR Insomnia OR Dream* OR Nightmare*) AND (Delus* OR Hallucinat* OR Psychosis OR Psychotic OR Schizophren*).

### Inclusion criteria

Papers were required to have reported all of the below:

1. Explicit measures of psychotic experiences or positive symptoms;
2. Objective or subjective measure of sleep dysfunction;
3. Analysis testing a relationship between these two factors.

### Exclusion criteria

Papers fulfilling any of the below criteria were excluded:

1. Single case studies;
2. Relating primarily to:
    a. Dementias or other neurological conditions;
    b. Bipolar Disorder or other affective psychoses (including post-partum psychosis);
    c. Schizotypy or dissociation;
    d. Hypnogogic or hypnopompic hallucinations;
    e. Narcolepsy.

This search revealed 2657 papers (July 2015). Titles and abstracts were scanned, and if appropriate the whole paper, in order to ascertain whether each item fulfilled the inclusion and exclusion criteria. The reference lists of relevant papers were also scanned for further citations. This yielded a total of 66 papers, which for the purposes of discussion have been divided into investigations on non-clinical and clinical groups. The search was repeated in April 2017 and six additional articles fitting the criteria were added. See Figure 1 for a PRISMA flow diagram of the systematic review process.

The diversity of participant groups, measures, and methodologies revealed by the search, and the finding that many studies did not themselves aim to investigate the sleep and psychosis relationship, meant that it was not possible to apply a systematic methodological assessment tool. Methodological or other limitations are instead discussed in the results as required.

# 1.3 Results

## 1.3.1 General population

Eighteen papers investigating the relationship between sleep dysfunction and psychotic experiences in the general population were found (see Table 3). The majority of studies utilise subjective reports of either insomnia symptoms (8 papers) or other sleep disorder symptoms such as nightmares (7 papers), while the remaining three papers focus on sleep deprivation.

### Insomnia and psychotic experiences

Of the individual psychotic experiences, the relationship between paranoia and insomnia has received the most attention in the literature. Evidence from multiple sources suggests that insomnia and paranoia co-occur. For example, in national epidemiological surveys, a diagnosis of insomnia was associated with odds ratios (OR) of 1.78 – 2.54 for reporting concomitant paranoia (Freeman et al., 2011), with chronic insomnia linked to a 5 times increased likelihood of endorsing the statement "*a group of people are plotting to cause you serious harm or injury*" (Freeman, Brugha, et al., 2010). This relationship was partially mediated by depression and anxiety symptoms, and to a more limited extent by cannabis use, although an independent contribution of insomnia symptoms to paranoia remained even after controlling for these factors (Freeman et al., 2011, 2009).

In addition to the co-occurrence of insomnia with paranoia, longitudinal evidence indicates that insomnia predicts future paranoia. Insomnia was found to predict new paranoid thinking (OR 1.49 – 1.84) and persistence of existing paranoid thinking (OR = 1.2) at 18-month follow up in an epidemiological population survey (Freeman et al., 2012). In a smaller study, still using dimensional measures of insomnia and paranoia, insomnia was a significant predictor of paranoia and PTSD symptoms over 6 months (Freeman et al., 2013).

Insomnia has also been found to co-occur with and predict new hallucinatory experiences in the same general population samples, whilst controlling for both affective symptoms and paranoia (Sheaves, Bebbington, et al., 2016). Insomnia symptoms were cross-sectionally associated with a two to four times increased likelihood of endorsing hallucination items relating to hearing or seeing things that others couldn't, or hearing voices saying words or sentences. Longitudinal analysis further revealed that insomnia symptoms at baseline predicted new hallucinatory experiences at 18-month follow up.

More broadly, a large WHO study combining data from 56 countries (n=267,692) corroborates a cross-sectional relationship between sleep problems (indexed by a single self-report questionnaire item based on insomnia criteria) and several psychotic experiences. Self-reported sleep disruption significantly increased the likelihood of concomitant psychotic experiences (OR = 2.26 - 2.84 across different psychotic experiences), even after controlling for anxiety and depression (remaining ORs of 1.54 - 1.68) (Koyanagi & Stickley, 2015).

A recent cross-sectional study examined the genetic and environmental influences on sleep dysfunction and six individual psychotic experiences (Taylor, Gregory, Freeman, & Ronald, 2015). Five thousand 16-year old twin pairs completed self-report assessments for insomnia symptoms, subjective sleep quality, paranoia, hallucinations, cognitive disorganisation, grandiosity, anhedonia, and (parent rated) negative symptoms. The latter three factors were found to have only mild covariance with the sleep measures, but paranoia, hallucinations and cognitive disorganisation all demonstrated a strong association with the sleep dysfunction variables. Further analysis utilising modelling of genetic, environmental, and non-shared environment influences on the sleep and psychotic experience phenotypes demonstrated an aetiological overlap (i.e. shared genetic and environmental mechanisms). These relationships reduced, but again remained significant, after controlling for negative affect.

Overall there is strong evidence for insomnia co-occurring with a range of psychotic experiences, and some indications of insomnia predicting later psychotic experiences (limited to paranoia and hallucinations at this point). It should be noted that none of these longitudinal studies had the statistical power to test the reverse association (i.e. psychotic experiences predicting later sleep dysfunction). In terms of mediating factors for the relationship between insomnia and psychotic experiences, there is evidence of partial mediation by depression and anxiety.

## Other sleep disorders and psychotic experiences

A co-occurrence between psychotic experiences and sleep disorders other than insomnia is also supported by the literature. A number of sleep disorder symptoms (including excessive daytime sleepiness, cataplexy, and excessive snoring) were found to predict psychotic like experiences in two adolescent samples (Y. J. Lee, Cho, Cho, Jang, & Kim, 2012; Oshima et al., 2010). In the former study this relationship reduced but remained significant after controlling for depressive symptoms.

The likelihood of reporting psychotic experiences in another young sample (aged 11-12) increased with the number of reported sleep problems, including nightmares and daytime fatigue (Jeppesen et al., 2014). Distress associated with nightmares in a student sample was associated with increased paranoia, anxiety, and depression - as well as poorer occupational functioning (Levin & Fireman, 2002). Another student sample study found that several disturbances were associated with psychotic like experiences, including fragmented sleep and night anxiety – distress from psychotic like experiences was additionally associated with insomnia and unusual sensations at night (Andorko et al., 2017). Findings from the ALSPAC longitudinal cohort have also indicated that parasomnias during childhood (nightmares and night terrors) predict psychotic experiences at age 12 (Fisher et al., 2014), and that nightmares at age 12 predict psychotic experiences at 18 (Thompson et al., 2015) even after controlling for mood and psychotic experiences at age 12.

Altogether, these studies suggest that the relationship between sleep dysfunction and psychotic experiences is not limited to insomnia, but extends to other sleep disorders, and that these disorders co-occur with and may predict psychotic experiences. However, these findings are primarily based upon adolescent samples, and there is evidence that some sleep disorders may be more common in this group than in the adult population (e.g. parasomnias: Laberge, Tremblay, Vitaro, & Montplaisir, 2000). Therefore further investigation is needed to explore whether these links between parasomnias, excessive daytime sleepiness, and psychotic experiences are also present in the adult population.

## Sleep deprivation

Three studies have manipulated sleep via sleep deprivation to investigate its impact on psychotic-like experiences.

Kahn-Greene and colleagues (2007) deprived 25 non-clinical military volunteers of sleep for 56 hours, administering the Personality Assessment Inventory (PAI; Morey, 1991) at baseline and after sleep deprivation. Following sleep deprivation, increases were observed in the anxiety, depression and paranoia factors, but not in 'manic related symptoms' or 'schizophrenia symptoms' factors of the PAI. However, with the exception of paranoia, the scale dimensions do not appear to differentiate positive psychotic experiences from negative symptoms or affective symptoms. It is therefore difficult to interpret these results with regard to particular psychotic experiences.

In the second sleep deprivation study a student sample underwent a night of sleep deprivation or normal sleep in two counterbalanced sessions under laboratory conditions (Petrovsky et al., 2014). The psychotomimetic states inventory (PSI; Mason, Morgan, Stefanovic, & Curran, 2008) - a scale previously utilised for the self-report of effects of cannabis and ketamine on non-clinical volunteers in research contexts - was administered in the evening and morning for both conditions. The sleep deprivation condition resulted in significantly higher ratings in several PSI subscales (perceptual distortions, cognitive disorganisation, and anhedonia) but not others (mania, paranoia, or delusional thinking). No data on mood changes were collected. Given the robust link between insomnia and paranoia discussed previously (Freeman et al., 2011, 2012, 2009; Freeman, Brugha, et al., 2010), it is intriguing that no effects of sleep deprivation on paranoia were reported in this study. One potential rationale could be that the 8 item PSI subscale for paranoia includes several items which are less specific to persecutory ideation (e.g. "you feel that you deserve to be punished", "you feel that no-one understands you") than questionnaire items used in the paranoia-focused studies e.g. the Green et al. Paranoid Thoughts Scale (2008).

The last sleep deprivation study identified by the review took a somewhat different approach in utilising natural conditions of sleep deprivation – in this case by competitors taking part in a 168km ultramarathon event. Wrist actigraphy was used to track volunteer competitors in this event (involving an average of 46 h 38 min of wakefulness for this group), and on completion of the event a short questionnaire was filled out including an open-ended item asking about experiences of sleep deprivation (including hallucinations). Four of the seventeen volunteers reported experiencing hallucinations during the event.

These studies do indicate that experimentally reducing sleep increases psychotic-like experiences, although the evidence is inconsistent with respect to particular psychotic experiences. Besides the issues already highlighted in the questionnaires employed, these studies are limited by small sample sizes, and no analyses for mediating factors. In the case of the last study, there was also no baseline measurement or control group. Furthermore, no studies have yet attempted to treat insomnia in a non-psychosis population to test the effect on psychotic-like experiences.

### 1.3.2 Clinical populations

Tables 4 – 8 contain the fifty-four clinical studies retrieved by the search terms. Research in these clinical groups is complicated by the heterogeneity of individuals with psychosis, such as differing medication status, age, and current symptom presentation. Furthermore, many of the studies in clinical populations poorly differentiate between individual psychotic experiences, both in recruitment and in the measures used.

Over three quarters of studies retrieved were carried out with a group recruited for a diagnosis of schizophrenia or another psychotic disorder (41 papers), regardless of symptom presentation. Other participants were recruited based on broadly defined psychotic symptoms (5 papers). Another four studies utilise differing criteria (based on a mixture of positive psychotic and other symptoms) for selecting a sample at high risk of psychosis. Only four studies have addressed individual psychotic experiences in relation to sleep, and these predominantly focus on paranoia and persecutory delusions.

#### Polysomnography

Polysomnographic methods have been widely applied in this clinical population (Table 4). All of the studies are cross-sectional designs, using small samples, often seeking to associate clinical severity or symptom profiles with particular differences in sleep architecture.

The most consistently reported findings related to positive psychotic symptoms are REM sleep alterations. Positive symptoms have been found to be associated with a lowered REM onset latency in unmedicated and medication naive patients (Lauer, Schreiber, Pollmächer, Holsboer, & Krieg, 1997; Poulin, Daoust, Forest, Stip, & Godbout, 2003; Tandon et al., 1992; Yang & Winkelman, 2006) although there are inconsistent results, mostly from studies with smaller sample sizes (Ganguli, 1987; Tandon, Shipley, Eiser, & Greden, 1989; Taylor, Tandon, Shipley, Eiser, & Goodson, 1991). Similarly, reduced REM onset latency and an increased percentage of time in REM sleep were correlated with positive symptom severity (Sarkar, Katshu, Nizamie, & Praharaj, 2010). Another sleep EEG study found that positive symptom scores partially explained the variation (63%) in high frequency EEG activity during REM sleep (Tekell et al., 2005). An association between increased positive psychotic symptoms and reduced REM density has also been reported (Rotenberg et al., 1997; Yang & Winkelman, 2006).

The interpretation of these REM sleep abnormalities is opaque, as the function of REM sleep and the impact of alterations to it are still the subject of debate (e.g. Wamsley, 2014). Regardless, these changes do at the very least point to a disruption in neural regulation of sleep in individuals with psychosis, which could have an impact throughout the sleep period. For example, a reduced REM sleep onset latency may mean that less time is spent in slow wave sleep prior to first REM epoch.

In contrast to REM sleep, alterations in slow wave sleep have been more traditionally associated with negative symptoms (e.g. Keshavan *et al.* 1995, 1998; Kajimura *et al.* 1996). Yet three recent polysomnographic studies have reported that a reduced number and amplitude of spindles recorded during slow wave sleep is associated with greater positive symptom severity (Ferrarelli et al., 2010; Sarkar et al., 2010; Wamsley et al., 2012). Notably in one case a reverse association (increased sleep spindle amplitude with increased positive symptom score) was reported (Manoach et al., 2014).

Another PSG study tested if sleep state misperception (i.e. difference between PSG measured sleep duration and self reported sleep duration) was associated with clinical presentation among a large sample (n=148) of inpatients with schizophrenia (Bian et al., 2016). The only associations found were with negative symptoms, with no siginficiant link found between sleep state misperecption and positive psychotic symptoms

Importantly, the cross-sectional nature of these polysomnographic studies mean that they are unable to provide any conclusions on the direction of the relationship between REM sleep changes and psychosis. Furthermore, clinical participants were not recruited on the basis of particular psychotic experiences in any of the studies, and the measures used amalgamate multiple psychotic experiences. As a result, it is not possible to speculate on whether particular psychotic experiences have differing associations with the sleep architecture changes described.

## Actigraphy and circadian rhythm

Several recent studies have used actigraphy to assess sleep wake patterns and circadian dysfunction in psychosis, with the aim of linking circadian profiles to clinical features (Table 5).

Two longitudinal studies found that nightly variations in objective and subjective sleep disturbances were associated with increased paranoia and increased hallucinations the next day in outpatients with schizophrenia (Mulligan, Haddock, Emsley, Neil, & Kyle, 2016; Waters et al., 2011). Furthermore, both found that increases in negative affect partly explained this association between sleep disturbance

and psychotic experiences. A cross sectional study with a large sample of outpatients with schizophrenia (n=75) identified a relationship between reduced activity and positive symptom severity (Wichniak et al., 2011). On the other hand, two other cross-sectional studies utilising melatonin profiling as well as actigraphy (Bromundt et al., 2011; Wulff, Dijk, Middleton, Foster, & Joyce, 2012) did not find any significant association between positive symptom scores and sleep-wake or circadian phase abnormalities. Another report from an actigraphic monitoring study on older patients with schizophrenia found no associations between any clinical variables (including positive symptoms) and activity levels (Martin et al., 2001). From these initial findings, it seems likely that circadian dysfunction plays a part in the observed sleep dysfunction in individuals with psychosis.

Two more recent longitudinal studies have investigated sleep and circadian rhythm among a group identified as at high risk for transition to psychosis. Both studies, from the same group, indicate that sleep wake and circadian abnormalities are highly prevalent in this group – and in both cases they found that the sleep and circadian variables predict positive symptoms at baseline and one year follow up (Lunsford-Avery et al., 2016; Lunsford-Avery, LeBourgeois, Gupta, & Mittal, 2015).

Further studies utilising circadian profiling to link particular characteristics (e.g. advanced phase, delayed phase, free running) with symptomatology are a clear next step. The high diversity of sleep and circadian phenotypes reported in these initial small samples indicates that much larger studies will be required to identify if there are any particular associations by psychotic experience type.

### Sleep and clinical course of psychosis

Several different types of studies have linked sleep with the clinical course of psychosis, including investigations of individuals at risk of transition to first episode psychosis, retrospective reports following first psychotic episode, and quality of life in patients with non-affective psychosis (Table 6).

An intriguing subset of studies have investigated the link between sleep dysfunction and psychotic experiences in groups identified as at ultra-high risk of psychosis. Ruhrmann and colleagues (2010) utilised the sleep disruption item from the Structured Interview for Prodromal Symptoms (SIPS; Miller et al., 1999) as one of six predictors in a model predicting transition to psychosis from a high risk state. This resulting model predicted transition to psychosis over 18 months with a sensitivity of only 41.7% but a high specificity of 97.9%. Another high risk population study reported a high proportion of high risk individuals reporting sleep difficulties (78.4%), with a cross-sectional

association between sleep disorders and increased positive symptoms -but no significant predictive effect of sleep disorders on psychotic experiences at 2.5 year follow up (Poe et al., 2017). Lunsford-Avery and colleagues (2015) found that several actigraphically measured sleep variables (including decreased sleep efficiency and waking after sleep onset) were predictive of positive psychotic symptoms at baseline and 12 month follow up. A second study reported that circadian disruption was similarly linked to positive symptoms (Lunsford-Avery et al., 2016). An earlier cross-sectional study from the same authors on a similar sample (recording only self-reported sleep disruption) had found an association with negative symptoms but not positive symptoms (Lunsford-Avery et al., 2013).

Retrospective reports similarly indicate that sleep dysfunction is notable before transition to first episode psychosis. Tan & Ang (2001) surveyed the most commonly reported prodromal symptoms across a group of first episode non-psychotic (major depression or anxiety disorders) and psychotic disorder inpatients at a military hospital. Sleep disruption was one of the most common symptoms reported in the prodrome of psychotic disorders (77%), although this is non-specific as sleep disruption was even more common (97%) in the non-psychotic clinical group.

Sleep disruption is also known to be a common symptom prior to relapse, accounting for its typical inclusion in scales developed to predict relapse in clinical populations. The 34-item Early Signs Scale (ESS), which includes an item on recent sleep disruption, has demonstrated reasonable sensitivity (81%) and selectivity (79%) in identifying individuals who go on to relapse (Birchwood et al., 1989; Jørgensen, 1998a). The Warning Signals Scale, a shortened version of the ESS which retains self-reported sleep disruption as one of eight items, also demonstrated acceptable specificity (68%) and selectivity (77%) in detecting individuals prior to relapse in delusions in a large sample of 131 patients (Jørgensen, 1998b). These findings suggest that the presence of sleep dysfunction is predictive of relapse in to psychosis.

Sleep has also been linked to the broader well-being of individuals with psychosis. Several studies have indicated an association between the severity of positive psychotic symptoms and poorer sleep quality and quality of life (Afonso, Brissos, Figueira, & Paiva, 2011; Afonso, Figueira, & Paiva, 2014), including in a large sample (n=505) of patients with schizophrenia (Xiang et al., 2009). However two other studies with smaller samples found no direct link between self-reported sleep quality and positive symptoms (Ma, Song, Xu, Tian, & Chang, 2016; Ritsner, Kurs, Ponizovsky, & Hadjez, 2004).

Some research links sleep duration as a standalone variable to psychotic symptoms. One study, based on data from 623 individuals with schizophrenia, found that self-reported short (<7h) and long sleeper (>8) groups both had increased positive symptoms in comparison to normal sleepers (7-8h) (Hou et al., 2016). Reduced sleep duration (as indexed from clinical records during an inpatient stay) was found to be strongly associated with increased positive symptom severity within a group of patients with childhood-onset schizophrenia (Mattai et al., 2006).

From these studies it seems likely that sleep dysfunction among individuals with psychosis is associated with poorer clinical outcomes. The role of sleep dysfunction in predicting transition to first episode psychosis or relapse is especially intriguing. However, the majority of studies on this topic to date do not attempt to measure the influence of sleep on individual psychotic experiences and the measure of sleep dysfunction is often a single self-report item on duration or quality of sleep, limiting further interpretation of this association.

### Sleep disorders and their relationship to psychotic experiences in clinical groups

Only six studies identified by the review directly investigated whether sleep disorders are associated with positive symptoms or individual psychotic experiences (Table 7a).

Freeman and colleagues (2009) studied the relationship between insomnia and paranoia in a sample of 30 patients with persecutory delusions and a community sample of 300 individuals. High rates of insomnia were seen in the clinical group: 54% of the individuals with persecutory delusions had moderate or severe insomnia, versus 7.4% of the community sample. Within each group dimensional measures of paranoia and insomnia severity were positively associated, with the relationship partly mediated by depression and anxiety. A more recent cross-sectional study reported a potential role of dysfunctional emotion regulation strategies in mediating the relationship between insomnia and paranoia, in addition to supporting a role for negative affect in this relationship (Grezellschak, Jansen, & Westermann, 2017).

A large study on outpatients with schizophrenia in Hong Kong and Beijing (n=505) found that patients reporting one or more insomnia symptoms exhibited more severe positive symptoms than patients who slept well (Xiang et al., 2009). Severity of depressive symptoms was also a significant contributor to poor sleep in this sample. In contrast to the above findings, Palmese and colleagues (2011) found no correlation between insomnia symptoms and positive symptoms – although

insomnia prevalence was again found to be elevated in this clinical group, with 79% of participants reporting some sleep difficulty.

A high proportion of patients with psychotic disorders have also been found to experience weekly distressing nightmares: 55% , in comparison to a 0.9-6.8% estimated prevalence in the general population (Sheaves, Onwumere, et al., 2015). The authors found that the level of distress associated with the nightmares correlated with the severity of delusions, with this association remaining significant after controlling for nightmare frequency. Another study reported no association between nightmare frequency and positive symptoms, although patients and individuals at high risk for psychosis did show elevated nightmare frequency compared to controls (Michels et al., 2014).

The above studies are only cross-sectional and therefore cannot provide conclusions on the direction of causal effect. However, four recently-published trials have begun to investigate whether improving sleep in patients with schizophrenia would also reduce psychotic experiences, though all are substantially underpowered to address the connection adequately (Table 7b).

A double-blinded randomised controlled trial of a pharmacological treatment for insomnia (eszopiclone) in patients with schizophrenia found that positive psychotic symptoms showed greater reduction of insomnia symptoms in the treatment group (CI -3.1;0.4) versus the group receiving placebo (Tek et al., 2014). The confidence interval indicates the potential impact of the sleep intervention. While this difference was not statistically significant, such pilot trials are underpowered to produce effects significant at conventional levels (E. C. Lee, Whitehead, Jacques, & Julious, 2014). Furthermore, only 39 of the intended sample of 80 were recruited, which would have also reduced the study power.

An open-label non-randomised trial of a sodium oxybate (unlicensed for treatment of insomnia but used to treat sleep deficits in narcolepsy) on a small sample (n=8) of inpatients with schizophrenia (Kantrowitz et al., 2010) found large effect size improvements in several PSG sleep variables (including an increase in SWS time and REM onset latency), an improvement in self-rated sleep quality, and a reduction in total Positive and Negative Symptom Scale score (PANSS; Kay, Fiszbein, & Opfer, 1987). However, there was no reported significant specific effect on the positive symptoms subscale, and the reported outcomes do not provide mean changes or confidence intervals.

A case series study of cognitive behavioural therapy for insomnia (CBTi) reported a clear improvement in psychotic experiences and sleep. Fifteen outpatients with persecutory delusions received 4 sessions of CBTi in an un-blinded uncontrolled trial (Myers, Startup, & Freeman, 2011). In this case, large effect size improvements in insomnia symptoms and persecutory delusions were observed with additional reductions in anxiety, depression, and anomalies of experience. A subsequent single-blind randomised controlled trial testing the efficacy of CBT for sleep problems in 50 patients with persistent delusions and hallucinations has been completed (Freeman, Waite, Startup, et al., 2015). CBT was highly efficacious in improving insomnia in this population (Cohen's d = 1.9), but was inconclusive about the impact on psychotic experiences.

## Sleep and treatment for psychosis

A number of studies indicate that improvement in symptoms following antipsychotic treatment is associated with improvement in sleep variables (Taylor, Tandon, Shipley, & Eiser, 1991; Yamashita et al., 2004, 2005). Sleep dysfunction may also predict poorer clinical outcome following medication withdrawal (Chemerinski et al., 2002; Neylan, van Kammen, Kelley, & Peters, 1992), although in one smaller study sleep variables displayed no relationship with clinical symptoms (Nofzinger, Kammen, Gilbertson, Gurklis, & Peters, 1993). On balance such studies do appear to support an association between changes in positive psychotic symptoms and sleep. However, in this context it is difficult to associate any changes reported in sleep variables directly to changes in symptoms due to the likely direct effect of antipsychotic medication on sleep via their influence on multiple neurotransmitter systems (Cohrs, 2008). This effect particularly complicates interpretation of studies such as these on the impact of withdrawing or changing antipsychotic medications.

A recent randomised controlled trial indicated that improvement in positive psychotic symptoms following electroconvulsive therapy (ECT) is associated with an improvement in sleep variables (Zhang et al., 2012). The magnitude of reduction in positive symptoms following ECT significantly correlated with increases in sleep efficiency, REM onset latency, and REM density. Furthermore, sleep efficiency and positive psychotic symptoms improved further in the group which received ECT in addition to treatment as usual (antipsychotic medication) compared to a control group receiving only treatment as usual. The method of action of ECT on psychosis or sleep remains unclear (N. Kato, 2009) although it has been proposed that the mechanism of action of ECT is to mimic the EEG characteristics of slow wave/delta sleep (Charlton, 1999).

## 1.4 Discussion

There are surprisingly few studies that have assessed both individual psychotic experiences and sleep dysfunction. Currently the best quality evidence is in non-clinical populations, primarily utilising subjective reports of sleep. Here there is convincing evidence that psychotic experiences and sleep dysfunction co-occur (especially with respect to insomnia and paranoia). Yet this does not elucidate the direction of causal effects. There are fewer studies testing longitudinal data, but those that do indicate that sleep dysfunction (particularly symptoms of insomnia and nightmares) predicts later psychotic experiences. The opposite direction of effect (i.e. whether psychotic experiences predict later sleep dysfunction) remains to be tested. Evidence from manipulation studies, the strongest research design, is so far limited to sleep deprivation protocols using small sample sizes. Regardless, these studies do indicate that reducing sleep elicits psychotic-like experiences, as consistent with a causal role for sleep dysfunction in psychosis.

The clear next step for manipulation studies in the general population would be to test whether treatment of insomnia affects the occurrence of psychotic experiences. Such a study is already underway (Freeman, Sheaves, Goodwin, et al., 2015). Another focus for future research in non-clinical populations would be to determine the mechanisms underlying the association between sleep and psychotic experiences. Anxiety and depression are consistently found to act as partial mediators, but these are typically the only potential mediating factors tested. Furthermore, assessment of sleep disorders should move beyond insomnia given the association with other sleep disorders such as parasomnias reported here.

The studies in clinical populations are so far less conclusive. Issues include the heterogeneity of the populations studied (compounded by small sample sizes), and limited psychotic experiences assessment, although objective sleep assessments such as PSG and actigraphy have been widely applied – in contrast to the non-clinical studies. It seems likely that sleep dysfunction and psychotic experiences do co-occur, and that sleep might be a predictor of clinical change. The field requires much more attention. Assessing a wide variety of sleep processes in relation to individual psychotic experiences at different stages in the clinical course of psychotic disorders would be beneficial. Substantial tests of a potential reciprocal relationship between sleep dysfunction and psychotic experiences are also required. Further prospective studies are needed on the causal role that sleep problems may play in those at high risk of psychosis, particularly in relation to transition to first

episode psychosis. The typical sleep changes in adolescence, in particular exhibiting a preference for a later chronotype (Gau & Soong, 2003; Gradisar, Gardner, & Dohnt, 2011; Keyes, Maslowsky, Hamilton, & Schulenberg, 2015) are especially interesting in this regard, as this is the age at which psychotic experiences typically begin to manifest. More thorough assessments of sleep at this period of elevated risk would be an advantage for future studies – in particular, considering individual sleep disorders rather than single item measures of sleep disruption. As one example, a recent student population survey found that insomnia, nightmare frequency, and nightmare distress increased risk for mental illness in a dose-response fashion (Sheaves, Porcheret, et al., 2016).

### 1.4.1 Theoretical integration

It is likely that further development in the understanding of the connection between sleep and psychosis could be made by integrating the findings with the existing theoretical literature in each of the two areas.

Previous studies drawing upon a cognitive model of persecutory delusions (Freeman et al., 2002) have shown that negative affect (anxiety and depression) may be an important link between sleep and paranoia. Another shared factor between this model of psychosis and cognitive models of insomnia that remains to be tested is the thinking style of worry. Other important mechanisms proposed in this model of paranoia– such as anomalous experiences and reasoning biases – also remain to be investigated for their relationship with sleep dysfunction.

Cognitive models of hallucinations, while yet to be explicitly linked with sleep, have similarly emphasised negative affect as having a key role in the source, form, and content of hallucinatory experiences (Waters, Allen, et al., 2012). Furthermore, it is possible that sleep dysfunction could contribute to cognitive processes associated with hallucinatory experiences such as changes in source monitoring and inhibitory control. It is also possible that disturbances in sleep could mediate the relationship between trauma, PTSD, and hallucinatory experience (Morrison, Frame, & Larkin, 2003).

Parasomnias have historically received less attention than insomnia, yet the findings from this review indicate that these disorders may have an important relationship to psychotic experiences, particularly in the case of nightmares. Dreams and nightmares have a longstanding association with psychosis owing to perceived phenomenological similarity (Limosani, D'Agostino, Manzone, & Scarone, 2011; Mason & Wakerley, 2012). The notion that in both states internally generated images or ideas are

experienced as having an external origin, and as being intrinsically believable, has been carried through to modern theorising (Feinberg, 2011; Hobson, 2004). Cognitive models of nightmares (e.g. Nielsen & Levin, 2007) provide a link to models of paranoia and hallucinations via a shared emphasis on affective disturbance (in particular anxiety), as well as biases towards negative appraisals, for example of the nightmare event. Nightmares are most associated with REM sleep activity, which has been found to have an earlier onset and perhaps make up a higher percentage of total sleep time in psychotic populations – with both these characteristics correlating with increased positive psychotic symptom severity (Sarkar et al., 2010). An intriguing further direction for this research would be to directly investigate whether these REM sleep characteristics are associated with nightmare reports and psychotic experiences in clinical and non-clinical groups.

A neurodevelopmental model, where psychosis is seen as resulting from aberrant synaptic pruning during adolescence, has been linked to sleep dysfunction in psychosis (Keshavan, Anderson, & Pettergrew, 1994; Lunsford-Avery & Mittal, 2013). This account provides a plausible physiological underpinning for sleep dysfunction in psychosis, as structural abnormalities in key regions for promoting and maintaining sleep (e.g. the thalamus) are present in patients with first episode and chronic schizophrenia (Adriano, Spoletini, Caltagirone, & Spalletta, 2010), and in individuals who are at risk of schizophrenia (Lunsford-Avery et al., 2013). In the latter case the thalamic abnormalities were found to predict sleep dysfunction. Further work based on this model would need to establish a mechanism by which neurodevelopmental abnormalities or lack of sleep specifically lead to the experiences of individual psychotic experiences such as delusions or hallucinations.

Another body of research linking sleep and psychosis focuses on the impact of dysfunctional circadian rhythms in patients with schizophrenia. Studies utilising melatonin profiling in patients with schizophrenia have illuminated a range of circadian misalignments, such as delayed or advanced sleep phase, irregular sleep patterns, and free-running rest and activity patterns (where the circadian phase does not align to 24 hours and therefore sleep and wake phases occur at different times each day) (Bromundt et al., 2011; Wulff et al., 2012). The melatonin profile in individuals with schizophrenia has been described as 'blunted', with reduced circadian variation in melatonin secretion, and a reduced correlation between rise in melatonin and sleep efficiency (Afonso, Figueira, & Paiva, 2011). Two small RCTs have indicated that melatonin supplements improve sleep quality in patients with schizophrenia (Kumar, Andrade, Bhakta, & Singh, 2007; Shamir et al., 2000), although neither

investigated the effect of this treatment on psychotic experiences. A particular area of interest is the interaction of melatonin with dopamine and other key neurotransmitter systems associated with psychosis and the action of antipsychotic medications (Anderson & Maes, 2012; Monti et al., 2013). A range of animal studies have shown that melatonin inhibits dopamine release, increases dopamine turnover, and alters dopamine receptor activation (Monti et al., 2013), therefore one influence of a disturbed melatonin secretion profile could be the dopamine dysregulation thought to represent a 'final common pathway' to psychosis (Howes & Kapur, 2009). Again, further development based upon this model would need to specify mechanisms linked to individual psychotic experiences.

The salience model of psychosis (Kapur, 2003; Kapur, Mizrahi, & Li, 2005) has been linked to sleep dysfunction via the proposed role of sleep in synaptic homeostasis (Tononi & Cirelli, 2014). According to the synaptic homeostasis hypothesis, the need for sleep (or sleep pressure) arises physiologically as a result of synaptic potentiation in wakefulness (new connections are constantly made in response to the environment while awake, but there is no corresponding downscaling or removing of associations). Slow wave sleep, in this theory, mediates a downscaling of synaptic strength, allowing informational efficiency to be restored for the next day. This would imply that, if sleep were disturbed as it is in psychosis, downscaling would be disrupted, and therefore the ability of the neural network to correctly detect novel associations may be disrupted. This would allow abnormal associations to arise and persist without contextual corrections, and may result in type 1-style errors in assessing the informational value (or salience) of these associations. Reports of individuals with psychosis as being more likely to perceive meaning in ambiguous stimuli would support this account (Catalan et al., 2014; Galdos et al., 2011). On the other hand, the synaptic homeostasis hypothesis is primarily proposed as a theory of the function slow wave sleep, whereas the primary sleep architecture changes directly related to psychosis in the research literature to date involve REM sleep. Regardless, this theory does provide testable hypotheses for future research – for example, does sleep deprivation in non-clinical individuals cause similar changes in information processing? However, the model does not differentiate how this process could contribute to the emergence of individual psychotic experiences, which have been shown to be independent (e.g. Ronald, 2015).

A recent theory of positive psychotic symptoms provides a computational account based on Bayesian inference (Adams, Stephan, Brown, Frith, & Friston, 2013; Davies & Egan, 2013). Bayesian

conceptualisations of psychosis describe delusions and hallucinations as both arising from faulty inference. A belief can be held with great precision or confidence – this corresponds to a narrowed variance in the probability distribution. In Bayesian inference, prior beliefs (or expectations) are transformed to posterior beliefs by combination with the current sensory evidence, its perceived accuracy, and the predicted likelihood of that sensory data occurring given the prior belief. If a piece of evidence is thought to be accurate, but unlikely given previous beliefs, these older beliefs will be altered. Such a system can be thought of as having confidence in the accuracy of an existing belief.

One model based on this theory proposes that psychosis results from a reduction of this confidence in relation to current sensory evidence (Adams et al., 2013). An impact of this would be that beliefs or perceptions are more malleable in the face of sensory evidence, i.e. there is a reduced influence of previous beliefs due to their estimated low precision. One example of evidence for this model is that individuals with schizophrenia have been found to be less susceptible to visual illusions (Notredame, Pins, Deneve, & Jardri, 2014). As visual illusions work by capitalising on pre-existing beliefs about the environment, resistance to visual illusions in individuals with psychosis could be an expression of reduced influence of such beliefs. Some studies have reported that this reduced susceptibility to illusions correlates with the severity of positive psychotic symptoms (e.g. Silverstein et al., 2013) – and furthermore, sleep deprived non-clinical volunteers have been found to exhibit a similar resistance to visual illusions (Schmeider, Leweke, Sternemann, Emrich, & Weber, 1996; Sternemann et al., 1997). Further development of this model would need to provide an account of how sleep dysfunction could contribute to this change in inferential processing. For example, whether sleep dysfunction could contribute to the dopaminergic modulations that have been suggested as instantiating this computational change in psychosis (Adams et al., 2013; Castelnovo, Ferrarelli, & D'Agostino, 2015). However, these models again are limited by the absence of differentiation between different psychotic experiences.

In conclusion, there is an increasing acknowledgement of the potential role of sleep in the occurrence of psychotic experiences. It is clear from existing research that these two phenomena are connected. However, the direction of effect is yet to be demonstrated. Furthermore, the mechanisms by which sleep and psychotic experiences are linked remain to be established, although there are many plausible different routes for further investigation. It is likely that sleep dysfunction is a contributory cause to psychosis, or more specifically, an 'INUS' condition: an insufficient but non-redundant condition

which is itself unnecessary but sufficient for the occurrence of the effect (Mackie, 1965). In other words, sleep dysfunction by itself is unlikely to lead to psychosis in isolation and as itself, but in contribution with and by exacerbating various other factors (low mood, worry, cognitive impairments, neurotransmitter imbalance, neurodevelopmental impairment etc.). Sleep is a highly interesting area for research given the implications in terms of prevention and treatment of psychosis. Furthermore, even if future research indicates no causal connections between sleep and psychosis, it could be argued that a high prevalence of sleep problems in patients with psychosis should still become a target in clinical services, since it is an important problem in its own right, for which effective treatments exist (Freeman, Waite, Startup, et al., 2015).

## 1.5 Aims for the thesis

This systematic review has highlighted several areas where further research is needed in order to explore the possible role of sleep dysfunction in psychosis. Firstly, a manipulation test of whether insomnia causes psychotic experiences is required. The majority of evidence identified in this review is correlational, and the experimental studies focused on sleep deprivation rather than attempting to model insomnia-like sleep loss. Furthermore, there has been no examination of mechanisms by which sleep dysfunction increases psychosis in any manipulation study. An experimental study aiming to address this these issues is described in Chapter 2.

A priority identified in this review is the relationship between sleep dysfunction and the development of a first episode of psychosis from the 'at-risk' state. If sleep dysfunction is associated with increased severity of psychotic experiences or transition, this would have implications for the etiology of psychosis, and might indicate sleep treatment could prevent worsening of psychotic symptoms in this group. Accordingly, a large cohort dataset from an at-risk patient group is analysed in Chapter 3, with the aim of investigating the predictive value for sleep dysfunction on psychotic experiences in this group.

Another issue raised in this review is the lack of attention to date on sleep disorders in psychosis. Insomnia in psychosis has been investigated in very few studies, and only one study has investigated nightmares among individuals with psychosis. However, clinical impressions are that sleep disorders in psychosis are common and complex (Rehman et al., 2016). If so, there may be an unmet clinical need in this group for sleep disorder assessment and treatment, even independently of any role that

sleep dysfunction might have in contributing to psychotic experiences. A descriptive study, reported in Chapter 4, provides an initial assessment and report of sleep disorders presenting in a group of individuals with non-affective psychosis. The associations of these sleep disorders to other clinically relevant factors are also assessed.

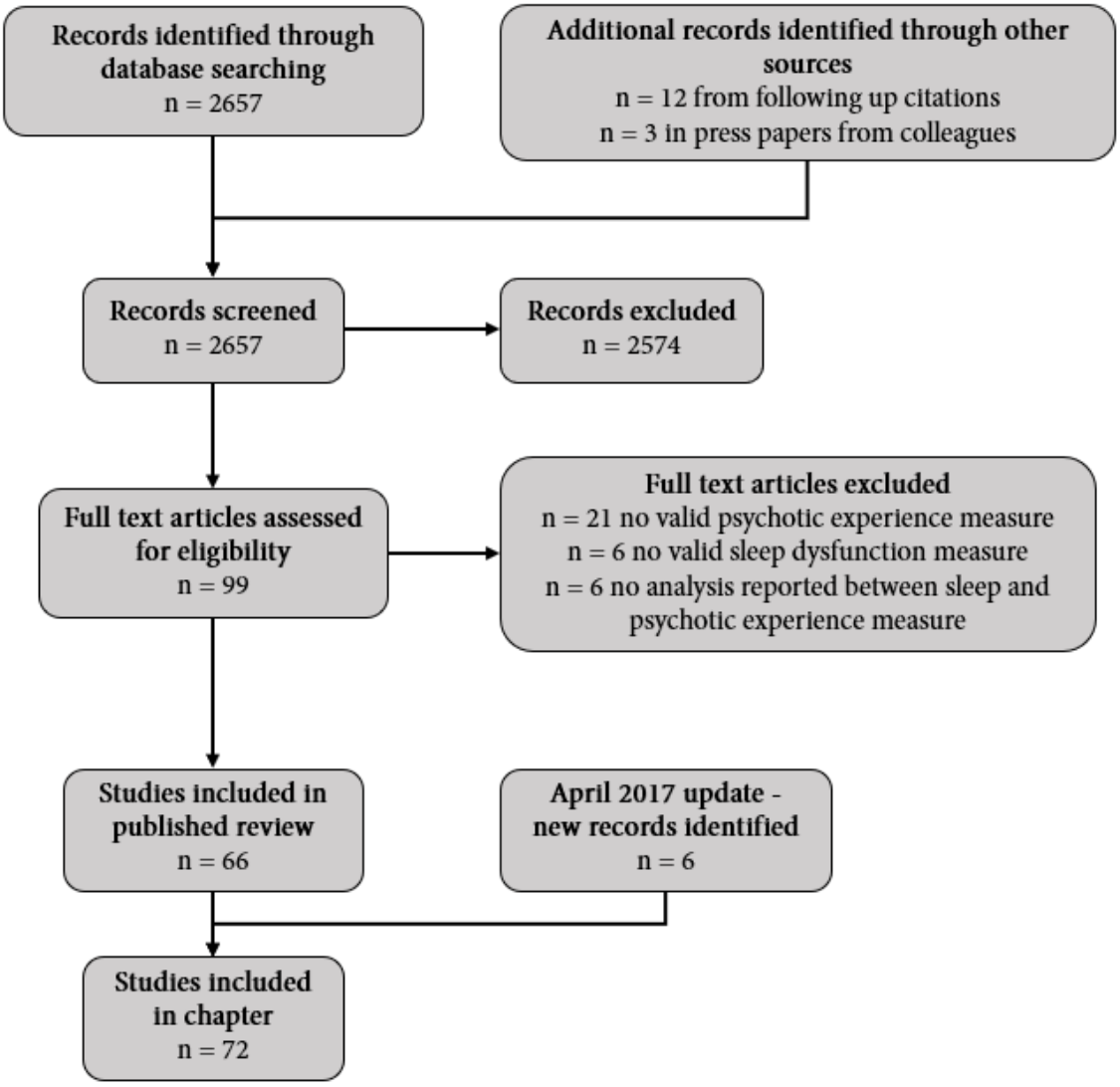
The review in this chapter has sought to investigate whether sleep dysfunction has a role in psychotic experiences. However, no research was identified that assessed the opposite direction of effect (i.e. psychotic experiences predicting later sleep dysfunction). It is likely that some contribution to sleep dysfunction is made by this route, but it is important to assess how much (especially in comparison with the contribution of sleep dysfunction to later psychotic experiences). In Chapter 5 these directions of effect are tested against each other using longitudinal data from a subgroup of the Chapter 4 participants.

In carrying out the research for the above chapters, it became clear that oversleeping and sleepiness were common sleep difficulties among individuals with psychosis, but had received little attention in the clinical and research literature. Therefore Chapter 6 describes an exploratory analysis of the presentation and issues associated with sleepiness and oversleeping in a group of individuals with psychosis.

It is hoped that this programme of research will shed light on the mechanisms linking sleep dysfunction and psychotic experiences, and thereby provide information of etiological and clinical relevance to the literature.

## 1.6 Figures

### 1.6.1 Figure 1: PRISMA Cohort Diagram



## 1.7 Tables

### 1.7.1 Table 1a: Objective sleep measurement methods

| Sleep or circadian variable | Definition |
|---|---|
| Polysomnography (PSG) | Recording of electrical activity during sleep from multiple sources – typically including electroencephalography, electrooculography, electromyography, and electrocardiogram respectively monitoring electrical activity in the brain, eyes, muscles and heart. May also include respiratory indicators or other measurements. |
| Actigraphic monitoring | Continuous activity monitoring, usually carried out over several days via a device worn on the wrist, allows objective measurement of sleep-wake patterns (time to sleep, time to wake, sleep onset, night wakings etc.) |
| Melatonin concentration | Melatonin production rises during evening and peaks during the night. Irregular peaks or reduced amplitude in melatonin cycles are associated with circadian rhythm sleep-wake disorders (Table 2). Regular collection of saliva or urine allows measurement of concentrations of melatonin throughout the day, which can be combined with actigraphic monitoring to assess circadian functioning |

## 1.7.2 Table 1b: Commonly assessed sleep variables

| Sleep or circadian variable | Definition |
|---|---|
| Sleep latency | Time from lights out until first occurrence of sleep |
| Sleep Period Time (SPT) | Time from sleep onset until final awakening, including intermittent waking periods |
| Total Sleep Time (TST) | Total time spent in any REM or NREM sleep stage |
| Sleep efficiency (SE) | Percentage of time in bed (TIB) spent asleep |
| REM onset latency | Time between sleep onset and the first occurrence of REM |
| REM density | Measure of frequency of rapid eye movements during REM sleep |
| Slow wave sleep (SWS) | Amount of non-REM sleeps stages 3 and 4 (also known as delta sleep) |

### 1.7.3 Table 2: Sleep disorders and their symptoms

| Sleep disorder/symptom | Definition/key symptoms | Population prevalence (from DSM-V APA, 2013) |
|---|---|---|
| Insomnia | Difficulty initiating or maintaining sleep or nonrestorative sleep causing significant functional impairment. | 6-10% |
| Sleep apnoea | A breathing related sleep disorder where breathing is obstructed during sleep, blocking off airflow and disturbing sleep. The primary symptoms are loud snoring and daytime sleepiness. | 2-4% |
| Hypersomnia | Characterised by symptoms of excessive daytime sleepiness, and/or extended nocturnal sleep period, | 1% |
| Parasomnias | A group of sleep disorders linked by abnormal behaviours, emotions, and dreams during sleep that lead to intermittent awakenings and difficulty resuming sleep. | Varies across disorder |
| Nightmare Disorder | A disorder within the parasomnia group, characterised by frequent nightmares causing clinically significant distress or impairment in functioning – one or more episodes a week is classed as moderate severity. | 6% |
| Circadian rhythm sleep-wake disorders | A group of sleep disorders resulting primarily from alteration of the circadian system or to misalignment between the endogenous circadian rhythm and the sleep-wake schedule required by an individual's environment. These disorders are split in to type by the alteration seen for example - delayed sleep phase, advanced sleep phase and non-24 hour sleep-wake type. | Varies across sub-type |

### 1.7.4 Table 3: Studies addressing the link between sleep and psychotic experiences in non-clinical populations

| Citation | Design | N | Sample characteristics | Psychosis measure(s) | Sleep dysfunction measure(s) | Comment on findings | Linked? |
|---|---|---|---|---|---|---|---|
| (Andorko et al., 2017) | Cross-sectional | 420 | Undergraduate psychology students | *Psychotic experiences*<br>PQ-B | *Sleep disorder symptoms*<br>IOWA | Insomnia (fragmented sleep, night anxiety) and sleep onset hallucinations significantly associated with PLE frequency. Initial insomnia, movements at night, and sensations at night linked with PLE distress | Y |
| (Fisher et al., 2014) | Longitudinal | 6796 | Children (aged 12) from population cohort (ALSPAC) | *Psychotic experiences*<br>PLIKSi | *Sleep disorder symptoms*<br>Postal questionnaires (completed by mothers) at age 2.5, 3.5, 4.75, 6.75, and 9 years.<br>Sleep problems at 12 years assessed in semi-structured diagnostic-based interview with child. | Children with more frequent nightmares between 2.5 and 9 years more likely to report psychotic experiences at age 12.<br>Children reporting any parasomnia at age 12 also found to have higher rates of psychotic experiences. | Y |
| (Freeman et al., 2009) | Cross-sectional | 300 | Convenience sample from community | *Paranoia*<br>G-PTS | *Insomnia symptoms*<br>ISI, Sleep-50 | Insomnia associated with paranoid thinking, association partly accounted for by anxiety and depression. | Y |
| (Freeman, Brugha, et al., 2010) | Cross-sectional | 8580 | National epidemiological survey (British National Survey of Psychiatric Morbidity) | *Paranoia*<br>PSQ, SCID-II | *Insomnia symptoms*<br>CIS-R | Insomnia associated with an increase in paranoid thinking, association partly accounted for by affective symptoms or cannabis use. | Y |
| (Freeman et al., 2011) | Cross-sectional | 7281 | National epidemiological survey (USA - Adult Psychiatric Morbidity Survey) | *Paranoia*<br>Paranoia items from survey (3) | *Insomnia symptoms*<br>CIS-R | Paranoia associated with insomnia, Odds ratios of insomnia diagnosis increases with level of paranoia. | Y |

| Citation | Design | N | Sample characteristics | Psychosis measure(s) | Sleep dysfunction measure(s) | Comment on findings | Linked? |
|---|---|---|---|---|---|---|---|
| (Freeman et al., 2012) | Longitudinal | 2382 | National epidemiological survey (British Psychiatric Morbidity Survey 2000) | *Paranoia*<br>PSQ (3 items)<br>SCID-II (at baseline and 18 month follow up) | *Insomnia symptoms*<br>CIS-R (at baseline and 18 month follow up) | Insomnia symptoms predicted new paranoid thinking or persistence of existing paranoid thinking at 18 month follow-up. | Y |
| (Freeman et al., 2013) | Longitudinal | 106 | Individuals attending hospital after an assault | *Paranoia*<br>G-PTS<br>SSPS<br>PANSS<br>PSYRATS<br>4 paranoia and threat related visual analogue scales<br>(all at baseline and 6 month follow up) | *Insomnia symptoms*<br>ISI (at baseline and 6 month follow up) | Insomnia at baseline was found to predict paranoia (G-PTS) and post-traumatic stress disorder symptoms at 6 month follow up.<br>Current insomnia was also a significant predictor of paranoia scores at 6 months. | Y |
| (Hurdiel et al., 2014) | Manipulation (sleep deprivation) | 17 | Volunteers completing ultramarathon event | *Psychotic experiences*<br>Hallucinations – open ended question on completion | *Objective sleep*<br>Wrist watch actigraphy throughout event<br>*Sleep deprivation*<br>Average 46h 38min | 4 out of 17 participants reported experiencing hallucinations during the exercise event. | Y |
| (Jeppesen et al., 2014) | Cross-sectional | 1623 | Adolescents (aged 11/12 years) from population cohort | *Psychotic experiences:*<br>K-SADS-PL | *Subjective sleep*<br>Self-report of sleep disruption in structured interview | Likelihood of psychotic experiences increased with sleep problems and emotional or neurodevelopmental disorders.<br>Increased prevalence of sleep disorders among children with psychotic experiences. | Y |

| Citation | Design | N | Sample characteristics | Psychosis measure(s) | Sleep dysfunction measure(s) | Comment on findings | Linked? |
|---|---|---|---|---|---|---|---|
| (Kahn-Greene et al., 2007) | Manipulation (sleep deprivation) | 25 | Non-clinical volunteers (recruited from military) | *Psychotic experiences*<br>PAI (pre and post sleep deprivation) | *Sleep deprivation*<br>56 hours | Sleep deprivation resulted in increase in anxiety, depression and paranoia, but not manic-related symptoms or schizophrenia symptom factors. | Y |
| (Koyanagi & Stickley, 2015) | Cross-sectional | 267692 | WHO population based survey (56 countries) | *Psychotic experiences*<br>Single items from CIDE for delusional mood, delusions of persecution/reference, delusions of control, hallucinations | *Insomnia symptoms*<br>1 item for presence of insomnia symptoms (5 point scale of 'none' to 'extreme') | Sleep problems associated in dose-response fashion with psychotic symptoms in almost all countries with significant ORs from 2.26 - 2.84 (1.54 - 1.68 after controlling for anxiety and depression). | Y |
| (Y. J. Lee et al., 2012) | Cross-sectional | 7172 | 23 high school cohorts of students (aged 12-17) | *Psychotic-experiences*<br>ESI<br>*Psychosis risk:*<br>Y-PARQ | *Insomnia*<br>Self report questionnaire modelled on ICD-10 diagnostic criteria for insomnia<br>*Excessive Daytime Sleepiness*<br>ESS<br>*Cataplexy*<br>Single item, muscle weakness<br>*Snoring*<br>Single item, frequency of snoring | Insomnia and excessive daytime sleepiness predicted psychotic like experiences (and higher risk scores for psychosis) in adolescent group, independent of depressive symptoms. | Y |

| Citation | Design | N | Sample characteristics | Psychosis measure(s) | Sleep dysfunction measure(s) | Comment on findings | Linked? |
|---|---|---|---|---|---|---|---|
| (Levin & Fireman, 2002) | Cross-sectional | 116 | Undergraduate psychology students selected for high nightmare prevalence (at least 3 – 10a year) from screening survey | *Psychoticism/Paranoia*<br>SCL-90-R | *Nightmares*<br>Dream Log | Nightmare distress (not frequency) associated with paranoia, anxiety, depression.<br>Nightmare frequency associated with psychoticism scale score. | Y |
| (Oshima et al., 2010) | Cross-sectional | a) 279<br>b) 62 | High school cohort of students (aged 12-17)<br>a) singletons<br>b) twin students (31 pairs) | *Psychotic-experiences*<br>Custom self-report questionnaire (4 items) | *Subjective sleep*<br>GHQ-12 | Poor sleep associated with psychotic like experiences. | Y |
| (Petrovsky et al., 2014) | Manipulation (sleep deprivation) | 24 | Student volunteers | *Psychotic-experiences*<br>PSI (pre and post sleep deprivation) | *Sleep deprivation*<br>Overnight sleep deprivation<br>*Sleepiness*<br>SSS at 9pm and from 7 – 10am following morning (6 time points in total) | Sleep deprivation induced perceptual distortions, cognitive disorganisation and anhedonia, but not mania, paranoia or delusional thinking. | Y |
| (Sheaves, Bebbington, et al., 2016) | Longitudinal | a) 8580<br>b) 7403<br>c) 2046 | National epidemiological surveys:<br>a) British Psychiatric Morbidity Survey 2000<br>b) British Psychiatric Morbidity Survey 2007<br>c) British Psychiatric Morbidity Survey 2000 18 month follow up | *Paranoia and hallucinations*<br>PSQ (2 items) (at baseline and 18 month follow up) | *Insomnia symptoms*<br>CIS-R (at baseline and 18 month follow up) | Insomnia predicted new hallucinatory experiences at 18 month follow up.<br>Presence of insomnia raised likelihood of reporting hallucinations cross-sectionally.<br>All remained significant when controlling for depression, anxiety and paranoia. | Y |

| Citation | Design | N | Sample characteristics | Psychosis measure(s) | Sleep dysfunction measure(s) | Comment on findings | Linked? |
|---|---|---|---|---|---|---|---|
| (Taylor et al., 2015) | Cross-sectional | 5000 | Twin pairs (aged 16) from population cohort | *Psychotic-experiences*<br>SPEQ | *Subjective sleep*<br>PSQI<br>*Insomnia symptoms*<br>ISI | Shared genetic and environmental mechanisms for psychotic experiences and sleep dysfunction – association reduced but remained significant after controlling for negative affect. | Y |
| (Thompson et al., 2015) | Longitudinal | 4270 | 18 year old population cohort sample (ALSPAC) | *Psychotic-experiences*<br>*PLIKSi* (at age 12 and 18) | *Sleep disorder symptoms*<br>Postal questionnaires (completed by mothers) at age 2.5, 3.5, 4.75, 6.75, and 9 years.<br>Sleep problems at 12 years assessed in semi-structured diagnostic-based interview with child. | Nightmares at age 12 a significant predictor of psychotic experiences at age 18, remaining after adjustment for mood and other confounders. | Y |

CIDI =(Kessler & Ustün, 2004); CIS-R = Clinical Interview Schedule (revised) (Lewis, Pelosi, Araya, & Dunn, 1992); ESI = Eppendorf Schizophrenia Inventory (Mass, 2000); ESS = Epworth Sleepiness Scale (M. W. Johns, 1991); GHQ-12 = 12 item version of the General Health Questionnaire (Goldberg & Williams, 1988); G-PTS = Green et al. paranoid thoughts scale (Green et al., 2008); ISI = Insomnia Severity Index (C M Morin, 1993); K-SADS-PL- Schedule for schizophrenia and affective disorders for school-age children, present and lifetime edition (Kaufman et al., 1997); PAI = Personality Assessment Inventory (Morey, 1991); PANSS = Positive and Negative Symptom Scale (Kay et al., 1987); PLIKSi = Psychosis-Like Symptom Interview (Horwood et al., 2008); PSI = Psychotomimetic States Inventory (Mason et al., 2008); PSQ = Psychosis Screening Questionnaire (P. Bebbington & Nayani, 1995); PSQI = Pittsburgh Sleep Quality Index (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989); PSYRATS = Psychotic symptom rating scales (Haddock, McCarron, Tarrier, & Faragher, 1999); SCID-II =Structured Clinical Interview for DSM-IV disorder (First, Gibbon, Spitzer, Williams, & Benjamin, 1997); SCL-90-R = Symptom Checklist 90 (Revised) (Derogatis, 1994); Sleep-50 = (Spoormaker, Verbeek, van den Bout, & Klip, 2005); SPEQ = Specific Psychotic Experiences Questionnaire (Ronald et al., 2014); SSPS = State Social Paranoia Scale (Freeman et al., 2007); SSS = Stanford Sleepiness Scale (Hoddes, Zarcone, Smythe, Phillips, & Dement, 1973); Y-PARQ = Youth Psychosis at Risk Questionnaire (Ord, Myles-Worsley, Blailes, & Ngiralmau, 2004)

## 1.7.5 Table 4: Studies addressing the link between positive symptoms and sleep measured with polysomnography in clinical groups

| Citation | N | Sample characteristics | Psychosis Measure(s) | # PSG nights | Comment on findings | Linked? |
|---|---|---|---|---|---|---|
| (Benson & Zarcone, 1993) | a) 21<br>b) 24<br>c) 13 | a) Patients with schizophrenia (at least 2 weeks medication free)<br>b) Patients with major depressive disorder<br>c) Non-clinical controls | *Positive symptoms*<br>BPRS | 2 | No significant differences in REM eye movements across groups, one positive correlation for a hallucinatory behaviour item and REM density in the schizophrenia group. | Y (partly) |
| (Bian et al., 2016) | 148 | Inpatients with schizophrenia | *Positive symptoms*<br>PANSS | 2 | Sleep misperception (self rated vs PSG) not associated with positive psychotic symptoms | N |
| (Ferrarelli et al., 2010) | a) 49<br>b)20<br>c) 44 | a) Patients with schizophrenia<br>b) Patients with other diagnoses receiving antipsychotic medication<br>c) Non-clinical controls | *Positive symptoms*<br>PANSS | 1 | Negative correlation between sleep spindle activity and number and positive symptoms. | Y |
| (Ganguli, 1987) | a) 8<br>b) 16<br>c) 16<br>d) 10 | Patients with:<br>a) Schizophrenia (medication naïve)<br>b) Delusional depression<br>c) Depression<br>d) Non-clinical controls | *Positive symptoms*<br>BPRS | 2 | Positive correlation between REM latency and severity of psychosis, but trend failed to reach statistical significance. | Y (partly) |
| (Kajimura et al., 1996) | a) 6<br>b) 6 | a) Patients with schizophrenia (outpatients)<br>b) Non-clinical controls | *Positive symptoms*<br>BPRS | 1 | Negative correlation between slow wave sleep and negative symptom scale.<br>No associations reported between PSG variables and positive symptoms. | N |
| (Keshavan et al., 1995) | a) 24<br>b) 5<br>c) 4<br>d) 5 | Patients with:<br>a) Schizophrenia<br>b) Schizoaffective bipolar<br>c) Schizoaffective depressed<br>d) Delusional disorder | *Positive symptoms*<br>BPRS<br>SAPS | 2 or 3 | Negative correlation between slow wave sleep and negative symptom scale.<br>No association reported between SWS and positive symptoms. | N |

| Citation | N | Sample characteristics | Psychosis Measure(s) | # PSG nights | Comment on findings | Linked? |
|---|---|---|---|---|---|---|
| (Keshavan et al., 1998) | a) 30<br>b) 30 | c) Unmedicated patients with schizophrenia (medication naïve or medication free for average of 40 weeks)<br>d) Non-clinical age and sex matched controls | *Positive symptoms*<br>BPRS | 2 or 3 | Patients with schizophrenia had reduced slow wave sleep.<br>No correlations between positive symptoms and slow wave sleep. | N |
| (Lauer et al., 1997) | a) 22<br>b) 20 | a) Drug naïve, first episode or acute exacerbation patients with schizophrenia<br>b) Non-clinical age and sex matched controls | *Positive symptoms*<br>BPRS | 1 | Positive symptoms scores correlate negatively with REM onset latency, but reported to be driven by conceptual disorganisation factor rather than all positive symptom factors. | Y |
| (Manoach et al., 2014) | a) 26<br>b) 25<br>c) 19<br>d) 23 | a) Patients with schizophrenia (inpatient and outpatient, n=11 early course)<br>b) Non-clinical age and sex matched controls (to patient group)<br>c) First degree relatives of patients with schizophrenia<br>d) Non-clinical age, sex and education matched controls (to relatives group) | *Positive symptoms*<br>SAPS | 1 | Positive correlation increased amplitude of spindles during stage 2 sleep and positive symptoms (only found in patients with schizophrenia). | Y |
| (Poulin et al., 2003) | a) 11<br>b) 11 | a) Patients with first episode psychosis (medication naïve)<br>b) Non-clinical controls | *Positive symptoms*<br>BPRS | 1 or 2 | Positive symptom scores correlated negatively with REM onset latency.<br>Other sleep measures correlate with total symptom severity. | Y |
| (Rotenberg et al., 1997) | 20 | Patients with schizophrenia (medicated) | *Positive symptoms*<br>PANSS | 3 | Positive symptoms correlated with lowered REM density. | Y |
| (Sarkar et al., 2010) | a) 20<br>b) 14<br>c) 20 | a) Patients with schizophrenia<br>b) First degree relatives of patients<br>c) Non-clinical age and sex matched controls | *Positive symptoms*<br>BPRS<br>PANSS | 1 | Positive symptoms correlated positively with percentage of time in REM sleep, and negatively correlated with REM sleep onset latency. | Y |

| Citation | N | Sample characteristics | Psychosis Measure(s) | # PSG nights | Comment on findings | Linked? |
|---|---|---|---|---|---|---|
| (Tandon et al., 1989) | 10 | Patients with schizophrenia (inpatients) | *Positive symptoms* BPRS | 1 | No difference in BPRS score between patients with and without REM abnormalities. | N |
| (Tandon et al., 1992) | a) 20<br>b) 20<br>c) 15 | a) Drug-naïve schizophrenia patients<br>b) Previously medicated but drug free schizophrenia patients<br>c) Non-clinical controls | *Positive symptoms* BPRS | 1 | Positive symptoms scores correlate negatively with REM onset latency, but effect only found in previously treated group, not in the drug naïve group. | Y (partly) |
| (S. F. Taylor et al., 1991) | 36 | Patients with schizophrenia (inpatients) | *Positive symptoms* BPRS | 1 | No difference in BPRS positive scale score in patients with REM at sleep onset (n=6) versus patients without REM at sleep onset (n=30). | N |
| (Tekell et al., 2005) | a) 17<br>b) 15<br>c) 17 | a) Patients with schizophrenia<br>b) Patients with major depression<br>c) Non-clinical controls | *Positive symptoms* BPRS SAPS | 1 | Positive symptom scores explained significant amount of variance in high frequency EEG activity during REM sleep. | Y |
| (Tesler et al., 2015) | a) 9<br>b) 15 | a) Adolescents (aged 14-18) meeting criteria for early onset schizophrenia spectrum disorder<br>b) Non-clinical age and sex matched controls | *Positive symptoms* PANSS | 1 | Reduced sleep spindle density in clinical group correlated with positive symptom severity. | Y |
| (Wamsley et al., 2012) | a) 21<br>b) 17 | a) Chronically medicated patients with schizophrenia<br>b) Non-clinical age and sex matched controls | *Positive symptoms* PANSS | 1 | Reduced amplitude and power of individual spindles correlated with greater severity of positive symptoms. | Y |
| (Yang & Winkelman, 2006) | a) 15<br>b) 15 | a) Inpatients with schizophrenia (at least 2 weeks drug free)<br>b) Non-clinical controls | *Positive symptoms* BPRS | 1 | Positive symptoms correlated with lowered REM density. | Y |

BPRS = Brief Psychiatric Rating Scale (Overall & Gorham, 1962); SAPS = Scale for Assessment of Positive Symptoms (Andreasen, 1984); PANSS = Positive and Negative Symptom Scale (Kay et al., 1987)

### 1.7.6 Table 5: Studies addressing the link between positive symptoms and sleep measured with actigraphy in clinical groups

| Citation | Design | N | Sample characteristics | Psychosis measure(s) | Sleep dysfunction measure(s) | Comment on findings | Linked? |
|---|---|---|---|---|---|---|---|
| (Afonso, Brissos, et al., 2011) | Cross sectional | 23 | Patients with schizophrenia (outpatients) | *Positive symptoms*<br>PANSS (used to divide in to predominant positive (n=11) and predominant negative (n=12) groups) | *Subjective sleep*<br>PSQI<br>*Circadian sleep measures*<br>Wrist-actigraphy (7 days continuous) | Patients with more positive symptoms report reduced sleep quality and quality of life in comparison to patients with predominantly negative symptoms. | Y |
| (Afonso et al., 2014) | Cross sectional | a) 34<br>b) 24 | a) Patients with schizophrenia (outpatients)<br>b) Age and gender matched non-clinical controls | *Positive symptoms*<br>PANSS | *Subjective sleep*<br>PSQI<br>*Circadian sleep measures*<br>Wrist-actigraphy | Increased positive symptoms associated with reduced sleep quality and more disturbed sleep-wake patterns in patient group. | Y |
| (Bromundt et al., 2011) | Cross-sectional | 14 | Patients with schizophrenia (outpatients) | *Positive symptoms*<br>PANSS | *Subjective sleep*<br>PSQI<br>*Circadian sleep measures*<br>Wrist-actigraphy (21 days)<br>Melatonin profiling (48 hour window collected weekly) | No relationship found between positive symptoms and cognitive performance or sleep-wake measures. | N |

| Citation | Design | N | Sample characteristics | Psychosis measure(s) | Sleep dysfunction measure(s) | Comment on findings | Linked? |
|---|---|---|---|---|---|---|---|
| (Lunsford-Avery et al., 2015) | Longitudinal | a) 36<br>b) 31 | a) Ultra high risk youth<br>b) Non-clinical controls | *Psychotic symptoms*<br>SIPS<br>SCID<br>(both at baseline and 12 month follow up) | *Circadian sleep measures*<br>Wrist-actigraphy<br>*Subjective sleep*<br>PSQI | Sleep disturbance significantly associated with increased positive symptoms at baseline in high risk group, and predict clinical symptoms at 12 months when controlling for age, depression and baseline psychotic symptoms. | Y |
| (Lunsford-Avery, Dean, & Mittal, 2017) | Longitudinal | a) 34<br>b) 32 | a) Clinical high risk youth<br>b) Non-clinical controls | Psychotic symptoms<br>SIPS<br>SCID | *Circadian sleep measures*<br>Wrist-actigraphy (5 days) | CHR showed significantly more disrupted circadian activity than HCs; circadian disturbance predicted increased positive symptoms at 12 month follow up | Y |
| (Martin et al., 2001) | Cross-sectional | 28 | Older patients with schizophrenia (mean age = 58 yrs) | *Positive symptoms*<br>BPRS<br>SAPS | *Objective sleep*<br>Wrist actigraphy (activity and light exposure – 3 days) | No clinical or demographic variables were related to sleep wake characteristics. | N |
| (Mulligan et al., 2016) | Longitudinal | 22 | Patients with schizophrenia (outpatients) | *Psychotic symptoms*<br>Auditory hallucinations, paranoia, delusions of control (single items) | *Subjective sleep*<br>Sleep diaries<br>*Objective sleep*<br>Wrist actigraphy<br>Both completed for 7 days | Subjective and objective sleep parameters (TST, SE, SQ) found to be linked with psychotic symptoms the next day; relationship partly accounted for by increased negative affect | Y |

| Citation | Design | N | Sample characteristics | Psychosis measure(s) | Sleep dysfunction measure(s) | Comment on findings | Linked? |
|---|---|---|---|---|---|---|---|
| (Waters et al., 2011) | Longitudinal | a) 6<br>b) 7 | a) Patients with schizophrenia (outpatients)<br>b) Age and gender matched non-clinical controls | *Positive symptoms*<br>BPRS<br>*Psychotic experiences*<br>12 item questionnaire including 8 items on psychotic experiences, 4 on mood (daily) | *Subjective sleep*<br>PSQI<br>*Circadian measures*<br>Wrist actigraphy (up to 28 days) | Sleep variations in the clinical group predicted daily changes in positive symptoms and negative mood. | Y |
| (Wichniak et al., 2011) | Cross-sectional | 73 | Patients with schizophrenia spectrum disorder (treated with olanzapine or risperidone) | *Positive symptoms*<br>PANSS | *Objective sleep*<br>Wrist actigraphy (7 days) | Positive symptom severity correlated with reduced activity. | Y |
| (Wulff et al., 2012) | Cross sectional | a) 20<br>b) 21 | a) Patients with schizophrenia (outpatients)<br>b) Age, gender and employment matched non-clinical controls | *Positive symptoms*<br>Clinician scored presence or absence of positive symptoms | *Subjective sleep*<br>PSQI<br>*Circadian measures*<br>Wrist-actigraphy<br>Melatonin profiling (48 hour window collected weekly) | Presence or absence of positive symptoms did not predict differences in circadian sleep/wake disruptions. | N |

BPRS = Brief Psychiatric Rating Scale (Overall & Gorham, 1962); PANSS = Positive and Negative Symptom Scale (Kay et al., 1987); PSQI = Pittsburgh Sleep Quality index (Buysse et al., 1989); SCID =Structured Clinical Interview for DSM-IV disorder (First et al., 1997); SIPS = Structured Interview for Prodromal Symptoms (Miller et al., 1999)

## 1.7.7 Table 6: Studies addressing the link between sleep and clinical course of psychosis

| Citation | Design | N | Sample characteristics | Psychosis Measure(s) | Sleep dysfunction measure(s) | Comment on findings | Linked? |
|---|---|---|---|---|---|---|---|
| (Afonso, Brissos, et al., 2011) | Cross sectional | 23 | Patients with schizophrenia (outpatients) | *Positive symptoms*<br>PANSS (used to divide in to predominant positive (n=11) and predominant negative (n=12) groups) | *Subjective sleep quality*<br>PSQI<br>Circadian sleep measures<br>Wrist-actigraphy (7 days continuous) | Patients with more positive symptoms report reduced sleep quality and quality of life in comparison to patients with predominantly negative symptoms. | Y |
| (Afonso et al., 2014) | Cross sectional | a) 34<br>b) 24 | a) Patients with schizophrenia (outpatients)<br>b) Age and gender matched non-clinical controls | *Positive symptoms*<br>PANSS | *Subjective sleep*<br>PSQI<br>*Circadian measures*<br>Wrist actigraphy | Negative correlation found between positive symptoms and self-reported sleep quality in patient group. | Y |
| (Birchwood et al., 1989) | Longitudinal | 19 | Patients with schizophrenia (outpatients) | *Positive symptoms*<br>PAS (repeated monthly)<br>Relapse (defined as readmission or incipient readmission) | *Subjective sleep*<br>ESS (repeated every 2 weeks for 18weeks) | Sleep disruption item formed part of self-report scale predicting relapse – sleep disruption reported prior to positive symptoms on PAS. | Y |
| (Jørgensen, 1998a) | Longitudinal | 60 | Patients with schizophrenia (outpatients) | *Positive symptoms*<br>Psychotic scale of PANSS (repeated every 2 weeks for 6 months or to relapse), relapse defined as increase in 2 in any item | *Subjective sleep*<br>ESS (repeated every 2 weeks for 6 months or to relapse) | Increase of 10 points on ESS predicted relapse with sensitivity of 81% and selectivity of 79%. | Y |

| Citation | Design | N | Sample characteristics | Psychosis Measure(s) | Sleep dysfunction measure(s) | Comment on findings | Linked? |
|---|---|---|---|---|---|---|---|
| (Jørgensen, 1998b) | Longitudinal | 131 | Patients with schizophrenia (outpatients) | *Positive symptoms*<br>Psychotic scale of PANSS (repeated every 2 weeks), delusion relapse defined as increase of 2 in delusions scale | *Subjective sleep*<br>WSS (repeated every 2 weeks for 6 months or to relapse) | 8-item Warning Signals Scale (condensed from ESS found to have sensitivity of 77% and specificity of 68% in detecting delusion formation. | Y |
| (Kim, Lee, Kim, Jung, & Lee, 2009) | Retrospective | 20 | Patients with first episode psychosis | *Psychotic symptoms*<br>K-NOS (Korean version) | *Subjective sleep*<br>K-NOS (Korean version) | Sleep changes reported in prodrome of 16 – 43% of patients. | Y |
| (Lunsford-Avery et al., 2013) | Cross sectional | a) 33<br>b) 33 | a) Adolescents (aged 12-21 years)<br>b) Satisfying UHR criteria<br>c) Age matched non-clinical controls | *Prodromal positive symptoms*<br>SIPS<br>SCID | *Subjective sleep*<br>PSQI | Sleep dysfunction associated with negative symptom severity but not positive symptoms. | N |
| (Lunsford-Avery et al., 2015) | Longitudinal | a) 36<br>b) 31 | a) Ultra high risk youth<br>b) Non-clinical controls | *Psychotic symptoms*<br>SIPS<br>SCID<br>(both at baseline and 12 month follow up) | *Objective sleep*<br>Wrist actigraphy<br>*Subjective sleep*<br>PSQI | Sleep disturbance associated with increased positive symptoms at baseline in high-risk group, and predict clinical symptoms at 12 months when controlling for age, depression and baseline psychotic symptoms. | Y |
| (Lunsford-Avery et al., 2017) | Longitudinal | a) 34<br>b) 32 | a) Clinical high risk youth<br>b) Non-clinical controls | *Psychotic symptoms*<br>SIPS<br>SCID | *Circadian sleep measures*<br>Wrist-actigraphy (5 days) | CHR showed significantly more disrupted circadian activity than HCs; circadian disturbance predicted increased positive symptoms at 12 month follow up | Y |

| Citation | Design | N | Sample characteristics | Psychosis Measure(s) | Sleep dysfunction measure(s) | Comment on findings | Linked? |
|---|---|---|---|---|---|---|---|
| (Ma et al., 2016) | Cross-sectional | 104 | Patients with schizophrenia (first episode) | *Positive symptoms*<br>BPRS | *Subjective sleep*<br>PSQI | No association between PSQI scores and BRPS positive symptom dimension | N |
| (Martin et al., 2001) | Cross-sectional | 28 | Older patients with schizophrenia (mean age = 58 yrs) | *Positive symptoms*<br>BPRS<br>SAPS | *Objective sleep*<br>Wrist actigraphy (activity and light exposure) | No clinical or demographic variables were related to sleep wake characteristics. | N |
| (Mattai et al., 2006) | Manipulation (observed over medication wash out period of 5- 7 days) | 61 | Patients with childhood onset schizophrenia (mean age = 10 yrs) | *Positive symptoms*<br>BPRS<br>SAPS | *Sleep duration*<br>Nursing notes and safety records - used to divide sample in to good sleepers (>6 hrs sleep) and poor sleepers (<6 hours sleep) | Poor sleepers had significantly increased positive symptoms scores in comparison to good sleepers. | Y |
| (Poe et al., 2017) | Longitudinal | a) 194<br>b) 66 | a) Patients at clinical high risk of psychosis<br>b) Non-clinical controls | *Positive symptoms*<br>SIPS | *Subjective sleep*<br>SIPS (sleep disruption item) | Patients reported significantly more sleep disruption than healthy controls. Sleep disruption was associated with higher positive symptoms at baseline but not 2.5 yr follow up | Y |
| (Ritsner et al., 2004) | Cross sectional | 145 | Patients with schizophrenia (inpatient and outpatient) | *Positive symptoms*<br>PANSS | *Subjective sleep*<br>PSQI - used to split sample in to good sleepers (<5, n= 79) and bad sleepers (>=5, n = 66)) | No significant difference in positive or negative symptoms across the good sleeper and poor sleeper groups. | N |

| Citation | Design | N | Sample characteristics | Psychosis Measure(s) | Sleep dysfunction measure(s) | Comment on findings | Linked? |
|---|---|---|---|---|---|---|---|
| (Ruhrmann et al., 2010) | Longitudinal | 245 | Youth satisfying ultra high risk criteria or basic symptom based criterion cognitive disturbances | *Prodromal positive symptoms*<br>SIPS | *Subjective sleep*<br>SIPS (sleep disruption item); | Model predicting transition from high risk status includes sleep disruption as one of 6 predictors, predicts 18 month outcomes with sensitivity of 41.7% and specificity of 97.9%. | Y |
| (Tan & Ang, 2001) | Retrospective | a) 30<br>b) 34 | Patients in military hospital with:<br>a) first episode psychosis<br>b) first episode non-psychotic and non-organic psychiatric conditions | *Positive symptoms*<br>Unstructured and semi-structured interviews of patients and informants | *Subjective sleep*<br>Unstructured and semi-structured interviews of patients and informants | Sleep disruption seen in prodrome of 77% of psychotic patients, but 97% of non-psychotic. | Y |
| (Xiang et al., 2009) | Cross sectional | 505 | Outpatients with schizophrenia | *Positive symptoms*<br>BPRS | *Insomnia symptoms*<br>3 DSM-IV based items – classification as 'poor sleeper' following positive answer to 1 item or more | 36% of sample classified as 'poor sleepers'. Poor sleep significantly associated with positive symptom severity and reduced quality of life. | Y |

BPRS = Brief Psychiatric Rating Scale (Overall & Gorham, 1962); ESS = Early Signs Scale (Birchwood et al., 1989); G-PTS = Green et al. paranoid thoughts scale (Green et al., 2008); ISI = Insomnia Severity Index (C M Morin, 1993); K- NOS = Korean version of the Nottingham interview schedule (Kim et al., 2009); PANSS = Positive and Negative Symptom Scale (Kay et al., 1987); PAS = Psychiatric Assessment Scale (Krawiecka, Goldberg, & Vaughan, 1977); PSQI = Pittsburgh Sleep Quality index (Buysse et al., 1989); SAPS = Scale for Assessment of Positive Symptoms (Andreasen, 1984); PSYRATS = Psychotic symptom rating scales (Haddock et al., 1999); SCID =Structured Clinical Interview for DSM-IV disorder (First et al., 1997); SIPS = Structured Interview for Prodromal Symptoms (Miller et al., 1999); Sleep-50 = (Spoormaker et al., 2005); WSS = Warning Signals Scale (Jørgensen, 1998b)

## 1.7.8 Table 7a: Studies addressing the link between sleep disorders or sleep disorder symptoms and psychosis

| Citation | Design | N | Sample characteristics | Psychosis Measure(s) | Sleep dysfunction measure(s) | Comment on findings | Linked ? |
|---|---|---|---|---|---|---|---|
| (Freeman et al., 2009) | Cross-sectional | a) 300<br>b) 30 | a) Non-clinical community sample<br>b) Individuals with persecutory delusions and diagnosis of non-affective psychosis. | *Paranoia*<br>G-PTS | *Insomnia symptoms*<br>ISI<br>Sleep-50 | Insomnia associated with paranoid thinking, relationship largely accounted for by anxiety and depression | Y |
| (Grezellschak et al., 2017) | Cross-sectional | a) 46<br>b) 23<br>c) 267 | a) Patients with psychosis<br>b) Relatives of patients with psychosis<br>c) Non-clinical controls | *Paranoia*<br>PC | *Insomnia symptoms*<br>ISI | The effect of insomnia on paranoia ideation is mediated by emotion regulation difficulties (increased suppression, decreased reappraisal) | Y |
| (Michels et al., 2014) | Cross-sectional | a) 17<br>b) 14<br>c) 17<br>d) 29 | a) Inpatients with schizophrenia<br>b) ARMS outpatients<br>c) Non-clinical relatives of patients with schizophrenia<br>d) Non-clinical controls | *Positive symptoms*<br>PANSS | *Nightmares*<br>Frequency scale (past 2 months) | Positive symptoms did not correlate with nightmare frequency, although nightmares were more common in ARMS outpatients and schizophrenia groups. | N |
| (Palmese et al., 2011) | Cross-sectional | 175 | Patients with schizophrenia or schizoaffective disorder (outpatients) | *Positive symptoms*<br>CGI | *Insomnia symptoms*<br>ISI<br>PSQI<br>*Night eating*<br>NEQ | No significant relationship between positive symptom score and insomnia severity. No relationship reported between night eating and positive symptom score | N |
| (Sheaves et al., 2015) | Cross sectional | 40 | Patients with psychotic symptoms (inpatient and outpatient) | *Psychotic experiences*<br>PSYRATS | *Subjective sleep*<br>PSQI<br>*Nightmares*<br>Dream Log | High proportion of sample reported weekly distressing nightmares, distress associated with severity of delusions. | Y |
| (Xiang et al., 2009) | Cross sectional | 505 | Outpatients with schizophrenia | *Positive symptoms*<br>BPRS | *Insomnia symptoms*<br>3 DSM-IV based questions –classified as 'poor sleeper' following positive screen for >=1 | 36% of sample classified as 'poor sleepers'. Poor sleep significantly associated with positive symptom severity and reduced quality of life. | Y |

ARMS = At Risk Mental State (Rausch et al., 2013); BPRS = Brief Psychiatric Rating Scale (Overall & Gorham, 1962); CGI = Clinical Global Impression Scale (Haro et al., 2003); G-PTS = Green et al. paranoid thoughts scale (Green et al., 2008); ISI = Insomnia Severity Index (C M Morin, 1993); NEQ = Night Eating Questionnaire (Allison et al., 2008); PC = Paranoia Checklist (Freeman et al., 2005b); PSQI = Pittsburgh Sleep Quality Index (Buysse et al., 1989); PSYRATS = Psychotic symptom rating scales (Haddock et al., 1999); SLEEP-50 = (Spoormaker et al., 2005)

## 1.7.9 Table 7b: Studies addressing the link between positive psychotic symptoms and treatment for sleep disorders

| Citation | N | Sample characteristics | RCT | Treatment | Psychosis Measure(s) | Sleep dysfunction measure(s) | Comment on findings | Linked? |
|---|---|---|---|---|---|---|---|---|
| (Freeman, Waite, Startup, et al., 2015) | 50 | Outpatients with persistent persecutory delusions or hallucinations and insomnia | Y | CBT for insomnia (CBTi – 8 sessions in max 12 weeks) | *Psychotic experiences*<br>PSYRATS<br>PANSS<br>(pre and post treatment, 12 week follow up) | *Insomnia symptoms*<br>*ISI*<br>(pre and post treatment, 12 week follow up) | CBT for insomnia led to large effect size reductions in insomnia symptoms. Direction of changes to delusions and hallucinations unclear. | N |
| (M. Kato et al., 1999) | 7 | Male outpatients with schizophrenia | N | Change to insomnia medication (benzodiazapene to 8 weeks of zopiclone | *Positive symptoms*<br>BPRS<br>(pre and post treatment) | *Objective sleep*<br>Polysomnography<br>(pre and post treatment) | Slow wave sleep improved following move to zopiclone treatment, negative symptoms significantly improved (positive symptoms improved but non-significant) | N |
| (Kantrowitz et al., 2010) | 8 | Inpatients with schizophrenia and insomnia | N | Insomnia medication (sodium oxybate – 4 weeks) | *Positive symptoms*<br>PANSS<br>(pre and post-treatment) | *Subjective sleep*<br>PSQI (baseline and post-treatment)<br>ESS (baseline and post-treatment)<br>*Objective sleep*<br>PSG (2 nights at baseline and last nights of treatment) | Pharmaceutical treatment of insomnia improved sleep (large improvements in SWS time, reduced sleep latency, and increased REM latency) and positive symptoms | Y |
| (Myers et al., 2011) | 15 | Outpatients with persistent persecutory delusions and insomnia | N | CBTi – 4 sessions, over max 8 weeks | *Paranoia*<br>G-PTS<br>*Psychotic symptoms*<br>PSYRATS<br>*Anomalous perceptions*<br>CAPS<br>(pre and post treatment, and one month follow up) | *Insomnia symptoms*<br>ISI<br>*Subjective sleep*<br>PSQI<br>(pre and post treatment, and one month follow up) | CBTi led to improvements in insomnia symptoms and persecutory delusions, with reductions also observed in anxiety, depression, and anomalies of experience. | Y |

| Citation | N | Sample characteristics | RCT | Treatment | Psychosis Measure(s) | Sleep dysfunction measure(s) | Comment on findings |
|---|---|---|---|---|---|---|---|
| (Tek et al., 2014) | 39 | Clinically stable outpatients with schizophrenia and insomnia | Y | Insomnia medication (eszopiclone – 8 weeks) | *Positive symptoms*<br>PANSS<br>(every 2 weeks) | *Insomnia symptoms*<br>ISI (weekly)<br>*Subjective sleep*<br>Sleep diary (every day) | Psychotic symptoms showed greater reduction in the treatment group (CI -3.1; 0.4) compared to the group receiving placebo. |

CAPS = Cardiff Anomalous Perceptions Scale (Bell, Halligan, & Ellis, 2006); ESS = Epworth Sleepiness Scale (M. W. Johns, 1991); G-PTS – Green et al. Paranoid Thoughts Scale (Green et al., 2008); ISI =Insomnia Severity Index (C M Morin, 1993); PANSS = Positive and Negative Symptom Scale (Kay et al., 1987); PSQI = Pittsburgh Sleep Quality index (Buysse et al., 1989); PSYRATS = Psychotic symptom rating scales (Haddock et al., 1999)

## 1.7.10 Table 8: Studies addressing the link between treatment of positive psychotic symptoms and sleep

| Citation | N | Sample Characteristics | Treatment manipulation | Psychosis Measure(s) | Sleep dysfunction measure(s) | Comment on findings | Linked? |
|---|---|---|---|---|---|---|---|
| (Chemerinski et al., 2002) | 122 | Patients with schizophrenia | Withdrawal of antipsychotic medication | *Positive symptoms* SAPS (weekly) | *Insomnia symptoms* HAM-D insomnia items (weekly) | Patients reporting insomnia prior to withdrawal had more severe psychotic symptoms during medication-free period | Y |
| (Neylan et al., 1992) | 18 | Clinically stable patients with schizophrenia inpatients | Withdrawal of antipsychotic medication | *Positive symptoms* Bunney-Hamburg (daily) | *Objective sleep* PSG (3 nights pre and post withdrawal) | Psychosis scale score correlated with REM time, inversely correlated with REM onset latency. This did not predict status following withdrawal of antipsychotic Increased symptoms after withdrawal were associated with reduced sleep continuity and decrease in total REM and NREM time. | Y |
| (E. Nofzinger et al., 1993) | 10 | Male patients with schizophrenia | Withdrawal of antipsychotic medication | *Positive symptoms* BPRS (at 2 weeks and 6 weeks post withdrawal) | *Objective sleep* PSG (3 nights at 2 weeks and 6 weeks post withdrawal) | Changes in EEG sleep during withdrawal period did not correlate with positive symptoms. | N |
| (S. Taylor et al., 1991) | 14 | Inpatients with schizophrenia | Administered antipsychotic medication (medication free at baseline) | *Positive symptoms* BPRS (pre-treatment and after average of 24.4 days of treatment) | *Objective sleep* PSG (one night pre-treatment and two nights after average of 24.4 days of treatment) | Positive symptoms correlate with shortened REM latency prior to antipsychotic treatment, but no symptom measure and sleep variable correlations found after treatment. | Y |
| (Yamashita et al., 2004) | 92 | Inpatients with schizophrenia - same sample as (Yamashita et al., 2005), average age 61.5 | Observed over change from conventional to atypical antipsychotics | *Positive symptoms* PANSS (baseline and 8 weeks post change completion) | *Subjective sleep* PSQI (baseline and 8 weeks post change completion) | Improvement in negative symptoms significantly correlated with improvement in PSQI scores, trend correlation (p=0.08) with positive symptoms following medication switch. | Y |

| Citation | N | Sample Characteristics | Treatment manipulation | Psychosis Measure(s) | Sleep dysfunction measure(s) | Comment on findings | Linked? |
|---|---|---|---|---|---|---|---|
| (Yamashita et al., 2005) | a) 35<br>b) 51 | Inpatients with schizophrenia:<br>a) Elderly (age => 65)<br>b) Middle-aged (age<65) | Observed over change from conventional to atypical antipsychotics | *Positive symptoms* PANSS (baseline and 8 weeks post change completion) | *Subjective sleep* PSQI (baseline, and 8 weeks post completion of change) | Improvement in sleep satisfaction was significantly correlated with improvement in all subscales of the PANSS (including positive symptoms), but only in the middle aged group. Correlation limited to negative symptoms and self-rated sleep quality in elderly group. | Y |
| (Zhang et al., 2012) | a) 40<br>b) 18 | First episode psychosis patients | a) Electroconvulsive therapy and antipsychotic medication<br>b)Antipsychotic medication only | *Positive symptoms* PANSS (baseline and then repeated weekly during hospital stay) | *Objective sleep* PSG (overnight, recorded at baseline and week 2) | Reduction in positive symptoms significantly correlated with improvements in sleep efficiency, REM latency, and REM density.<br>Sleep efficiency and positive symptoms improved further from baseline in the ECT and antipsychotic group versus the antipsychotic only group. | Y |

SAPS = Scale for Assessment of Positive Symptoms (Andreasen, 1984); HAM-D = Hamilton Depression Rating Scale (Hamilton, 1960); Bunney-Hamburg Scale (Bunney & Hamburg, 1963); PSG = Polysomnography (see Table 1 for definition); BPRS = Brief Psychiatric Rating Scale (Overall & Gorham, 1962); PANSS = Positive and Negative Symptom Scale (Kay et al., 1987)

# Chapter 2

# Disrupting sleep: the effects of sleep loss on psychotic experiences tested in an experimental study with mediation analysis

## 2.1 Chapter abstract


### Background

Insomnia appears to be associated with psychotic experiences, but no studies have directly tested its causal role in an experimental study, or investigated mediating mechanisms.

### Aim

This chapter aims to investigate the causal role of insomnia in psychosis by assessing the effect of an insomnia-like sleep loss on psychotic experiences and mediating variables in a non-clinical sample.

### Method

The study was a within-subjects crossover design that included a planned mediation analysis. Sixty-eight nonclinical volunteers underwent a sleep loss condition (restricted to four hours sleep for three nights) and a control condition (standard sleep) in randomized order in two consecutive weeks, with a weekend washout period. Psychotic experiences (paranoia, hallucinations, grandiosity, and cognitive disorganization) and candidate mediating variables (negative affect and related processes, working memory, decision making, and perceptual processing) were assessed before and after each condition.

### Results

Actigraphy verified an average sleep duration of 5h15 min in the sleep loss condition, vs 6h58 min in the control condition. After the sleep loss condition, relative to the control condition, participants reported significant increases in paranoia, hallucinations, and cognitive disorganization, with no significant changes in grandiosity. The sleep loss condition resulted in significant increases in negative affect, negative self and other cognitions, worry, and working memory impairment. Mediation analyses indicated that changes in psychotic experiences were mediated by changes in negative affect and related processes, but not memory impairment.

### Conclusion

The overall conclusion is that insomnia has a causal role in the occurrence of certain psychotic experiences, and that a key route is via negative affect.

**This chapter is adapted from the following paper, attached in Appendix 2.1*

*Reeve, S., Emsley, R., Sheaves, B., & Freeman, D. (2017). Disrupting sleep: the effects of sleep loss on psychotic experiences tested in an experimental study with mediation analysis. Schizophrenia Bulletin.*

## 2.2 Introduction

From Chapter 1 it is clear that there is an association between insomnia and psychotic experiences. However, no direct test of the causal role has been carried out, and there is little understanding of the mechanisms linking insomnia with psychotic experiences. Such findings would inform the understanding of the aetiology of psychotic experiences, and would also contribute to developing sleep interventions for patients with non-affective psychosis (Freeman, Waite, Startup, et al., 2015). In order to establish causation, studies are needed which manipulate the proposed causal variable (insomnia) to test the effect (on psychotic experiences) (Pearl, 2000).

One approach is to improve insomnia while measuring psychotic experiences among individuals with existing sleep problems with or without a psychotic disorder diagnosis (Freeman, Sheaves, Goodwin, et al., 2015; Freeman, Waite, Startup, et al., 2015). An improvement in sleep should lead to a lessening in psychotic experiences. A second approach is to disrupt sleep, with the prediction that psychotic experiences should worsen. In effect, with non-clinical individuals this would temporarily simulate the development of psychotic experiences. One advantage of this approach, as compared to treating an existing insomnia condition, is that it allows a more controlled investigation. Confounds such as the chronicity and severity of the disorder are controlled, as all participants effectively have the same amount of disorder induced.

Table 1 lists the three experimental sleep deprivation studies measuring psychotic experiences reported to date (Hurdiel et al., 2014; Kahn-Greene et al., 2007; Petrovsky et al., 2014). These studies are consistent with the idea that sleep loss results in an increase in psychotic experiences. However, the findings in relation to individual psychotic experiences are inconsistent. For example, paranoia is increased following sleep deprivation in Kahn-Green *et al.* (2007) but not Petrovsky *et al.* (2014). Furthermore, these studies manipulate sleep via total sleep deprivation, whereas insomnia is characterised by insufficient sleep over a period of time. It is has been shown that total deprivation has differing effects to reducing sleep, even when the same amount of sleep is lost (Drake et al., 2001)

therefore findings from sleep deprivation cannot necessarily be extrapolated to insomnia. Lastly, none of these studies included measurement or analysis of potential mediating factors.

Cognitive models of psychotic experiences suggest multiple potential mechanisms by which insomnia could lead to psychotic experiences. One primary candidate would be negative affect (anxiety and depression). Changes in negative affect have been found to explain a proportion of the relationship between insomnia and psychotic experiences in non-manipulation studies (Chapter 1), and reducing sleep is known to increase negative affect (Banks & Dinges, 2007). This mechanism would be consistent with models of paranoia and hallucinations which place anxiety and depression at the centre of the development and maintenance of positive psychotic symptoms (Freeman, 2016; Garety et al., 2001; Waters, Allen, et al., 2012). Affect-related processing such as worry and core beliefs about self and others have also been linked to psychotic experiences, especially paranoia (Freeman, 2016; Freeman et al., 2014; Freeman, Dunn, Startup, et al., 2015). No studies have investigated changes in these factors relating to sleep loss, however it seems plausible that insomnia or sleep loss might increase worry or negative core beliefs, given their relationship with negative affect.

Furthermore, there are other untested factors which could mediate the relationship between sleep dysfunction and psychosis. Working memory deficits are a commonly noted consequence of sleep loss and insomnia (Alhola & Polo-Kantola, 2007; Fortier-Brochu, Beaulieu-Bonneau, Ivers, & Morin, 2012) and have been linked to the jumping to conclusions reasoning bias (Garety, Joyce, et al., 2013), which is itself a key component of cognitive models of delusions (Garety et al., 2001). Changes in top-down perceptual processing (i.e. influence of beliefs on sensory processing) are a common feature in cognitive models of hallucinations (Waters, Allen, et al., 2012). These changes can be investigated with tasks based on visual or auditory illusions which leverage beliefs regarding the environment to produce their sensory effects. Individuals with schizophrenia and sleep deprived volunteers have both been shown to be less susceptible to the effects of visual and auditory illusions (Notredame et al., 2014; Sternemann et al., 1997), therefore reduced top-down processing could represent another route from sleep loss to hallucinatory experiences.

Therefore, there is a strong theoretical basis for testing the contribution of mediating factors such as affect and related processing, working memory, perceptual processing, and decision making in the relationship between insomnia and psychotic experiences.

### 2.2.1 The current study

The current study aims to investigate the causal role of insomnia in psychosis by assessing the effect of sleep loss on psychotic experiences and mediating variables in a non-clinical sample.

In the sleep loss condition, sleep was restricted to four hours sleep each night for three consecutive nights. A review of the literature indicated that this would be appropriate for causing noticeable changes, while still being reversible in a weekend washout period (Banks & Dinges, 2007; Banks, Van Dongen, Maislin, & Dinges, 2010; Belenky et al., 2003; Rupp, Wesensten, Bliese, & Balkin, 2009; Van Dongen, Maislin, Mullington, & Dinges, 2003). This sleep restriction was self-enforced by participants at home, and participants continued their daily activities (study, work, etc.) during the study. This level of self-enforced sleep restriction has successfully been achieved in previous studies (Kahn, Fridenson, Lerer, Bar-Haim, & Sadeh, 2014; Sadeh, Dan, & Bar-Haim, 2011). Adherence was monitored by actigraphic recording, responses to SMS (text message) prompts, and sleep diaries. Sleep was restricted by participants delaying their sleep onset. In other studies modelling insomnia, for example by Finan and colleagues (2015), sleep has been restricted by waking participants during the night. However, this is challenging to administer outside of a sleep laboratory, which in turn limits ecological validity.

The following hypotheses were tested in order to establish a causal relationship between the sleep loss condition and psychotic experiences, and to test the role of mediating factors in this relationship.

1. Sleep loss will cause an increase in (sub-clinical) psychotic experiences.
2. Sleep loss will cause changes in mood and cognition that may underlie the development of psychotic experiences.
3. Changes in mood and cognition will mediate the changes in psychotic experiences.

## 2.3 Method

### 2.3.1 Recruitment

Eight-five participants consented to take part, of which 75 completed the study. Seven participants were excluded for non-completion or late completion of an assessment, resulting in a final sample of 68 on which all analyses were carried out. Participants were recruited via advertisements from the student and wider community in Oxford. The language used in the advertisements, and by the lead investigator at the initial screening meeting, was kept broad ("psychological changes") in order to minimise expectancy effects relating to changes in psychotic experiences. See Appendix 2.2 for more details on the recruitment process.

Participants were aged 18-30 in order to reduce confounding by changes in sleep with age (Duffy, Zitting, & Chinoy, 2015). This is also the age at which psychotic symptoms generally emerge for those who go on to receive a diagnosis of clinical disorder. Other inclusion criteria were: good quality sleep (scoring ≤ 5 on the Pittsburgh Sleep Quality Index; Buysse, Reynolds, Monk, Berman, & Kupfer, 1989)), no history of psychiatric disorder, and no current mood disorder (indicated by scoring below clinical cut-off on the Beck Depression Inventory; Beck, Guth, Steer, & Ball, 1997, and the Mood Disorder Questionnaire; Hirschfeld et al., 2014). The exclusion criteria were: travel across time zones in the preceding two weeks; employment requiring shift work; consumption of drugs or medication (besides contraceptives or vitamins); requirement to drive, cycle, or operate heavy machinery during the study period; and non-fluency in English. The study received approval from Oxford University Research Ethics Committee, and written informed consent was received from all participants. Participants were compensated up to £50 for their involvement in the study, contingent on their responses to adherence checks (see study design below).

### 2.3.2 Study design

A within-subjects crossover design was chosen. Following consent, participants were randomised to the sleep loss condition (four hours sleep a night for three nights) or the control condition (standard sleep) for their first week in the study, with the alternate condition carried out in the second week. Both conditions were carried out Monday-Thursday or Tuesday-Friday, such that there was a minimum three-night washout period over Friday, Saturday and Sunday nights. Assessments were carried out at the start and end of both conditions. A diagram of the study design is included in Appendix 2.3.

Sleep recording was carried out in both study conditions. A self-report sleep diary based on the Consensus Sleep Diary (Carney et al., 2012) was completed, and objective recording of sleep-wake patterns was conducted using wrist actigraphy (CamNTech MotionWatch 8). MotionWare software was used to provide an estimate of total sleep time in each 24 hour period from the actigraphic recordings. Alcohol, caffeine, and nicotine consumption was recorded in the diary. Further information on the sleep recording and enforcement can be found in Appendix 2.4.

Sleep loss condition (restricted sleep): Participants set their own four-hour sleep period based on delaying sleep time while keeping wake time constant. For example, a participant who normally slept from 2300h until 0700h would sleep from 0300h to 0700h each night in the restricted condition. Participants responded to automated hourly text (SMS) messages to demonstrate they were awake, with compensation reduced by £5 for each text not responded to within this window. The messages were sent from 2200h until the hour before the participant's chosen sleep time.

Control condition (standard sleep): In this condition, participants could sleep however they wished for the three nights, and were not required to respond to any text messages.

### 2.3.3 Assessments

All assessments were administered online via the Inquisit platform ("Inquisit 4.0.7.4 [Computer software]," 2014) – see Appendix 2.5 for further details. Participants were emailed individual links to the assessment platform at 1800h on the first and fourth day of the sleep condition, and completed the assessment before 0000h. The timescale of all questionnaires was adjusted to the previous three days in order to allow for repeated administration. In all measures higher scores indicate greater severity. The assessment battery comprised:

#### Psychotic experiences

Specific Psychotic Experience Questionnaire (Ronald et al., 2014): The SPEQ is a self-report measure assessing psychotic experiences over the past month. The subscales for paranoia, hallucinations, cognitive disorganisation, and grandiosity were used in the current study. The paranoia subscale is formed of 15 statements rated by the participant for frequency of the thought from 0 ("Not at all") up to 5 ("Nearly all the time"), with a maximum possible score of 75. The subscale for hallucinations is comprised of nine items rated on the same scale to comprise a maximum score of 45. For cognitive disorganisation eleven statements are marked as "Yes" (this does apply to me) or "No" (this doesn't

apply to me), scored as 1 and 0 respectively. The grandiosity subscale is formed of eight statements rated for agreement by the participant on a 0 ("Not at all") to 3 ("Completely") scale, with a maximum score of 24. Higher scores indicate more severe psychotic experiences. See Appendix 2.6 for further details and a copy of the questionnaire.

### Negative affect

Depression Anxiety Stress Scale (short form) (Lovibond & Lovibond, 1995): The DASS is a 21 item self-report questionnaire assessing 3 dimensions of negative affect (depression, anxiety, and stress). Each dimension is indexed by seven items. Each item is marked on a 0-3 Likert scale where 0 is "Did not apply to me" and 3 is "Applied to me very much or nearly all the time". The outcome measures are the total of each of the depression, anxiety, and stress subscale – the minimum score is 0 and the maximum score is 21 in each. See Appendix 2.7 for further details and a copy of the questionnaire.

### Affective processes

Worry questionnaire (Freeman et al, in prep): This scale assesses frequency of worry and cognitions about worry. It is formed of ten statements ranked on 5 point Likert scale for agreement, where 0 is "None of the time" and 4 is "All of the time". Items include "There was little I could do to stop worrying" and "Worry has caused me to feel upset". The outcome variable is the total sum of responses, with a maximum score of 40. See Appendix 2.8 for further details and a copy of the questionnaire.

Brief Core Schema Scale (Fowler et al., 2006): The BCSS is a 24-item scale assessing positive and negative beliefs about self and others. The participant rates each belief on a 0 - 4 agreement scale, where 0 is "Do not have this belief" and 4 is "Believe this totally". Outcome variables are the total score for each subscale (negative self, positive self, negative other, positive other), for which the maximum score in each is 24. See Appendix 2.9 for further details and a copy of the questionnaire.

### Perception

Ebbinghaus illusion task: Participants decide which of two orange circles appear larger. Grey surrounding circles present a misleading illusory effect on a third of trials, a helpful illusory effect on another third, and there are no surrounding circles in the remainder of trials (control trials). The outcome variable is the average of the absolute difference in percentage of correct identifications between each illusory condition and the control condition. A higher average difference indicates

stronger top-down processing, a smaller difference indicates weaker. The hypothesis is that sleep loss leads to a reduced top-down processing. The current task was modelled on that used in Doherty et al. (2010). See Appendix 2.10 for further details.

Perceptual vigilance task (Balkin et al., 2004): Participants click as soon as possible when a red dot appears in one of nine locations on screen (at intervals randomly chosen from 1 – 10 seconds) over five minutes. Outcome variables were number of lapses (≥500ms response time) and average reaction time. See Appendix 2.11 for further details.

### Decision making

Jumping to conclusions (Garety & Freeman, 1999) task: The 85:15 ratio version of the task was used. Participants requested 'randomly selected' beads one at a time with replacement until they were certain which jar the beads were from (the beads are actually in a predetermined sequence). The outcome variable is the number of beads taken to make a decision. Individuals with paranoia have been found to exhibit a jumping to conclusions bias in this task, in which they ask for fewer beads before making their decision. See appendix 2.12 for further details.

### Working memory

N-Back task (Ragland et al., 2002). Participants are presented with a sequence of letters, and click when the current letter matches the letter 1 position, 2 position, or 3 positions back in the sequence. Participants completed two blocks of each of the 1, 2, and 3 back tasks in a random order. Each block contained 20 letters, with a 1/3 rate of matching letters. The outcome variable is the decision value, calculated by the below formula:

$$\text{Decision Value} = (\text{Correct Hits} - \text{False Alarms}) / \text{Total Number of Trials}$$

The minimum value is 0, maximum score is 0.3. A lower score indicates greater working memory impairment. See Appendix 2.13 for details.

## 2.3.4 Statistical analysis

Data for this two-condition two-period crossover trial were analysed using Stata version 14 (StataCorp, 2015). Demographic and adherence data were analysed using SPSS 22.0 (IBM Corp. Released, 2011). There were no missing data. Statistical significance was set at $p<0.05$.

Actigraphic and sleep diary estimates of sleep, and nicotine, alcohol, and caffeine consumption where checked for adherence using paired t-tests.

The primary data analysis was performed using multilevel modelling to account for the repeated measures within an individual and the two measures of 'baseline' prior to each of the sleep conditions. For each outcome, a linear mixed model was fitted with a fixed effect for order, the sleep condition, and the 'baseline' measure of the outcome, with a random intercept for each participant. This modelling was repeated for each putative mediator as an outcome. Effect sizes were calculated using the first baseline standard deviation (pooled across conditions and order groups) as the denominator (Feingold, 2009), which can be interpreted as equivalent to Cohen's d.

Whilst there has been considerable discussion of the underlying assumptions in statistical mediation analysis (Emsley, Dunn, & White, 2010), a crossover experimental design is a scenario in which these assumptions will plausibly hold. Mediation was therefore evaluated using the strategy suggested by Baron and Kenny (1986). In the final mediation analysis, only mediators and outcomes with a significant condition effect ($p<0.05$) from the previous analysis were examined (i.e. where significant changes in psychotic experiences and mood or cognitive changes were detected following sleep restriction). For each significant outcome, this involved fitting the additional linear mixed model as above with the addition of the putative mediators at 'baseline' and end of intervention as fixed effects. The total effect is the effect of sleep condition on outcome in the first model. The direct effect is the effect of sleep condition on outcome in the model including the mediators. The indirect effect is the product of the coefficient of sleep condition on the mediator, and the coefficient of the mediator on outcome. All three models were bootstrapped with 1000 replications to obtain valid standard errors and significance tests. If the direct effect is smaller than the total effect, it becomes non-significant in the presence of the mediator, and the indirect effect itself is statistically significant, then mediation would be concluded. As each mediator was considered individually, this sample size was considered to provide sufficient power to detect indirect effects. The proportion mediated was calculated as the ratio of the indirect effect to the total effect.

# 2.4 Results

### Demographics

The 68 study participants were balanced with respect to gender (54% female, n=37), were predominantly white British (69%, n=47), and the majority (76%, n=52) were undergraduate or postgraduate students. Further details can be found in Table 2.

### Adherence to sleep restriction

Nine hundred and seventy seven of the 993 SMS messages (98.4%) sent to the participants were responded to within the 15-minute window. The total sleep time recorded in the diaries (3h54 sleep loss condition vs 7h21 control condition) and by actigraphy (5h15 vs 6h58) show a significant reduction in sleep time (both $p<0.001$). No significant difference was found in alcohol (0.81 vs 1.02 units, $p=0.223$) or nicotine (1.47mg vs 1.26mg, $p=0.211$) intake across the two weeks. A slight but significant increase in caffeine intake was recorded in the sleep loss condition (104.32mg vs 87.23mg, $p=0.006$). However, the magnitude of this difference was small (17.09mg, which is less than half of the caffeine in a standard cup of black tea). Further details can be found in Table 3.

## 2.4.1 Changes in outcomes by condition

### Psychotic experiences

In Table 4 it can be seen that, in comparison to the control condition, the sleep loss condition was associated with significant increases in hallucinations, paranoia, and cognitive disorganisation. Distress from psychotic experiences also significantly increased relative to the control condition. All these changes had moderate to large effect sizes (ranging from 0.38 to 0.87). However, no significant changes due to sleep condition were found in grandiosity. An expanded table of mean changes across conditions, broken down by order of conditions, is available in Appendix 2.14.

There was a significant interaction between baseline scores and the sleep condition effect in paranoia (effect = 0.535 (SE=0.156), $p=0.001$), hallucinations (1.228 (0.280), $p<0.001$), and psychotic experience distress (0.388 (0.154), $p=0.012$), indicating that a higher baseline score resulted in a proportionally higher sleep condition effect. Further details can be found in Appendix 2.15.

### Mediators

Table 4 also illustrates that highly significant and large effect size increases were seen in depression, anxiety, and stress following the sleep loss condition, as compared to the control condition. Significant

and moderate effect size increases in worry (effect=0.402) and in endorsement of negative beliefs about self (0.463) and others (0.363) were also found following sleep loss. There were no significant changes in endorsements of positive beliefs about self or others.

Working memory task performance significantly worsened following the sleep loss condition as compared to the control condition (effect=0.55). No significant changes were seen in the number of beads requested prior to decision in the jumping to conclusions task. There were no significant changes in the illusion effect in the Ebbinghaus task. There was no significant effect of sleep condition on vigilance (reaction time or lapses).

### 2.4.2 Mediation analysis

The outcome of mediation analyses can be seen in Table 5. The effect of sleep loss on paranoia is almost completely mediated by negative affect (all >90%). Affective processes, in particular negative beliefs about others, also mediated a proportion of the effect. Working memory change was not a significant mediator for paranoia or for any other psychotic experience (i.e. the indirect effect via working memory did not reach significance for any outcome). The results for cognitive disorganisation are similar to those for paranoia, with significant mediation by negative affect, negative beliefs about self, and worry. However, the proportion mediated by these factors (26.2%-39.2%) was smaller than for paranoia. The only significant mediator found for hallucinations was stress (43.4%). Distress from psychotic experiences was again predominantly mediated by negative affect (51.4%-57.0% across dimensions), with no other mediators reaching significance.

Of all these mediators, only the negative affect and worry pathways for paranoia indicated full mediation (i.e. the direct effect of sleep on paranoia became non-significant in the presence of the mediator). In all other cases where a significant indirect effect was found, the direct effect pathway remained significant – this indicates that these other mediators are only partially mediating the effects seen.

## 2.5 Discussion

This is the first study to test the aetiology of psychotic experiences by simulating insomnia-like sleep loss in non-clinical volunteers. Participants adhered to the self-enforced sleep restriction, as demonstrated by the SMS responses and actigraphy. Compared to the control condition, sleep loss resulted in moderate to large effect size increases in paranoia, hallucinations, and cognitive disorganisation. There was no change in grandiosity. The significant interaction between baseline psychotic experience scores and sleep condition indicates a greater effect of sleep restriction on those endorsing more psychotic experiences at baseline. Large increases in depression and anxiety were found following the sleep loss condition (compared to the control condition), along with moderate increases in endorsement of negative beliefs about self and others, and in worry. There were no significant changes in positive beliefs about self or others. Significant impairment in working memory was found following the sleep loss condition. However, no changes were found for perceptual processing (illusory effects or vigilance), or decision making. Overall, the results are consistent with a causal role for insomnia in certain psychotic experiences.

The lack of change in grandiosity could be understood within the context of the large increase in negative affect. Emotion congruent models of grandiosity would predict that negative affective states are not conducive to the development of these beliefs (N. Smith, Freeman, & Kuipers, 2005). The absence of an effect of restricted sleep on perceptual vigilance is notable, given this is a common consequence of sleep restriction in previous laboratory-based studies (Banks & Dinges, 2007; Belenky et al., 2003; Rupp et al., 2009). In the current study vigilance decreased across the week in both sleep conditions. While there was a greater decrease in vigilance in the sleep loss condition, a social jet-lag effect in the control condition may have reduced the contrast with the sleep loss (Wittmann, Dinich, Merrow, & Roenneberg, 2006). The lack of change in jumping to conclusions bias suggests that this is not a route by which reduced sleep leads to increased psychotic experiences.

The mediation analysis sheds light on the link between disrupted sleep and psychotic experiences. This shows that negative affect is by far the most relevant factor in explaining the effect of sleep loss on psychotic experiences. These findings join others in demonstrating the importance of negative affect in this relationship (in both clinical and non-clinical populations) (B. Smith et al., 2006; Vorontsova, Garety, & Freeman, 2013).

Conversely, despite there being significant deficits in working memory following reduced sleep, these changes did not mediate any significant proportion of the effect on psychotic experiences. This was especially the case for paranoia, where 90% or more of the relationship was mediated by depression, anxiety, or stress. This pattern is identical to that found in a previous study, which tested the mechanisms underlying paranoia by the administration of Δ9-tetrahydrocannabinol (the principal psychoactive ingredient of cannabis; Freeman, Dunn, Murray, et al., 2015). As in the current study this induced increases in negative affect, working memory impairment, and paranoia. The increased negative affect mediated the relationship between the experimental manipulation and increased paranoia, with no significant role for the working memory impairment. The significant mediation by both worry and negative self belief in this study is also interesting in the context of clinical trials demonstrating that addressing these affective processes can improve symptoms of paranoia in individuals with persecutory delusions (Foster et al., 2010; Freeman et al., 2014). These results emphasise the key role of negative affect and affective cognitions in paranoia (Freeman & Garety, 2003), above neuropsychological factors.

Cognitive disorganisation shared many of the same mediators as paranoia, although in all cases the mediation was incomplete. This indicates that further factors might be responsible for the increase in cognitive disorganisation reported. As there is a dearth of psychological models for cognitive disorganisation it is not possible to speculate on further factors. Regardless, it is still intriguing that working memory impairment did not mediate cognitive disorganisation, given the apparent link between these phenomena. The increase in hallucinations was least well accounted for by the mediators tested. Only one aspect of negative affect (stress) was identified as a possible (partial) mediator. This implies that different mechanistic factors may link sleep dysfunction to hallucinations, and sleep dysfunction to cognitive disorganisation, supporting the need to research and measure psychotic experiences individually rather than grouping together as a unitary 'psychosis' (Beards & Fisher, 2014; van Os, 2009; Wigman et al., 2011).

### 2.5.1 Limitations and future directions

This study models insomnia by delaying sleep onset to decrease total sleep time. However insomnia is also characterised by decreases in sleep efficiency (more time spent in bed awake), and decreased sleep continuity (waking during the night), which are not simulated in the manipulation. Nevertheless, the ecological validity of the design, wherein participants were required to go about their daily lives while

suffering from the consequences of reduced sleep, offers a significant advantage in allowing replication of some aspects of insomnia as experienced by the clinical population. It may also be worth considering that a study comparing delayed onset sleep loss versus sleep loss by disrupting sleep continuity found that continuity disruptions resulted in even greater increases in negative affect than delayed sleep onset (Finan et al., 2015). Therefore the current study may underestimate the impact of insomnia on mood and psychotic experiences.

One potential limitation is that the actigraphic recording indicated incomplete adherence to the sleep restriction (5h15 of sleep, rather than the 4h target). An explanation for this can be that the actigraphic analysis algorithm assumes periods of inactivity amount to sleep, therefore sleep can be overestimated when individuals are tired and less active. Regardless, as the study aimed to investigate the effects of reduced sleep (rather than precisely the effect of four hours of sleep), the conclusions of the study remain.

It was not possible to test for expectancy effects that participants may have had regarding sleep loss. However, attempts were made to minimise these by referring to "psychological changes" as the main outcome, rather than specifically relating the study to psychotic experiences. The lack of change in grandiosity following sleep loss indicates that the changes were more selective than would be expected if caused by expectancy effects.

Psychotic experiences were generally endorsed at a low level in the study group, and all changes remained in the non-clinical range. However it should be noted that this was screened to be a 'psychologically healthy' sample, and that this was a mild sleep restriction manipulation. Furthermore, the interaction analysis shows that those endorsing more psychotic experiences at baseline had a greater relative increase in psychotic experiences after sleep restriction. Therefore it could be hypothesised that the effect of sleep loss on psychotic experiences in a more vulnerable group might be correspondingly more severe.

Besides the theoretical importance of these findings, there are some implications for clinical practice. Firstly, monitoring or treating insomnia in individuals at risk of psychosis may reduce transition to first episode psychosis. Secondly, sleep problems may be maintaining negative emotional states, which themselves may be maintaining distressing psychotic experiences. Treatment of insomnia in psychosis has recently been shown to be highly effective (Freeman, Waite, Startup, et al., 2015) and well-

accepted by patients (Waite, Evans, et al., 2016). However, while clinicians recognise the importance of sleep, sleep problems are rarely formally assessed or treated (Rehman et al., 2016), and are traditionally considered a consequence of psychosis. The current study shows that sleep problems themselves may be causally relevant to the onset or maintenance of distressing psychotic experiences.

## 2.6 Tables

### 2.6.1 Table 1: Existing sleep deprivation studies addressing psychotic experiences

| Citation | N | Sample characteristics | Psychotic experience measure | Sleep deprivation | Findings |
|---|---|---|---|---|---|
| (Hurdiel et al., 2014) | 17 | Volunteers completing ultramarathon event | Hallucinations – open ended question on completion | Average 46h 38min (measured by actigraphy) | 4 out of 17 participants reported experiencing hallucinations during the exercise event. |
| (Kahn-Greene et al., 2007) | 25 | Non-clinical volunteers (recruited from military) | PAI (pre and post sleep deprivation) | 56 hours (in lab) | Sleep deprivation resulted in increase in anxiety, depression, and paranoia, but not manic-related symptoms or schizophrenia symptom factors. |
| (Petrovsky et al., 2014) | 24 | Non-clinical volunteers (students) | PSI (pre and post sleep deprivation) | Overnight sleep deprivation (in lab) | Sleep deprivation induced perceptual distortions, cognitive disorganisation and anhedonia, but not mania, paranoia or delusional thinking. |

PAI = Personality Assessment Inventory (Morey, 1991); PSI = Psychotomimetic States Inventory (Mason et al., 2008)

## 2.6.2 Table 2: Demographics of study sample

| | Total sample | First week restricted | Second week restricted |
|---|---|---|---|
| | *N=68* | *(n=33)* | *(n=35)* |
| Mean age in years (SD) | 22.5 (3.4) | 21.9 (3.1) | 23.0 (3.7) |
| **Gender – n (%)** | | | |
| Male | 31 (45.6) | 14 (42.4) | 17 (48.6) |
| Female | 37 (54.4) | 19 (57.6) | 18 (51.4) |
| **Ethnicity – n (%)** | | | |
| White/White British | 47 (69.1) | 22 (66.7) | 25 (71.4) |
| Asian/Asian British | 12 (17.6) | 6 (18.1) | 6 (17.1) |
| Mixed/multiple ethnic groups | 5 (7.4) | 1 (3.0) | 4 (11.4) |
| Black/African/Caribbean/Black British | 2 (2.9) | 2 (6.1) | 0 (0.0) |
| Other | 2 (2.9) | 2 (6.1) | 0 (0.0) |
| **Occupation – n (%)** | | | |
| Undergraduate student | 33 (48.5) | 17 (51.5) | 16 (45.7) |
| Postgraduate student | 19 (27.9) | 9 (27.3) | 10 (28.6) |
| Part-time employed | 5 (7.4) | 2 (6.1) | 3 (8.6) |
| Full-time employed | 10 (14.7) | 5 (15.2) | 5 (14.3) |
| Unemployed | 1 (1.5) | 0 (0.0) | 1 (2.9) |

## 2.6.3 Table 3: Adherence to sleep conditions

| | Restricted Sleep | Standard Sleep | |
|---|---|---|---|
| | Mean (SD) | Mean (SD) | p-value.[a] |
| Avg mins sleep - sleep diary | 231 (18.6) | 432 (65.2) | <0.001 |
| Avg mins sleep - actigraphy *(n=60)*[b] | 315 (103.7) | 418 (71.8) | <0.001 |
| Daily caffeine (mg) | 104.32 (87.8) | 87.23 (77.3) | 0.006 |
| Daily alcohol (units) | .81 (2.0) | 1.02 (1.4) | 0.223 |
| Daily nicotine (mg) | 1.47 (5.8) | 1.26 (5.0) | 0.211 |

[a] Tested in paired samples t-test

[b] Actigraphic recordings were not available for eight participants. In six cases the watches failed , in one case the strap broke and the watch was unwearable, and in the last case the participant lost the watch.

## 2.6.4 Table 4: Changes in psychotic experiences and candidate mediators following sleep restriction and control condition

| Psychotic Experiences | Sleep | Baseline mean (SD) | Endpoint mean (SD) | Effect (SE), p-value | 95% CI | Effect size |
|---|---|---|---|---|---|---|
| Paranoia (SPEQ) | Restricted | 2.3 (3.4) | 3.8 (5.4) | 1.57 (0.54), 0.003 | 0.52, 2.63 | 0.383 |
| | Standard | 2.8 (4.7) | 2.5 (5.4) | | | |
| Hallucinations (SPEQ) | Restricted | 0.4 (0.8) | 1.2 (2.4) | 1.06 (0.28). <0.001 | 0.51, 1.62 | 0.869 |
| | Standard | 0.3 (1.5) | 0.1 (0.7) | | | |
| Cognitive Disorganisation (SPEQ) | Restricted | 2.6 (3.9) | 4.8 (4.2) | 2.44 (0.36), <0.001 | 1.73, 3.14 | 0.643 |
| | Standard | 2.7 (3.8) | 2.5 (3.5) | | | |
| Grandiosity (SPEQ) | Restricted | 6.6 (6.7) | 6.7 (6.6) | 0.14 (0.52), 0.780 | -0.87, 1.16 | 0.002 |
| | Standard | 6.4 (6.1) | 6.4 (6.5) | | | |
| Psychotic experience distress (SPEQ) | Restricted | 0.3 (0.8) | 0.7 (1.1) | 0.42 (0.12), 0.001 | 0.18, 0.66 | 0.521 |
| | Standard | 0.4 (0.8) | 0.3 (0.7) | | | |
| **Mediating Variables** | **Sleep** | **Baseline mean (SD)** | **Endpoint mean (SD)** | **Effect (SE), p-value** | **95% CI** | **Effect size** |
| Depression (DASS) | Restricted | 2.0 (3.9) | 4.6 (6.1) | 2.80 (0.61), <0.001 | 1.61, 3.99 | 0.776 |
| | Standard | 1.8 (3.2) | 1.6 (3.9) | | | |
| Anxiety (DASS) | Restricted | 2.2 (3.2) | 5.2 (5.2) | 3.53 (0.67), <0.001 | 2.22, 4.84 | 1.002 |
| | Standard | 3.0 (3.8) | 2.1 (3.9) | | | |
| Stress (DASS) | Restricted | 3.8 (6.2) | 7.8 (7.8) | 4.61 (0.85), <0.001 | 2.95, 6.27 | 0.806 |
| | Standard | 4.0 (5.3) | 3.3 (4.6) | | | |
| Negative beliefs about self (BCSS) | Restricted | 1.8 (2.2) | 2.6 (3.2) | 1.05 (0.28), <0.001 | 0.50, 1.60 | 0.463 |
| | Standard | 1.9 (2.3) | 1.6 (2.1) | | | |
| Positive beliefs about self (BCSS) | Restricted | 13.1 (5.3) | 12.0 (5.1) | -0.55 (0.53), 0.305 | -1.59, 0.50 | 0.113 |
| | Standard | 13.7 (4.4) | 130.0 (5.3) | | | |
| Negative beliefs about others (BCSS) | Restricted | 1.9 (2.7) | 2.6 (3.7) | 0.99 (0.36), 0.006 | 0.29, 1.68 | 0.363 |
| | Standard | 2.0 (2.8) | 1.7 (2.4) | | | |
| Positive beliefs about others (BCSS) | Restricted | 12.0 (5.0) | 11.8 (4.9) | 0.19 (0.56), 0.737 | -0.91, 1.28 | 0.044 |
| | Standard | 12.9 (3.7) | 12.1 (5.0) | | | |
| Worry (Worry scale) | Restricted | 5.9 (6.4) | 7.6 (7.3) | 2.59 (0.92), 0.005 | 0.80, 4.39 | 0.402 |
| | Standard | 6.0 (6.6) | 5.0 (6.0) | | | |
| Ebbinghaus – difference in scores | Restricted | 40.3 (9.3) | 39.7 (11.0) | 0.74 (1.19), 0.538 | -1.60, 3.06 | 0.079 |
| | Standard | 40.8 (9.2) | 39.4 (10.2) | | | |
| Perceptual vigilance - average RT (ms) | Restricted | 603.5 (975.3) | 613.2 (409.9) | 63.13 (56.11), 0.261 | -46.84, 173.10 | 0.233 |
| | Standard | 510.7 (300.8) | 539.0 (283.7) | | | |
| Perceptual vigilance – no. of lapses (RT ≤500ms) | Restricted | 12.0 (12.9) | 18.1 (15.5) | 2.65 (1.48), 0.072 | -0.24, 5.56 | 0.214 |
| | Standard | 11.1 (11.8) | 15.4 (12.4) | | | |
| Working memory (N-back decision value) | Restricted | 0.2 (0.1) | 0.2 (0.1) | -0.03 (0.01), 0.005 | -0.04, -0.01 | 0.545 |
| | Standard | 0.2 (0.0) | 0.2 (0.1) | | | |
| Jumping to conclusions (no. of. beads) | Restricted | 3.5 (4.1) | 4.6 (4.5) | 0.02 (0.27), 0.925 | -0.50, 0.55 | 0.005 |
| | Standard | 4.2 (3.6) | 4.3 (3.5) | | | |

## 2.6.5 Table 5 Mediation analysis for increases in psychotic experiences

| OUTCOME | TOTAL EFFECT<br>Estimate (SE), p-value | PUTATIVE MEDIATOR | DIRECT EFFECT<br>Estimate (SE), p-value | INDIRECT EFFECT<br>Estimate (SE), p-value | PROPORTION MEDIATED % |
|---|---|---|---|---|---|
| SPEQ Paranoia | 1.57 (0.59), 0.008 | Anxiety | 0.26 (0.79), 0.747 | 1.44 (0.59), 0.014 | **91.7** |
| | | Depression | -0.12 (0.54), 0.816 | 1.45 (0.42), 0.001 | **92.1** |
| | | Stress | 0.02 (0.63), 0.969 | 1.55 (0.51), 0.002 | **98.7** |
| | | Negative beliefs about self | 1.13 (0.50), 0.023 | 0.43 (0.33), 0.195 | **27.2** |
| | | Negative beliefs about others | 0.92 (0.54), 0.084 | 0.64 (0.24), 0.009 | **40.8** |
| | | Worry | 0.86 (0.73), 0.238 | 0.67 (0.39), 0.082 | **42.7** |
| | | Working Memory | 1.51 (0.66), 0.022 | 0.07 (0.18), 0.687 | **4.7** |
| SPEQ Hallucinations | 1.06 (0.29), <0.001 | Anxiety | 0.88 (0.28), 0.002 | 0.23 (0.18), 0.193 | **22.0** |
| | | Depression | 0.89 (0.32), 0.005 | 0.13 (0.12), 0.276 | **12.9** |
| | | Stress | 0.61 (0.22), 0.006 | 0.46 (0.23), 0.045 | **43.4** |
| | | Negative beliefs about self | 0.81 (0.27), 0.002 | 0.27 (0.16), 0.094 | **25.4** |
| | | Negative beliefs about others | 0.93 (0.28), 0.001 | 0.14 (0.08), 0.071 | **12.7** |
| | | Worry | 0.93 (0.30), 0.002 | 0.14 (0.12), 0.200 | **13.4** |
| | | Working Memory | 1.06 (0.30), <0.001 | 0.01 (0.07), 0.912 | **0.7** |
| SPEQ Cognitive disorganisation | 2.44 (0.40), <0.001 | Anxiety | 1.52 (0.41), <0.001 | 0.96 (0.31), 0.002 | **39.2** |
| | | Depression | 1.78 (0.40), <0.001 | 0.64 (0.25), 0.011 | **26.2** |
| | | Stress | 1.55 (0.40), <0.001 | 0.90 (0.28), 0.001 | **36.8** |
| | | Negative beliefs about self | 2.05 (0.38), <0.001 | 0.41 (0.18), 0.026 | **16.8** |
| | | Negative beliefs about others | 2.26 (0.37), <0.001 | 0.17 (0.15), 0.242 | **7.0** |
| | | Worry | 1.90 (0.36), <0.001 | 0.53 (0.26), 0.042 | **21.7** |
| | | Working Memory | 2.40 (0.43), <0.001 | 0.03 (0.09), 0.706 | **1.4** |
| SPEQ Distress | 0.42 (0.14), 0.002 | Anxiety | 0.18 (0.13), 0.174 | 0.24 (0.12), 0.048 | **56.9** |
| | | Depression | 0.17 (0.12), 0.145 | 0.24 (0.09), 0.009 | **57.0** |
| | | Stress | 0.20 (0.12), 0.080 | 0.22 (0.09), 0.022 | **51.4** |
| | | Negative beliefs about self | 0.27 (0.12), 0.020 | 0.15 (0.08), 0.056 | **34.8** |
| | | Negative beliefs about others | 0.37 (0.13), 0.005 | 0.05 (0.03), 0.111 | **12.3** |
| | | Worry | 0.28 (0.12), 0.022 | 0.14 (0.08), 0.082 | **33.3** |
| | | Working Memory | 0.34 (0.14), 0.012 | 0.08 (0.06), 0.162 | **18.4** |

# Chapter 3

# Sleep duration and psychotic experiences over time in patients at risk of psychosis: a secondary analysis of the EDIE-2 trial

The chapter originally presented here cannot be made freely available via ORA until July 2019 due to copyright.

# Chapter 4

# Sleep disorders in early psychosis

The chapter originally presented here cannot be made freely available via ORA until July 2019 due to copyright.

# Chapter 5

# Insomnia, negative affect, and psychotic experiences over time: modelling relationships in patients with early psychosis

The chapter originally presented here cannot be made freely available via ORA until July 2019 due to copyright.

# Chapter 6

## Hypersomnia in psychosis: an initial investigation

The chapter originally presented here cannot be made freely available via ORA until July 2019 due to copyright.

# Chapter 7
# Conclusions

*"The best bridge between despair and hope is a good night's sleep."* - E. Joseph Cossman

In this chapter a summary of the findings of the thesis and its limitations shall be presented, followed by an update on recent research. Based on these, future directions for research and clinical practice will be discussed.

## 7.1 Summary of the thesis

The research described in this thesis shows that sleep dysfunction does not occur solely as a consequence of psychosis, but may have a contributory role in the onset and maintenance of psychotic experiences. The systematic review in Chapter 1 gave an overview of the existing literature, finding that there was a lack of studies which directly tested the causal role of sleep in the occurrence of psychotic experiences, that empirical studies of mechanisms were very limited, and that very few studies had investigated the breadth of sleep disorders in individuals with psychosis. The remaining chapters of the thesis then attempted to start to address these shortcomings.

The sleep restriction study in Chapter 2 was the first clear demonstration of a causal role for insomnia in the occurrence of psychotic experiences. Furthermore, it was the first experimental study to show that negative affect was the primary mechanism linking insomnia to psychotic experiences, although the mechanisms differed somewhat among individual psychotic experiences, as negative affect was a complete mediator for the influence of insomnia on paranoia but only a partial mediator for hallucinations. The study also found that the effects of sleep loss on increasing psychotic experiences were stronger for individuals endorsing higher levels of psychotic experiences at baseline. The latter finding suggested that sleep may be particularly important in the at-risk psychosis population.

The potential role of sleep in the at-risk population was investigated in Chapter 3 via an opportunistic secondary analysis of the Early Detection and Intervention Evaluation (EDIE-2) trial cohort (Morrison et al., 2012). Sleep duration variables were tested for cross-sectional and longitudinal associations with psychotic experience severity. Significant relationships were found between shorter sleep duration and more severe delusions and hallucinations at the same and later time points,

although these relationships did not remain significant once conservative controls were added for previous levels of each psychotic experience. Nevertheless, the results still indicated a possible role of sleep dysfunction in predicting the clinical trajectory of the at-risk group.

In Chapter 4 the focus moved from the at-risk group to individuals who have a non-affective psychotic disorder diagnosis. The aim in this study was to carry out the first assessment of the breadth sleep disorders in this population, and the results confirmed clinician impressions (Rehman et al., 2016) that sleep disorders among individuals with psychosis are common and severe. The complexity of the sleep disorder presentation, with multiple sleep disorder comorbidities being the norm in the study group, was another novel finding, and further demonstrates the scale of sleep issues present in patients with psychosis. The study supported the importance of improving the assessment and treatment of sleep disorders in individuals with psychosis, as less than 10% of sleep disorders had been appropriately treated.

Chapter 5 focused specifically on insomnia, with a longitudinal observational study mapping the relationships between insomnia, negative affect, and psychotic experiences over time. Statistical models based on the hypothesised role of insomnia in predicting later psychotic experiences were tested against competing models where the direction of effects were reversed. The results demonstrated that the hypothesised models were a better fit to the observed data than the competing models, supporting the promise of insomnia interventions as an opportunity to improve negative affect and psychotic experiences, alongside treating the sleep disorder itself.

In Chapter 6 the focus moved from insomnia to hypersomnia, following a common theme of oversleeping, sleepiness, and sedation emerging from patient and clinician reports (Faulkner & Bee, 2017; Rehman et al., 2016; Waite, Evans, et al., 2016) and the high incidence of excessive sleep disorders reported in Chapter 4. This exploratory study found that hypersomnia in psychosis is not necessarily associated with longer sleep duration, but is associated with lower daytime activity, increased fatigue, and increased negative affect. This presentation is similar to that of hypersomnia in mood disorders, but also could be due to the high comorbidity of hypersomnia with other sleep disorders in the study group. Further research investigating the longitudinal clinical course of those with hypersomnia, and possible interventions, would be valuable given the prevalence of hypersomnia in psychosis, and lack of research on this issue to date.

In sum, the evidence gathered in this thesis is consistent with the hypothesis that sleep dysfunction has a causal role in psychotic experiences. The thesis has mainly focused on insomnia, for which a causal role has been demonstrated by a manipulation study (Chapter 2) and a longitudinal data analysis (Chapter 5). The primary mechanism by which insomnia was found to contribute to psychotic experiences was negative affect. It is plausible that other sleep disorders (e.g. nightmares) similarly contribute to psychotic experiences (via increasing negative affect, or via other mechanisms), however further studies will be needed to demonstrate a causal role of other sleep disorders.

Negative affect as a mechanism linking sleep dysfunction and psychotic experiences fits well within theoretical models for psychotic experiences, which increasingly emphasise a role of negative affect in the onset and maintenance of psychotic experiences (Garety et al., 2001). The findings in this thesis indicate that sleep dysfunction may be a contributory causal factor for hallucinations, paranoia, and cognitive disorganisation. However, the primary mechanisms by which it contributes appear to differ by psychotic experience and by aspect of sleep dysfunction. The relationship between sleep dysfunction and grandiosity also deserves further investigation – while it was not linked to insomnia or other sleep disorders in Chapter 2 or Chapter 4, in Chapter 6 it appears to be associated with hypersomnia. A key part of resolving the relationship between sleep dysfunction and grandiosity will be resolving the role of negative affect in grandiosity, which so far has been a source of debate (Knowles, McCarthy-Jones, & Rowse, 2011).

Separately from these conclusions regarding the mechanisms linking sleep dysfunction to psychosis, the secondary finding of this thesis is that sleep disorders are prevalent and severe in psychosis (as principally discussed in Chapter 4). These findings support the need for further investigation in to the mechanisms linking sleep dysfunction and psychosis, given the prevalence of many kinds of sleep dysfunction in this group. However, more importantly these findings emphasise the importance of improving assessment and treatment of sleep disorders in psychosis, even independently of the relationship between sleep disorders and psychotic experiences.

## 7.2 Limitations

There are of course limitations to the conclusions that can be drawn from this thesis, besides the specific limitations for each study. For instance, the research described in this thesis has focused on the positive symptoms of psychosis (paranoia, hallucinations, cognitive disorganization, and

grandiosity). However, this means that negative symptoms of psychosis (e.g. anhedonia, avolition, alogia, flat affect) were not assessed, despite a plausible link between these experiences and sleep dysfunction. The rationale for the focus on positive symptoms was based on the success of the single symptom approach in allowing detailed specification of mechanisms (e.g. Freeman 2016), and the availability of single symptom models for positive symptoms (particularly delusions and hallucinations) in comparison to a lack of single symptom models for negative symptoms. The importance of this relatively narrow focus has been supported by the complexity of the relationships found between sleep dysfunction and psychotic experiences, both within this thesis and elsewhere. Without a limitation on scope it would not have been possible to investigate the relationships with sleep dysfunction in such detail within this thesis.

The focus on this thesis has been on cognitive psychological models, but there are also neurodevelopmental, neurochemical, and computational theories that could be applied to the relationship between sleep and psychosis (see Chapter 1). The focus on cognitive psychological models was based on a necessity of limiting the scope of the thesis, but also because insomnia, the primary sleep problem investigated, is most frequently conceptualised within cognitive models (Espie, 1991; Harvey, 2002). Therefore, given the aim of the thesis was to draw links between sleep dysfunction and psychotic experiences, a matching focus on cognitive models in psychosis was the most sensible approach. However, given the complexity of the sleep disorders found in the clinical group, it is clear that further work will be needed to investigate the sleep and psychosis link at multiple levels – especially as other sleep disorders (e.g. restless legs syndrome) are understood to have a more physiological rather than cognitive etiology (Becker & Novak, 2014).

One methodological limitation in this thesis is the measurement of sleep disorders. In Chapter 4 and Chapter 6 the sleep disorder assessment relies on a structured diagnostic interview that has not been validated in the psychosis population. Adaptations were made to the scoring of to this interview in order to increase its applicability in the population (see Appendices 4.2 and 4.3). However, by moving the interview away from its original scoring its reliability and validity may have suffered, which is not possible to assess. Attempts were made to limit the impact of these changes in three ways. Firstly, the diagnostic criteria for each disorder (pooled between the International Classification of Sleep Disorder and Diagnostic and Statistical Manual of Mental Health and Disorders) were conservatively applied to the diagnostic interview responses. Secondly, the severity scoring was based on standardised

principles regarding rating the frequency, duration, distress and impairment caused by the disorder, with threshold guidelines from diagnostic guidance or the wider literature applied as appropriate. Finally, the algorithm for assessing diagnosis and severity for each disorder has been specified in detail in the appendices of the thesis to provide transparency and a rationale for all adaptations. This process in itself drew attention to the need for improved sleep assessment measures for individuals with psychosis and other mental health problems.

Another limitation of the thesis is the lack of patient voice. Including more patient input might have allowed additional theoretical mechanisms linking sleep dysfunction and psychosis to be identified. Furthermore, given that one of the conclusions of the thesis is that sleep disorders should be a greater target of assessment and intervention by clinicians, service user input on the acceptability and implementation of these recommendations would have been worthwhile. Qualitative research on patient perspectives on sleep problems and treatment has generally indicated that patients perceive their sleep as disturbed and would welcome treatment (Faulkner & Bee, 2016, 2017; Waite, Evans, et al., 2016). However, there are some important reservations that require further exploration: for example, patients may perceive their sleep problems as only treatable via medication, or may consider them as a permanent part of their condition and therefore untreatable (Faulkner & Bee, 2017). Another interesting finding in the same study was that patients were not necessarily motivated to improve their sleep in itself, but instead as a way of helping achieve their occupational, social, and recovery goals via improved daytime functioning. These are important results to consider alongside the findings of this thesis, and further service user input would be vital in future investigations of sleep dysfunction in psychosis.

## 7.3 Recent results

Even since the introduction to this thesis was updated in April 2017 there have been further publications on the topic of sleep and psychosis. These recent results are worth summarising before future directions are explored.

The most important among these new findings is the results from the OASIS trial (Freeman et al., 2017). This randomised controlled trial of an online CBT for insomnia (CBTi) intervention in a population of students with insomnia (n=3755) was specifically powered to test whether improving insomnia improved psychotic experiences. Significant improvements in paranoia (d=0.19) and

hallucinations (d=0.24) were indeed found following the insomnia treatment alongside larger improvements in depression (d=0.48) and anxiety (d=0.33). Clearly this study is an important piece of work for the conclusions from this thesis. Not only does it confirm a causal role of insomnia in psychotic experiences in support of the results in Chapter 2 (including a mediation analysis demonstrating that the improvement in psychotic experiences was a result of insomnia treatment), but it also demonstrates the potential for insomnia treatment as an early stage intervention for preventing or improving psychotic experiences.

Two other recent publications have focused on the youth or at-risk group. The first, an experience sampling study, sought to investigate the day-by-day interaction of sleep and paranoia (including an analysis of mediating factors) in a group of 61 non-clinical adolescents (Hennig & Lincoln, 2017). The findings were that shorter sleep duration and higher dreaming predicted increased paranoia, but with paranoia not significantly predicting sleep parameters (in contrast to Chapter 5). The second study, a case series, investigated the feasibility of treating sleep problems in young people at-risk of psychosis (Bradley et al., 2017). All eligible patients referred to the study agreed to take part, and 11 out of 12 participants completed the CBTi-based intervention. Large effect size improvements in insomnia were found, and improvements also reported in psychotic experiences, negative affect, and psychological wellbeing. This study, while only an uncontrolled case series, demonstrates some of the strengths of insomnia treatment as a brief, acceptable, effective, non-stigmatising intervention that may have wider benefits in preventing exacerbation of psychotic experiences in this crucial clinical population.

Another recently published trial tested the feasibility of a psychological treatment for sleep in an acute inpatient group (Sheaves et al., 2017). Forty male inpatients were recruited, with half receiving an acute sleep intervention over two weeks and the other half receiving treatment as usual. The twenty patients who had the sleep treatment showed large effect size improvements in insomnia post treatment (with significant effects still present at 12-week follow-up), and a small but significant improvement in psychological wellbeing, as well as being discharged from the ward on average 8.5 days earlier than the control group. No significant changes in psychotic experiences were found (although the study was not adequately powered for this), but the directions of effects indicate that the sleep treatment was beneficial to psychotic experiences and psychological wellbeing.

Recent results in non-clinical groups also provide new perspectives on the mechanisms linking sleep dysfunction and psychosis. Rehman and colleagues recruited a large group (n=401) to investigate the

mechanisms linking sleep quality and paranoia. The relationship was found to be partially mediated by alexithymia (the inability to recognise and describe emotions), perceptual anomalies, and negative affect, although in the replication model (with a second sample; n=402) these factors fully mediated the relationship between sleep quality and paranoia (Rehman, Gumley, & Biello, 2017). The instability in these findings may be due to the issues inherent to cross-sectional mediation analysis (Preacher, 2014), but regardless these findings support a role of negative affect as a mediator in the insomnia and paranoia relationship, and suggest emotion regulation and perceptual anomalies as further potential mediators for this relationship.

Another non-clinical survey study, with over 800 participants, investigated nightmares and their potential causal factors (Rek, Sheaves, & Freeman, 2017). Again, this study was cross-sectional, but nightmares were found to be linked with hallucinations and paranoia. Furthermore, these associations remained significant even once negative affect was controlled for. Depersonalisation (related to dissociation) and worry were also identified as potentially relevant factors associated with nightmares. Both these factors are also linked to psychotic experiences (Freeman et al., 2012; Humpston et al., 2016), therefore they would be worthwhile to test as mediators of a nightmare to psychotic experience relationship in further longitudinal design studies.

## 7.4 Future directions

It is clear that in recent years there has been progress in understanding the relationship between sleep dysfunction and psychosis, and that interest is growing in this field as reflected by an increasing number of publications (see Figure 1). However, there are many areas where further research is still required.

While there has been a focus in this thesis and elsewhere (e.g. Rehman et al., 2017) on identifying the mechanisms linking sleep dysfunction and psychotic experiences, the mechanistic picture is still far from complete. The primary mediator identified so far is negative affect, especially for paranoia – although even here additional possible mediators have been identified. However, mediators for hallucinations remain more uncertain, perhaps reflecting the relative lack of consensus on the cognitive causes of hallucinations. Possible mechanisms include emotion regulation (Grezellschak et al., 2017; Rehman et al., 2017) and dissociation (Koffel & Watson, 2009; Van Der Kloet et al., 2013), or perhaps trauma as a common cause for sleep disorders and psychotic experiences (Freeman et al.,

2013; Geddes, Ehlers, & Freeman, 2016; Kilicaslan et al., 2017). Future research seeking to investigate mechanisms should ensure that specific measurement is made of sleep disorders or sleep variables (e.g. focusing on nightmares, or on sleep duration), and that individual psychotic experiences are measured, as it seems likely that there may be shared and differential causal factors between these experiences.

The broader range of consequences of sleep disorders and sleep dysfunction also require further research. While the emerging consensus is that sleep dysfunction predicts poorer outcome in mental health, it is likely that sleep dysfunction also has an impact on outcomes such as engagement with or effectiveness of other interventions, occupational and social recovery, utilisation of services, and physical health. These need to be systematically assessed so that an economic case can be made for increasing investment in clinical approaches to sleep disorders in mental health services.

Improvement is also needed in treatments for sleep disorders beyond insomnia in individuals with psychosis. A potential barrier here is the general lack of research on treatment for sleep disorders besides insomnia, and in treatment approaches for where sleep issues are comorbid. One approach to resolving this issue would be to identify the other most common and impactful sleep disorders in psychosis (e.g. nightmares), and develop treatments for these that are feasible, acceptable, and effective in this population (e.g. Sheaves 2015), ideally based on existing evidence-based treatment guidelines (e.g. Aurora *et al.* 2010). Another valuable route would be to develop more generic sleep interventions that can be applied in specific clinical phases (e.g. if relapse signs are detected) or settings (e.g. inpatient care). Ideally these treatments would be modular and highly manualised such that they can be easily applied by clinicians who may not have specific expertise in sleep disorders. In order to develop this area qualitative research and service user input are needed to further specify treatment targets and preferences (Faulkner & Bee, 2016; Waters, Chiu, Janca, Atkinson, & Ree, 2015).

However, these advances in understanding of the relationship between sleep dysfunction and psychotic experiences also need to reach clinical practice. A historical issue in sleep research and clinical practice has been its placement between mental and physical health, which means both medical and psychological training typically lacks sufficient training on sleep disorders. A recent survey found that UK medical students only receive a median of 2.5 hours of training on sleep disorders or treatment, with 13% of medical schools surveyed providing no sleep training at all (Urquhart, Orme, & Suresh, 2012) – similar results were found in a survey of psychology training in

the USA (Meltzer, Phillips, & Mindell, 2009). This lack of training is apparent in current clinician approaches to sleep disorders in psychosis. A recent clinician survey found that while clinicians agree that sleep is important for mental health, they rarely utilise structured or quantitative assessment techniques with patients reporting sleep issues, and provision of recommended interventions was rare (Rehman et al., 2016). This is mirrored by the findings in Chapter 4, wherein patients reported a lack of assessment or treatment for their sleep disorders within mental health services. This training gap represents a significant challenge, compounded by the complexity and severity of sleep disorders reported by individuals with psychosis. A clear priority is therefore to improve clinician skills and knowledge in assessing and treating sleep problems.

Improving clinical practice in the assessment and treatment of sleep will require significant investment, however there are likely to be multiple benefits to improving sleep even beyond the treatment of the sleep disorder and the possible secondary benefits to psychotic experiences. The most robust evidence on these additional benefits exists for treating insomnia – for instance, treating insomnia leads to improvement in other mental health issues such as depression and anxiety (Christensen et al., 2016; Freeman et al., 2017). Insomnia is also linked with lower functional health, lower quality of life and reduced psychological wellbeing. An ongoing randomised controlled trial is directly testing if treating insomnia improves these outcomes (Espie et al., 2016). Insomnia is also linked with a range of physical health problems including heart disease, high blood pressure, breathing problems, and chronic pain (Taylor et al., 2007). A recent study also showed that treating insomnia leads to improvement in pain from osteoarthritis (Vitiello et al., 2013), and it seems likely that treating insomnia may also improve other aspects of physical health. Furthermore, improving insomnia has been found to lead to reduced health care costs from primary care visits and chronic disease (McCrae, Bramoweth, Williams, Roth, & Mosti, 2014).

It is also worth considering that while this thesis has focused on treating sleep dysfunction in psychosis, there is also significant evidence supporting a role of insomnia treatment as an early or preventative intervention in mental health more generally. Firstly, the early stages of psychiatric illness are often characterised by non-differentiated symptoms (including anxiety, depression, and sleep issues) (Sheaves, Porcheret, et al., 2016). It is possible that sleep interventions in the early non-differentiated stage might act as a transdiagnostic intervention to prevent transition to diagnosable disorder or more severe symptoms. A second advantage of sleep intervention is that it is generally

perceived as non-stigmatising in comparison to other mental health interventions (Faulkner & Bee, 2016). A third advantage is deliverability – CBTi has been effectively delivered both online (Espie et al., 2012) and by nursing staff with appropriate training (Espie et al., 2007), therefore delivering the clinically recommended insomnia treatment (National Institute for Health and Clinical Excellence (NICE), 2015; Qaseem et al., 2016) is feasible even within a resource limited health system. The focus of this research to date has again been on insomnia, however, it is likely that treatment of other sleep disorders would have similar advantages.

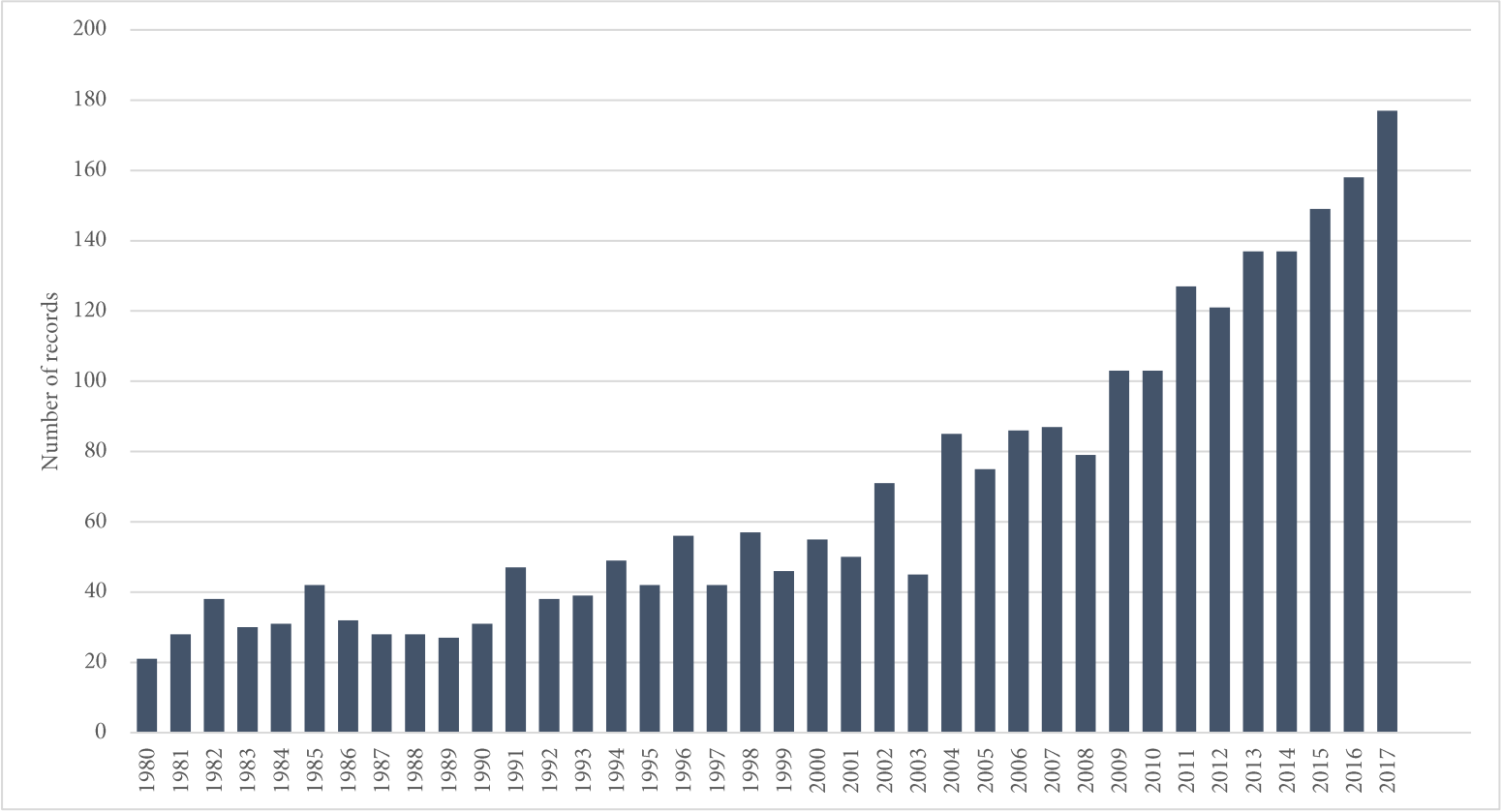
There are additional specific challenges with administering sleep treatments within the psychosis population. As mentioned above, the complexity and severity of the sleep issues that present in this group might appear to require highly developed assessment and treatment skills. However, by the same token, the severity of the sleep issues means that significant clinical benefits could be found from treating these disorders. Furthermore, the most common (insomnia, nightmares) have effective treatments that can be applied. Another factor to consider is medication – clearly antipsychotic medication has an effect on sleep, and many patients are receiving antidepressant or other medication types in addition to antipsychotic medication (Waters, Faulkner, et al., 2012). Medication is perceived as having both a positive and negative effect on sleep by clinicians and patients (Faulkner & Bee, 2017; Rehman et al., 2016), and research in this area is ongoing (Monti, Torterolo, & Pandi Perumal, 2017). Another challenge in this population can be engagement – patients with psychosis can be considered by clinicians as unlikely or unable to make behavioural changes, a belief that appears to carry over to sleep interventions (Rehman et al., 2016). However, sleep issues are something most patients are keen to receive treatment for (Faulkner & Bee, 2016, 2017; Waite, Evans, et al., 2016) as evidenced by the high treatment take up and retention rates in insomnia treatment studies (Bradley et al., 2017; Freeman, Waite, Startup, et al., 2015; Sheaves et al., 2017). The effectiveness of insomnia treatment when applied in this population (effect sizes of $d \geq 0.9$ were reported in all three insomnia treatment studies) can also assist with fostering engagement and hope. Indeed, sleep interventions could be used as a 'stepping stone' for building patient trust prior to attempting more challenging techniques (e.g. dropping safety behaviours). The last challenge is that existing sleep treatments may require adaptation to be effective in this population – however, this has been accomplished with insomnia (Freeman, Waite, Startup, et al., 2015; Waite, Myers, et al., 2016), and is likely to be possible for a range of other disorders (e.g. nightmares). Overall, the potential benefits of sleep treatment in this population appear to outweigh the challenges presented.

In conclusion, this thesis has contributed to the literature by demonstrating: a causal role of insomnia in non-clinical psychotic experiences; that sleep disruption predicts psychosis severity in an at-risk group; that sleep disorders are common, complex, and untreated in patients with psychosis; that insomnia predicts later negative affect and later psychotic experiences in clinical groups; and that hypersomnia in psychosis also appears to be associated with negative outcomes (and deserves further investigation). In short, it appears that sleep dysfunction has a rich and important relationship with psychotic experiences, and with the more general wellbeing of individuals with psychosis. This has consequences for understanding the etiology of psychotic experiences, but also great potential to transfer into clinical benefit.

*"There is a time for many words, and there is also a time for sleep."* - Homer

## 7.5 Figures

### 7.5.1 Figure 1: Number of PubMed records matching systematic search criteria (from Chapter 1) by year




Chapter 7 Figure 1: Number of PubMed records matching systematic search criteria (from Chapter 1) by year

# References


8.1 Chapter 1 References 179

8.2 Chapter 2 References 200

8.3 Chapter 3 References 206

8.4 Chapter 4 References 211

8.5 Chapter 5 References 216

8.6 Chapter 6 References 220

8.7 Chapter 7 References 225

## 8.1 Chapter 1 References

AASS. (2014). *International Classification of Sleep Disorders* (3rd ed.).

Adams, R., Stephan, K. E., Brown, H. R., Frith, C., & Friston, K. J. (2013). The computational anatomy of psychosis. *Frontiers in Psychiatry*, *4*(May), 47. https://doi.org/10.3389/fpsyt.2013.00047

Adriano, F., Spoletini, I., Caltagirone, C., & Spalletta, G. (2010). Updated meta-analyses reveal thalamus volume reduction in patients with first-episode and chronic schizophrenia. *Schizophrenia Research*, *123*(1), 1–14. https://doi.org/10.1016/j.schres.2010.07.007

Afonso, P., Brissos, S., Figueira, M. L., & Paiva, T. (2011). Schizophrenia patients with predominantly positive symptoms have more disturbed sleep-wake cycles measured by actigraphy. *Psychiatry Research*, *189*(1), 62–6. https://doi.org/10.1016/j.psychres.2010.12.031

Afonso, P., Figueira, M. L., & Paiva, T. (2011). Sleep-promoting action of the endogenous melatonin in schizophrenia compared to healthy controls. *International Journal of Psychiatry in Clinical Practice*, *15*(4), 311–5. https://doi.org/10.3109/13651501.2011.605954

Afonso, P., Figueira, M. L., & Paiva, T. (2014). Sleep-wake patterns in schizophrenia patients compared to healthy controls. *The World Journal of Biological Psychiatry : The Official Journal of the World Federation of Societies of Biological Psychiatry*, *15*(7), 517–24. https://doi.org/10.3109/15622975.2012.756987

Allison, K. C., Lundgren, J. D., O'Reardon, J. P., Martino, N. S., Sarwer, D. B., Wadden, T. A., … Stunkard, A. J. (2008). The Night Eating Questionnaire (NEQ): psychometric properties of a measure of severity of the Night Eating Syndrome. *Eating Behaviors*, *9*(1), 62–72. https://doi.org/10.1016/j.eatbeh.2007.03.007

Anderson, G., & Maes, M. (2012). Melatonin: An overlooked factor in schizophrenia and in the inhibition of anti-psychotic side effects. *Metabolic Brain Disease*, *27*(2), 113–119. https://doi.org/10.1007/s11011-012-9307-9

Andorko, N. D., Mittal, V., Thompson, E., Denenny, D., Epstein, G., Demro, C., … Schiffman, J. (2017). The association between sleep dysfunction and psychosis-like experiences among college students. *Psychiatry Research*, *248*, 6–12. https://doi.org/10.1016/j.psychres.2016.12.009

Andreasen, N. C. (1984). *Scale for the Assessment of Positive Symptoms*. University of Iowa.

APA. (2013). *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5). Diagnostic*

*and Statistical Manual of Mental Disorders 4th edition TR.* https://doi.org/10.1176/appi.books.9780890425596.744053

Auslander, L. A., & Jeste, D. V. (2002). Perceptions of problems and needs for service among middle-aged and elderly outpatients with schizophrenia and related psychotic disorders. *Community Mental Health Journal*, *38*(5), 391–402.

Bak, M., Drukker, M., van Os, J., & Delespaul, P. (2005). Hospital comorbidity bias and the concept of schizophrenia. *Social Psychiatry and Psychiatric Epidemiology*, *40*, 817–821. https://doi.org/10.1007/s00127-005-0971-0

Bebbington, P.., McBride, O., Steel, C., Kuipers, E., Radovanovič, M., Brugha, T., … Freeman, D. (2013). The structure of paranoia in the general population. *British Journal of Psychiatry*, *202*(6), 419–427. https://doi.org/10.1192/bjp.bp.112.119032

Bebbington, P., & Nayani, T. (1995). The Psychosis Screening Questionnaire. *International Journal of Methods in Psychiatric Research*, *5*(1), 11–19.

Bell, V., Halligan, P. W., & Ellis, H. D. (2006). The Cardiff Anomalous Perceptions Scale (CAPS): a new validated measure of anomalous perceptual experience. *Schizophrenia Bulletin*, *32*(2), 366–77. https://doi.org/10.1093/schbul/sbj014

Benson, K. L. (2006). Sleep in schizophrenia: impairments, correlates, and treatment. *The Psychiatric Clinics of North America*, *29*(4), 1033–45; abstract ix–x. https://doi.org/10.1016/j.psc.2006.08.002

Benson, K. L. (2008). Sleep in Schizophrenia. *Sleep Medicine Clinics*, *3*(2), 251–260. https://doi.org/10.1016/j.jsmc.2008.01.001

Benson, K. L., & Zarcone, V. (1993). Rapid eye movement sleep eye movements in schizophrenia and depression. *Archives of General Psychiatry*, *50*(2), 474–482. https://doi.org/10.1001/archpsyc.1993.01820180076008

Bian, Y., Wang, Z. X., Han, X. Le, Chen, L., Zhu, Y., & Wu, C. J. (2016). Sleep state misperception in schizophrenia: Are negative symptoms at work? *Comprehensive Psychiatry*, *67*, 33–38. https://doi.org/10.1016/j.comppsych.2016.02.008

Birchwood, M., Smith, J., Macmillan, F., Hogg, B., Prasad, R., Harvey, C., & Bering, S. (1989). Predicting relapse in schizophrenia: the development and implementation of an early signs monitoring system using patients and families as observers, a preliminary investigation.

*Psychological Medicine*, *19*(3), 649–56. https://doi.org/10.1017/S0033291700024247

Bleuler, E. (1950). *Dementia praecox or the group of schizophrenias.* (J. Zinkin & N. Lewis, Eds.). New York: International Universities Press.

Bliss, E., Clark, L., & West, C. (1959). Studies of sleep deprivation—relationship to schizophrenia. *AMA Archives of Neurology and Psychiatry*, *81*(3), 348–359. https://doi.org/10.1001/archneurpsyc.1959.02340150080009

Borbély, A. (1982). A two process model of sleep regulation. *Human Neurobiology*, *1*, 195–204.

Brauchi, J. T., & West, J. (1959). Sleep Deprivation. *The Journal of the American Medical Association*, *171*(1), 11–14. https://doi.org/10.1001/jama.1959.03010190013003

Bromundt, V., Köster, M., Georgiev-Kill, A., Opwis, K., Wirz-Justice, A., Stoppe, G., & Cajochen, C. (2011). Sleep-wake cycles and cognitive functioning in schizophrenia. *The British Journal of Psychiatry*, *198*(4), 269–76. https://doi.org/10.1192/bjp.bp.110.078022

Brown, R. E., Basheer, R., McKenna, J. T., Strecker, R. E., & McCarley, R. W. (2012). Control of Sleep and Wakefulness. *Physiological Reviews*, *92*(3), 1087–1187. https://doi.org/10.1152/physrev.00032.2011

Bunney, W., & Hamburg, D. (1963). Methods for reliable longitudinal observation of behaviour. *Archives of General Psyhicatry*, *9*, 280–294.

Buysse, D. J., Reynolds, C. F. 3Rd, Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The Pittsburgh Sleep Quality Index: A New Instrument for Psychiatric Practice and Research. *Psychiatry Research*, *28*, 193–213. https://doi.org/10.1016/0165-1781(89)90047-4

Castelnovo, A., Ferrarelli, F., & D'Agostino, A. (2015). Schizophrenia: from neurophysiological abnormalities to clinical symptoms. *Frontiers in Psychology*, *6*(April), 478. https://doi.org/10.3389/fpsyg.2015.00478

Catalan, A., Simons, C. J. P., Bustamante, S., Drukker, M., Madrazo, A., de Artaza, M. G., … Gonzalez-Torres, M. A. (2014). Novel evidence that attributing affectively salient signal to random noise is associated with psychosis. *PloS One*, *9*(7), e102520. https://doi.org/10.1371/journal.pone.0102520

Charlton, B. G. (1999). The "anti-delirium" theory of electroconvulsive therapy action. *Medical Hypotheses*, *52*(6), 609–11. https://doi.org/10.1054/mehy.1999.0857

Chemerinski, E., Ho, B.-C., Flaum, M., Arndt, S., Fleming, F., & Andreasen, N. C. (2002). Insomnia as a predictor for symptom worsening following antipsychotic withdrawal in schizophrenia. *Comprehensive Psychiatry*, *43*(5), 393–396. https://doi.org/10.1053/comp.2002.34627

Chouinard, S., Poulin, J., Stip, E., & Godbout, R. (2004). Sleep in untreated patients with schizophrenia: a meta-analysis. *Schizophrenia Bulletin*, *30*(4), 957–67.

Cohrs, S. (2008). Sleep disturbances in patients with schizophrenia. *CNS Drugs*, *22*(11), 939–962.

Davies, M., & Egan, A. (2013). Delusion: cognitive approaches–Bayesian inference and compartmentalization. *The Oxford Handbook of Philosophy and Psychiatry*, (September), 1–31. https://doi.org/10.1093/oxfordhb/9780199579563.013.0042

Derogatis, L. (1994). *SCL-90-R: Administration, scoring and procedure manual*. Minneapolis, MN: National Computer Systems.

Feinberg, I. (2011). Corollary discharge, hallucinations, and dreaming. *Schizophrenia Bulletin*, *37*(1), 1–3. https://doi.org/10.1093/schbul/sbq115

Ferrarelli, F., Peterson, M. J. M., Sarasso, S., Riedner, B. A., Murphy, M. J., Benca, R., … Tononi, G. (2010). Thalamic Dysfunction in Schizophrenia Suggested by Whole-Night Deficits in Slow and Fast Spindles. *American Journal of …*, *167*(November), 1339–1348. https://doi.org/10.1176/appi.ajp.2010.09121731

First, M., Gibbon, M., Spitzer, R., Williams, J., & Benjamin, L. (1997). *Structured Clinical Interview for DSM-IV Axis II Personality Disorders, (SCID-II)*. Washington DC: American Psychiatric Press, Inc.

Fisher, H., Caspi, A., & Poulton, R. (2013). Specificity of childhood psychotic symptoms for predicting schizophrenia by 38 years of age: a birth cohort study. *Psychological Medicine*, *43*(10), 2077–86. https://doi.org/10.1017/S0033291712003091

Fisher, H., Lereya, S. T., Thompson, A., Lewis, G., Zammit, S., & Wolke, D. (2014). Childhood parasomnias and psychotic experiences at age 12 years in a United Kingdom birth cohort. *Sleep*, *37*(3), 475–82. https://doi.org/10.5665/sleep.3478

Ford, J. M., Morris, S. E., Hoffman, R. E., Sommer, I., Waters, F., McCarthy-Jones, S., … Cuthbert, B. N. (2014). Studying hallucinations within the NIMH RDoC framework. *Schizophrenia Bulletin*, *40 Suppl 4*(Suppl_4), S295-304. https://doi.org/10.1093/schbul/sbu011

Foster, C., Startup, H., Potts, L., & Freeman, D. (2010). A randomised controlled trial of a worry intervention for individuals with persistent persecutory delusions. *Journal of Behavior Therapy and Experimental Psychiatry*, *41*(1), 45–51. https://doi.org/10.1016/j.jbtep.2009.09.001

Freeman, D., Brugha, T., Meltzer, H., Jenkins, R., Stahl, D., & Bebbington, P. (2010). Persecutory ideation and insomnia: findings from the second British National Survey of Psychiatric Morbidity. *Journal of Psychiatric Research*, *44*(15), 1021–6.

Freeman, D., Dunn, G., Startup, H., Pugh, K., Cordwell, J., Mander, H., … Kingdon, D. (2015). Effects of cognitive behaviour therapy for worry on persecutory delusions in patients with psychosis (WIT): a parallel, single-blind, randomised controlled trial with a mediation analysis. *The Lancet Psychiatry*, *2*(4), 305–313. https://doi.org/10.1016/S2215-0366(15)00039-5

Freeman, D., Garety, P., Bebbington, P., Smith, B., Rollinson, R., Fowler, D., … Dunn, G. (2005). Psychological investigation of the structure of paranoia in a non-clinical population. *The British Journal of Psychiatry*, *186*(5), 427–35. https://doi.org/10.1192/bjp.186.5.427

Freeman, D., Garety, P., Kuipers, E., Fowler, D., & Bebbington, P. (2002). A cognitive model of persecutory delusions. *The British Journal of Clinical Psychology*, *41*(Pt 4), 331–47.

Freeman, D., McManus, S., Brugha, T., Meltzer, H., Jenkins, R., & Bebbington, P. (2011). Concomitants of paranoia in the general population. *Psychological Medicine*, *41*(5), 923–36. https://doi.org/10.1017/S0033291710001546

Freeman, D., Pugh, K., Dunn, G., Evans, N., Sheaves, B., Waite, F., … Fowler, D. (2014). An early Phase II randomised controlled trial testing the effect on persecutory delusions of using CBT to reduce negative cognitions about the self: The potential benefits of enhancing self confidence. *Schizophrenia Research*, *160*(1), 186–192. https://doi.org/10.1016/j.schres.2014.10.038

Freeman, D., Pugh, K., Green, C., Valmaggia, L., Dunn, G., & Garety, P. (2007). A measure of state persecutory ideation for experimental studies. *The Journal of Nervous and Mental Disease*, *195*(9), 781–784. https://doi.org/10.1097/NMD.0b013e318145a0a9

Freeman, D., Pugh, K., Vorontsova, N., Antley, A., & Slater, M. (2010). Testing the continuum of delusional beliefs: an experimental study using virtual reality. *Journal of Abnormal Psychology*, *119*(1), 83–92. https://doi.org/10.1037/a0017514

Freeman, D., Pugh, K., Vorontsova, N., & Southgate, L. (2009). Insomnia and paranoia. *Schizophrenia Research*, *108*(1–3), 280–4. https://doi.org/10.1016/j.schres.2008.12.001

Freeman, D., Sheaves, B., Goodwin, G., Yu, L.-M., Harrison, P., Emsley, R., … Espie, C. (2015). A randomised controlled trial testing the effects of cognitive behavioural therapy for insomnia on the mental health of university students. *Trials*, *16*(236). https://doi.org/10.1186/s13063-015-0756-4.

Freeman, D., Stahl, D., McManus, S., Meltzer, H., Brugha, T., Wiles, N., & Bebbington, P. (2012). Insomnia, worry, anxiety and depression as predictors of the occurrence and persistence of paranoid thinking. *Social Psychiatry and Psychiatric Epidemiology*, *47*(8), 1195–203. https://doi.org/10.1007/s00127-011-0433-1

Freeman, D., Thompson, C., Vorontsova, N., Dunn, G., Carter, L.-A., Garety, P., … Ehlers, A. (2013). Paranoia and post-traumatic stress disorder in the months after a physical assault: a longitudinal study examining shared and differential predictors. *Psychological Medicine*, *43*(12), 2673–84. https://doi.org/10.1017/S003329171300038X

Freeman, D., Waite, F., Startup, H., Myers, E., Lister, R., McInerney, J., … Yu, L.-M. M. (2015). Efficacy of cognitive behavioural therapy for sleep improvement in patients with persistent delusions and hallucinations (BEST): A prospective, assessor-blind, randomised controlled pilot trial. *The Lancet Psychiatry*, *2*(11), 975–983. https://doi.org/10.1016/S2215-0366(15)00314-4

Galdos, M., Simons, C., Fernandez-Rivas, A., Wichers, M., Peralta, C., Lataster, T., … van Os, J. (2011). Affectively salient meaning in random noise: a task sensitive to psychosis liability. *Schizophrenia Bulletin*, *37*(6), 1179–86. https://doi.org/10.1093/schbul/sbq029

Ganguli, R. (1987). Electroencephalographic Sleep in Young, Never-Medicated Schizophrenics. *Archives of General Psychiatry*, *44*(1), 36. https://doi.org/10.1001/archpsyc.1987.01800130038006

Garety, P., Kuipers, E., Fowler, D., Freeman, D., & Bebbington, P. (2001). A cognitive model of the positive symptoms of psychosis. *Psychological Medicine*, *31*(2), 189–95.

Garety, P., Waller, H., Emsley, R., Jolley, S., Kuipers, E., Bebbington, P., … Freeman, D. (2014). Cognitive Mechanisms of Change in Delusions: An Experimental Investigation Targeting Reasoning to Effect Change in Paranoia. *Schizophrenia Bulletin*, sbu103-. https://doi.org/10.1093/schbul/sbu103

Gau, S. F., & Soong, W. T. (2003). The transition of sleep-wake patterns in early adolescence. *Sleep*, *26*(4), 449–454.

Goldberg, D., & Williams, P. (1988). *A user's guide to the General Health Questionnaire*. Windsor: NFER-Nelson.

Gradisar, M., Gardner, G., & Dohnt, H. (2011). Recent worldwide sleep patterns and problems during adolescence: a review and meta-analysis of age, region, and sleep. *Sleep Medicine*, *12*(2), 110–8. https://doi.org/10.1016/j.sleep.2010.11.008

Green, C. E. L., Freeman, D., Kuipers, E., Bebbington, P., Fowler, D., Dunn, G., & Garety, P. (2008). Measuring ideas of persecution and social reference: the Green et al. Paranoid Thought Scales (GPTS). *Psychological Medicine*, *38*(1), 101–11. https://doi.org/10.1017/S0033291707001638

Grezellschak, S., Jansen, A., & Westermann, S. (2017). Emotion regulation in patients with psychosis: A link between insomnia and paranoid ideation? *Journal of Behavior Therapy and Experimental Psychiatry*, *56*, 27–32. https://doi.org/10.1016/j.jbtep.2016.08.001

Haddock, G., McCarron, J., Tarrier, N., & Faragher, E. B. (1999). Scales to measure dimensions of hallucinations and delusions: the psychotic symptom rating scales (PSYRATS). *Psychological Medicine*, *29*(4), 879–889. https://doi.org/10.1017/S0033291799008661

Hamilton, M. (1960). A Rating Scale for Depression. *Journal of Neurology, Neurosurgery & Psychiatry*, *23*, 56–63.

Haro, J. M., Kamath, S. A., Ochoa, S., Novick, D., Rele, K., Fargas, A., … Jones, P. B. (2003). The Clinical Global Impression-Schizophrenia scale: a simple instrument to measure the diversity of symptoms present in schizophrenia. *Acta Psychiatrica Scandinavica. Supplementum*, (416), 16–23.

Harvey, A., & Murray, G. (2011). Sleep disturbance as transdiagnostic: consideration of neurobiological mechanisms. *Clinical Psychology Review*, *31*(2), 225–235. https://doi.org/10.1016/j.cpr.2010.04.003.Sleep

Hawley, C. J. (2006). Excessive daytime sleepiness in psychiatry: a relevant focus for clinical attention and treatment? *International Journal of Psychiatry in Clinical Practice*, *10*(2), 117–23. https://doi.org/10.1080/13651500600578904

Hawley, C. J., Gale, T. M., Sivakumaran, T., Paul, S., Kondan, V. R. G., Farag, A., & Shahzad, J. (2010). Excessive daytime sleepiness in psychiatric disorders: Prevalence, correlates and clinical significance. *Psychiatry Research*, *175*(1–2), 138–41. https://doi.org/10.1016/j.psychres.2008.10.037

Hobson, A. (2004). A model for madness? *Nature*, *430*(6995), 21. https://doi.org/10.1038/430021a

Hoddes, E., Zarcone, V., Smythe, H., Phillips, R., & Dement, W. C. (1973). Quantification of Sleepiness: A New Approach. *Psychophysiology*, *10*(4), 431–436. https://doi.org/10.1111/j.1469-8986.1973.tb00801.x

Horwood, J., Salvi, G., Thomas, K., Duffy, L., Gunnell, D., Hollis, C., … Harrison, G. (2008). IQ and non-clinical psychotic symptoms in 12-year-olds: results from the ALSPAC birth cohort. *The British Journal of Psychiatry : The Journal of Mental Science*, *193*(3), 185–91. https://doi.org/10.1192/bjp.bp.108.051904

Hou, C.-L., Zang, Y., Ma, X.-R., Cai, M.-Y., Li, Y., Jia, F.-J., … Xiang, Y.-T. (2016). The Relationship Between Sleep Patterns, Quality of Life, and Social and Clinical Characteristics in Chinese Patients With Schizophrenia. *Perspectives in Psychiatric Care*, *0*, 1–8. https://doi.org/10.1111/ppc.12186

Howes, O. D., & Kapur, S. (2009). The dopamine hypothesis of schizophrenia: version III--the final common pathway. *Schizophrenia Bulletin*, *35*(3), 549–62. https://doi.org/10.1093/schbul/sbp006

Hurdiel, R., Pezé, T., Daugherty, J., Girard, J., Poussel, M., Poletti, L., … Theunynck, D. (2014). Combined effects of sleep deprivation and strenuous exercise on cognitive performances during The North Face® Ultra Trail du Mont Blanc® (UTMB®). *Journal of Sports Sciences*, *33*(7), 670–674. https://doi.org/10.1080/02640414.2014.960883

Jeppesen, P., Clemmensen, L., Munkholm, A., Rimvall, M. K., Rask, C. U., Jørgensen, T., … Skovgaard, A. M. (2014). Psychotic experiences co-occur with sleep problems, negative affect and mental disorders in preadolescence. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*. https://doi.org/10.1111/jcpp.12319

Johns, L., & van Os, J. (2001). The continuity of psychotic experiences in the general population. *Clinical Psychology Review*, *21*(8), 1125–1141. https://doi.org/10.1016/S0272-7358(01)00103-9

Johns, M. W. (1991). A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep*, *14*(6), 540–545. https://doi.org/10.1016/j.sleep.2007.08.004

Jørgensen, P. (1998a). Early signs of psychotic relapse in schizophrenia. *British Journal of Psychiatry*, *172*(APR.), 327–330. https://doi.org/10.1192/bjp.172.4.327

Jørgensen, P. (1998b). Schizophrenic delusions: the detection of warning signals. *Schizophrenia Research*, *32*(1), 17–22. https://doi.org/10.1016/S0920-9964(98)00033-4

Kahn-Greene, E. T., Killgore, D. B., Kamimori, G. H., Balkin, T. J., & Killgore, W. D. S. (2007). The effects of sleep deprivation on symptoms of psychopathology in healthy adults. *Sleep Medicine*, *8*(3), 215–21. https://doi.org/10.1016/j.sleep.2006.08.007

Kajimura, N., Kato, M., Okuma, T., Sekimoto, M., Watanabe, T., & Takahashi, K. (1996). Relationship between delta activity during all-night sleep and negative symptoms in Schizophrenia: A Preliminary Study. *Biological Psychiatry*, *39*(6), 451–454. https://doi.org/10.1016/0006-3223(95)00376-2

Kalucy, M. J., Grunstein, R., Lambert, T., & Glozier, N. (2013). Obstructive sleep apnoea and schizophrenia - A research agenda. *Sleep Medicine Reviews*, *17*(5), 357–365. https://doi.org/10.1016/j.smrv.2012.10.003

Kantrowitz, J. T., Oakman, E., Bickel, S., Citrome, L., Spielman, A., Silipo, G., … Javitt, D. C. (2010). The importance of a good night's sleep: an open-label trial of the sodium salt of gamma-hydroxybutyric acid in insomnia associated with schizophrenia. *Schizophrenia Research*, *120*(1–3), 225–6. https://doi.org/10.1016/j.schres.2010.03.035

Kapur, S. (2003). Psychosis as a State of Aberrant Salience: A Framework Linking Biology, Phenomenology, and Pharmacology in Schizophrenia. *American Journal of Psychiatry*, *160*(1), 13. https://doi.org/10.1176/appi.ajp.160.1.13

Kapur, S., Mizrahi, R., & Li, M. (2005). From dopamine to salience to psychosis--linking biology, pharmacology and phenomenology of psychosis. *Schizophrenia Research*, *79*(1), 59–68. https://doi.org/10.1016/j.schres.2005.01.003

Kato, M., Kajimura, N., Okuma, T., Sekimoto, M., Watanabe, T., Yamadera, H., & Takahashi, K. (1999). Association between delta waves during sleep and negative symptoms in schizophrenia. Pharmaco-eeg studies by using structurally different hypnotics. *Neuropsychobiology*, *39*(3), 165–172. https://doi.org/26577

Kato, N. (2009). Neurophysiological mechanisms of electroconvulsive therapy for depression. *Neuroscience Research*, *64*(1), 3–11. https://doi.org/10.1016/j.neures.2009.01.014

Katz, S., & Landis, C. (1935). Psychologic and physiologic phenomena during a prolonged vigil. *Archives of Neurology & Psychiatry*, *34*(2), 307–317.

Kaufman, J., Birmaher, B., Brent, D., Rao, U., Flynn, C., Moreci, P., … Ryan, N. (1997). Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version

(K-SADS-PL): initial reliability and validity data. *Journal of the American Academy of Child and Adolescent Psychiatry*, *36*(7), 980–8. https://doi.org/10.1097/00004583-199707000-00021

Kay, S., Fiszbein, A., & Opfer, L. (1987). The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophrenia Bulletin*, *13*(2), 261–276.

Keshavan, M. S., Anderson, S., & Pettergrew, J. W. (1994). Is Schizophrenia due to excessive synaptic pruning in the prefrontal cortex? The Feinberg hypothesis revisited. *Journal of Psychiatric Research*, *28*(3), 239–265. https://doi.org/10.1016/0022-3956(94)90009-4

Keshavan, M. S., Miewald, J., Haas, G., Sweeney, J., Ganguli, R., & Reynolds, C. F. (1995). Slow-wave sleep and symptomatology in schizophrenia and related psychotic disorders. *Journal of Psychiatric Research*, *29*(4). https://doi.org/10.1016/0022-3956(95)00023-X

Keshavan, M. S., Reynolds, C. F., Miewald, J. M., Montrose, D. M., Sweeney, J. A., Vasko Jr, R. C., & Kupfer, D. J. (1998). Delta sleep deficits in schizophrenia: evidence from automated analyses of sleep data. *Archives of General Psychiatry*, *55*(5), 445–448. https://doi.org/10.1001/archpsyc.55.5.443

Kessler, R. C., & Ustün, T. B. (2004). The World Mental Health (WMH) Survey Initiative Version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI). *International Journal of Methods in Psychiatric Research*, *13*(2), 93–121.

Keyes, K. M., Maslowsky, J., Hamilton, A., & Schulenberg, J. (2015). The Great Sleep Recession: Changes in Sleep Duration Among US Adolescents, 1991-2012. *Pediatrics*, *135*(3), 460–468. https://doi.org/10.1542/peds.2014-2707

Kim, Y., Lee, J., Kim, Y. S., Jung, H., & Lee, K. (2009). Reliability of the Korean Nottingham Onset Schedule ( K-NOS ) in Korean First-episode Psychosis Patients. *Clinical Psychology and Neuroscience*, *7*(2), 51–56.

Kluge, M., Himmerich, H., Wehmeier, P. M., Rummel-Kluge, C., Dalal, M., Hinze-Selch, D., … Schuld, A. (2012). Sleep propensity at daytime as assessed by Multiple Sleep Latency Tests (MSLT) in patients with schizophrenia increases with clozapine and olanzapine. *Schizophrenia Research*, *135*(1–3), 123–127. https://doi.org/10.1016/j.schres.2011.12.017

Koranyi, E. K., & Lehmann, H. (1960). Experimental Sleep Deprivation in Schizophrenic Patients. *Archives of General Psychiatry*, *2*(5), 534. https://doi.org/10.1001/archpsyc.1960.03590110058007

Koyanagi, A., & Stickley, A. (2015). The Association between Sleep Problems and Psychotic Symptoms in the General Population: A Global Perspective. *Sleep*.

Kraepelin, E. (1919). *Dementia Praecox and Paraphrenia*. (R. Barclay & G. Robertson, Eds.). Chicago: Chicago Medical Book Co.

Krawiecka, M., Goldberg, D., & Vaughan, M. (1977). A standardized psychiatric assessment scale for rating chronic psychotic patients. *Acta Psychiatrica Scandinavica*, *55*(4), 299–308. https://doi.org/10.1111/j.1600-0447.1977.tb00174.x

Kumar, P. N. S., Andrade, C., Bhakta, S. G., & Singh, N. M. (2007). Melatonin in Schizophrenic Outpatients With Insomnia: A Double-Blind, Placebo-Controlled Study. *The Journal of Clinical Psychiatry*, *68*(2), 237–241.

Laberge, L., Tremblay, R. E., Vitaro, F., & Montplaisir, J. (2000). Development of parasomnias from childhood to early adolescence. *Pediatrics*, *106*(1 Pt 1), 67–74.

Lauer, C. J., Schreiber, W., Pollmächer, T., Holsboer, F., & Krieg, J. C. (1997). Sleep in schizophrenia: a polysomnographic study on drug-naive patients. *Neuropsychopharmacology*, *16*(1), 51–60. https://doi.org/10.1016/S0893-133X(96)00159-5

Lee, E. C., Whitehead, A. L., Jacques, R. M., & Julious, S. a. (2014). The statistical interpretation of pilot trials: should significance thresholds be reconsidered? *BMC Medical Research Methodology*, *14*(1), 41. https://doi.org/10.1186/1471-2288-14-41

Lee, Y. J., Cho, S.-J., Cho, I. H., Jang, J. H., & Kim, S. J. (2012). The relationship between psychotic-like experiences and sleep disturbances in adolescents. *Sleep Medicine*, *13*(8), 1021–7. https://doi.org/10.1016/j.sleep.2012.06.002

Levin, R., & Fireman, G. (2002). Nightmare prevalence, nightmare distress, and self-reported psychological disturbance. *Sleep*, *25*(2), 205–12.

Lewis, G., Pelosi, a J., Araya, R., & Dunn, G. (1992). Measuring psychiatric disorder in the community: a standardized assessment for use by lay interviewers. *Psychological Medicine*, *22*, 465–486. https://doi.org/10.1017/S0033291700030415

Limosani, I., D'Agostino, A., Manzone, M. L., & Scarone, S. (2011). The dreaming brain/mind, consciousness and psychosis. *Consciousness and Cognition*, *20*(4), 987–92. https://doi.org/10.1016/j.concog.2010.11.014

Linscott, R. J., & van Os, J. (2013). An updated and conservative systematic review and meta-analysis of epidemiological evidence on psychotic experiences in children and adults: on the pathway from proneness to persistence to dimensional expression across mental disorders. *Psychological Medicine*, *43*(6), 1133–49. https://doi.org/10.1017/S0033291712001626

Luby, E. D., Frohman, C. E., Grisell, J. L., Lenzo, J. E., & Gottlieb, J. S. (1960). Sleep deprivation: effects on behavior, thinking, motor performance, and biological energy transfer systems. *Psychosomatic Medicine*, *22*, 182–92.

Lunsford-Avery, J. R., Dean, D. J., & Mittal, V. A. (2017). *Self-reported sleep disturbances associated with procedural learning impairment in adolescents at ultra-high risk for psychosis*. *Schizophrenia Research*. https://doi.org/10.1016/j.schres.2017.03.025

Lunsford-Avery, J. R., Gonçalves, B. da S. B., Brietzke, E., Bressan, R., Gadelha, A., Auerbach, R. P., & Mittal, V. A. (2016). Adolescents at clinical-high risk for psychosis: Circadian rhythm disturbances predict worsened prognosis at 1-year follow-up. *Schizophrenia Research*. https://doi.org/10.1016/j.schres.2017.01.051

Lunsford-Avery, J. R., LeBourgeois, M. K., Gupta, T., & Mittal, V. A. (2015). Actigraphic-measured sleep disturbance predicts increased positive symptoms in adolescents at ultra high-risk for psychosis: A longitudinal study. *Schizophrenia Research*. https://doi.org/10.1016/j.schres.2015.03.013

Lunsford-Avery, J. R., & Mittal, V. A. (2013). Sleep Dysfunction Prior to the Onset of Schizophrenia: A Review and Neurodevelopmental Diathesis–Stress Conceptualization. *Clinical Psychology: Science and Practice*, *20*(3), 291–320. https://doi.org/10.1111/cpsp.12041

Lunsford-Avery, J. R., Orr, J. M., Gupta, T., Pelletier-Baldelli, A., Dean, D. J., Smith Watts, A. K., … Mittal, V. a. (2013). Sleep dysfunction and thalamic abnormalities in adolescents at ultra high-risk for psychosis. *Schizophrenia Research*, *151*(1–3), 148–53. https://doi.org/10.1016/j.schres.2013.09.015

Ma, X.-R., Song, G.-R., Xu, X.-B., Tian, T., & Chang, S.-H. (2016). The Prevalence of Sleep Disturbance and Its Socio-demographic and Clinical Correlates in First-episode Individuals With Schizophrenia in Rural China. *Perspectives in Psychiatric Care*. https://doi.org/10.1111/ppc.12197

Mackie, J. L. (1965). Causes and Conditions.

Manoach, D. S., Demanuele, C., Wamsley, E. J., Vangel, M., Montrose, D. M., Miewald, J., … Keshavan, M. S. (2014). Sleep spindle deficits in antipsychotic-naïve early course schizophrenia and in non-psychotic first-degree relatives. *Frontiers in Human Neuroscience*, *8*, 762. https://doi.org/10.3389/fnhum.2014.00762

Maric, N., Myin-Germeys, I., Delespaul, P., de Graaf, R., Vollebergh, W., & Van Os, J. (2004). Is our concept of schizophrenia influenced by Berkson's bias? *Social Psychiatry and Psychiatric Epidemiology*, *39*(8), 600–5. https://doi.org/10.1007/s00127-004-0803-z

Martin, J., Jeste, D. V., Caliguiri, M. P., Patterson, T., Heaton, R., & Ancoli-Israel, S. (2001). Actigraphic estimates of circadian rhythms and sleep/wake in older schizophrenia patients. *Schizophrenia Research*, *47*(1), 77–86. https://doi.org/10.1016/S0920-9964(00)00029-3

Mason, O., Morgan, C. J. M., Stefanovic, A., & Curran, H. V. (2008). The psychotomimetic states inventory (PSI): measuring psychotic-type experiences from ketamine and cannabis. *Schizophrenia Research*, *103*(1–3), 138–42. https://doi.org/10.1016/j.schres.2008.02.020

Mason, O., & Wakerley, D. (2012). The Psychotomimetic Nature of Dreams: An Experimental Study. *Schizophrenia Research and Treatment*, *2012*, 1–4. https://doi.org/10.1155/2012/872307

Mass, R. (2000). Characteristic subjective experiences of schizophrenia. *Schizophrenia Bulletin*, *26*, 921–931. https://doi.org/10.1093/oxfordjournals.schbul.a033506

Mattai, A. a, Tossell, J., Greenstein, D. K., Addington, A., Clasen, L. S., Gornick, M. C., … Gogtay, N. (2006). Sleep disturbances in childhood-onset schizophrenia. *Schizophrenia Research*, *86*(1–3), 123–9. https://doi.org/10.1016/j.schres.2006.04.020

Michels, F., Schilling, C., Rausch, F., Eifler, S., Zink, M., Meyer-Lindenberg, A., & Schredl, M. (2014, April 28). Nightmare frequency in schizophrenic patients, healthy relatives of schizophrenic patients, patients at high risk states for psychosis, and healthy controls. *International Journal of Dream Research*. https://doi.org/10.11588/ijodr.2014.1.11819

Miller, T. J., McGlashan, T. H., Woods, S. W., Stein, K., Driesen, N., Corcoran, C. M., … Davidson, L. (1999). Symptom assessment in schizophrenic prodromal states. *Psychiatric Quarterly*, *70*(4), 273–287. https://doi.org/10.1023/a:1022034115078

Monti, J. M., BaHammam, A. S., Pandi-Perumal, S. R., Bromundt, V., Spence, D. W., Cardinali, D. P., & Brown, G. M. (2013). Sleep and circadian rhythm dysregulation in schizophrenia. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, *43*, 209–16.

https://doi.org/10.1016/j.pnpbp.2012.12.021

Monti, J. M., & Monti, D. (2004). Sleep in schizophrenia patients and the effects of antipsychotic drugs. *Sleep Medicine Reviews*, *8*(2), 133–48. https://doi.org/10.1016/S1087-0792(02)00158-2

Morey, L. (1991). Personality Assessment Inventory (PAI).

Morin, C. M. (1993). *Insomnia: Psychological Assessment and management*. (D. Barlow, Ed.). New York: Guilford Press.

Morrison, A., Frame, L., & Larkin, W. (2003). Relationships between trauma and psychosis: a review and integration. *The British Journal of Clinical Psychology / the British Psychological Society*, *42*(Pt 4), 331–53. https://doi.org/10.1348/014466503322528892

Mulligan, L. D., Haddock, G., Emsley, R., Neil, S. T., & Kyle, S. (2016). High resolution examination of the role of sleep disturbance in predicting functioning and psychotic symptoms in schizophrenia: A novel experience sampling study. *Journal of Abnormal Psychology*, *125*(6), 788–797. https://doi.org/10.1037/abn0000180

Myers, E., Startup, H., & Freeman, D. (2011). Cognitive behavioural treatment of insomnia in individuals with persistent persecutory delusions: a pilot trial. *Journal of Behavior Therapy and Experimental Psychiatry*, *42*(3), 330–6. https://doi.org/10.1016/j.jbtep.2011.02.004

Neylan, T., van Kammen, D., Kelley, M., & Peters, J. (1992). Sleep in schizophrenic patients on and off haloperidol therapy: Clinically stable vs relapsed patients. *Archives of General Psychiatry*.

Nielsen, T., & Levin, R. (2007). Nightmares: a new neurocognitive model. *Sleep Medicine Reviews*, *11*(4), 295–310. https://doi.org/10.1016/j.smrv.2007.03.004

Nofzinger, E., Kammen, D. van, Gilbertson, M., Gurklis, J., & Peters, J. (1993). Electroencephalographic Sleep in Clinically Stable Schizophrenic Patients : Two-Weeks versus six weeks neuroleptic-free. *Biological Psychiatry*, 829–835.

Notredame, C.-E., Pins, D., Deneve, S., & Jardri, R. (2014). What visual illusions teach us about schizophrenia. *Frontiers in Integrative Neuroscience*, *8*, 63. https://doi.org/10.3389/fnint.2014.00063

Ord, L. M., Myles-Worsley, M., Blailes, F., & Ngiralmau, H. (2004). Screening for prodromal adolescents in an isolated high-risk population. *Schizophrenia Research*, *71*(2–3), 507–8. https://doi.org/10.1016/j.schres.2004.03.014

Oshima, N., Nishida, A., Fukushima, M., Shimodera, S., Kasai, K., Okazaki, Y., & Sasaki, T. (2010). Psychotic-like experiences (PLEs) and mental health status in twin and singleton Japanese high school students. *Early Intervention in Psychiatry*, *4*(3), 206–13. https://doi.org/10.1111/j.1751-7893.2010.00186.x

Overall, J., & Gorham, D. (1962). The Brief Psychiatric Rating Scale. *Psychological Reports*, *10*, 799–812.

Palmese, L. B., DeGeorge, P. C., Ratliff, J. C., Srihari, V. H., Wexler, B. E., Krystal, A. D., & Tek, C. (2011). Insomnia is frequent in schizophrenia and associated with night eating and obesity. *Schizophrenia Research*, *133*(1–3), 238–43. https://doi.org/10.1016/j.schres.2011.07.030

Pasnau, R., Naitoh, P., Stier, S., & Kollar, E. (1968). The psychological effects of 205 hours of sleep deprivation. *Archives of General Psychiatry*, *18*, 496–505.

Peralta, V., & Cuesta, M. J. (1999). Dimensional structure of psychotic symptoms: an item-level analysis of SAPS and SANS symptoms in psychotic disorders. *Schizophrenia Research*, *38*(1), 13–26. https://doi.org/10.1016/S0920-9964(99)00003-1

Petrovsky, N., Ettinger, U., Hill, A., Frenzel, L., Meyhöfer, I., Wagner, M., … Kumari, V. (2014). Sleep deprivation disrupts prepulse inhibition and induces psychosis-like symptoms in healthy humans. *The Journal of Neuroscience*, *34*(27), 9134–40. https://doi.org/10.1523/JNEUROSCI.0904-14.2014

Plomin, R., Haworth, C. M. A., & Davis, O. S. P. (2009). Common disorders are quantitative traits. *Nature Reviews. Genetics*, *10*(12), 872–8. https://doi.org/10.1038/nrg2670

Poe, S.-L., Brucato, G., Bruno, N., Arndt, L. Y., Ben-David, S., Gill, K. E., … Girgis, R. R. (2017). *Sleep disturbances in individuals at clinical high risk for psychosis*. *Psychiatry Research* (Vol. 249). https://doi.org/10.1016/j.psychres.2016.12.029

Poulin, J., Daoust, A. M., Forest, G., Stip, E., & Godbout, R. (2003). Sleep architecture and its clinical correlates in first episode and neuroleptic-naive patients with schizophrenia. *Schizophrenia Research*, *62*(1–2), 147–153. https://doi.org/10.1016/S0920-9964(02)00346-8

Pritchett, D., Wulff, K., Oliver, P. L., Bannerman, D. M., Davies, K. E., Harrison, P., … Foster, R. (2012). Evaluating the links between schizophrenia and sleep and circadian rhythm disruption. *Journal of Neural Transmission*, *119*(10), 1061–75. https://doi.org/10.1007/s00702-012-0817-8

Rausch, F., Eifler, S., Esser, A., Esslinger, C., Schirmbeck, F., Meyer-Lindenberg, A., & Zink, M. (2013).

The Early Recognition Inventory ERIraos detects at risk mental states of psychosis with high sensitivity. *Comprehensive Psychiatry*, *54*(7), 1068–76. https://doi.org/10.1016/j.comppsych.2013.04.016

Rehman, A., Waite, F., Sheaves, B., Biello, S., Freeman, D., & Gumley, A. (2016). Clinician perceptions of sleep problems, and their treatment, in patients with non-affective psychosis. *Psychosis*, 1–11. https://doi.org/10.1080/17522439.2016.1206955

Ritsner, M., Kurs, R., Ponizovsky, A., & Hadjez, J. (2004). Perceived quality of life in schizophrenia: relationships to sleep quality. *Quality of Life Research*. https://doi.org/10.1023/B:QURE.0000021687.18783.d6

Ronald, A. (2015). Recent quantitative genetic research on psychotic experiences: New approaches to old questions. *Current Opinion in Behavioral Sciences*. Elsevier Ltd. https://doi.org/10.1016/j.cobeha.2014.10.001

Ronald, A., Sieradzka, D., Cardno, A. G., Haworth, C. M. a, McGuire, P., & Freeman, D. (2014). Characterization of psychotic experiences in adolescence using the specific psychotic experiences questionnaire: Findings from a study of 5000 16-Year-Old Twins. *Schizophrenia Bulletin*, *40*(4), 868–877. https://doi.org/10.1093/schbul/sbt106

Ross, J. J. (1965). Neurological Findings After Prolonged Sleep Deprivation. *Archives of Neurology*, *12*, 399–403.

Ross, K., Freeman, D., Dunn, G., & Garety, P. (2011). A randomized experimental investigation of reasoning training for people with delusions. *Schizophrenia Bulletin*, *37*(2), 324–33. https://doi.org/10.1093/schbul/sbn165

Rotenberg, V. S., Indursky, P., Hadjez, J., Martin, T., Barak, Y., Gutman, Y., & Bichucher, A. (1997). Sleep structure in positive and negative schizophrenia. *Biological Psychiatry*, *42*(1), 69S. https://doi.org/10.1016/S0006-3223(97)87164-8

Ruhrmann, S., Schultze-Lutter, F., Salokangas, R., Heinimaa, M., Linszen, D., Dingemans, P., … Klosterkötter, J. (2010). Prediction of Psychosis in Adolescents and Young Adults at High Risk: results from the prospective european prediction of psychosis study. *Archives of General Psychiatry*, *67*(3), 241–251. https://doi.org/10.1001/archgenpsychiatry.2009.206

Sarkar, S., Katshu, M. Z. U. H., Nizamie, S. H., & Praharaj, S. K. (2010). Slow wave sleep deficits as a trait marker in patients with schizophrenia. *Schizophrenia Research*, *124*(1–3), 127–33.

https://doi.org/10.1016/j.schres.2010.08.013

Schmeider, U., Leweke, F. M., Sternemann, U., Emrich, H. M., & Weber, M. M. (1996). Visual 3D illusion: A systems-theoretical approach to psychosis. *European Archives of Psychiatry and Clinical Neuroscience*, *246*(5), 256–260. https://doi.org/10.1007/BF02190277

Shamir, E., Laudon, M., Barak, Y., Anis, Y., Rotenberg, V., Elizur, A., & Zisapel, N. (2000). Melatonin improves sleep quality of patients with chronic schizophrenia. *Journal of Clinical Psychiatry*, *61*(5), 373–377.

Sharafkhaneh, A., Giray, N., Richardson, P., Young, T., & Hirshkowitz, M. (2005). Association of psychiatric disorders and sleep apnea in a large cohort. *SLEEP*, *28*(11), 1405–1411.

Sheaves, B., Bebbington, P., Guy, M., Harrison, P., Espie, C., Foster, G., … Foster, R. (2016). Insomnia and hallucinations in the general population: Findings from the 2000 and 2007 British Psychiatric Morbidity Surveys. *Psychiatry Research*, *241*, 141–146. https://doi.org/10.1016/j.psychres.2016.03.055

Sheaves, B., Onwumere, J., Keen, N., Stahl, D., & Kuipers, E. (2015). Nightmares in patients with psychosis: the relationship with sleep, psychotic, affective and cognitive symptoms. *Canadian Journal of Psychiatry*, 60(8), 354–61. https://doi.org/10.1177/070674371506000804

Sheaves, B., Porcheret, K., Tsanas, A., Espie, C., Foster, R., Freeman, D., … Goodwin, G. (2016). Insomnia, Nightmares, and Chronotype as Markers of Risk for Severe Mental Illness: Results from a Student Population. *Sleep*, *39*(1), 173–81. https://doi.org/10.5665/sleep.5342

Silverstein, S. M., Keane, B. P., Wang, Y., Mikkilineni, D., Paterno, D., Papathomas, T. V, & Feigenson, K. (2013). Effects of short-term inpatient treatment on sensitivity to a size contrast illusion in first-episode psychosis and multiple-episode schizophrenia. *Frontiers in Psychology*, *4*, 466. https://doi.org/10.3389/fpsyg.2013.00466

Spoormaker, V. I., Verbeek, I., van den Bout, J., & Klip, E. C. (2005). Initial validation of the SLEEP-50 questionnaire. *Behavioral Sleep Medicine*, *3*(4), 227–246. https://doi.org/10.1207/s15402010bsm0304_4

Sternemann, U., Schneider, U., Leweke, F. M., Bevilacqua, C. M., Dietrich, D. E., & Emrich, H. M. (1997). [Pro-psychotic change of binocular depth inversion by sleep deprivation]. *Der Nervenarzt*, *68*(7), 593–6.

Tan, H.-Y., & Ang, Y.-G. (2001). First-episode psychosis in the military: a comparative study of

prodromal symptoms. *Australian and New Zealand Journal of Psychiatry*, *35*(4), 512–519. https://doi.org/10.1046/j.1440-1614.2001.00912.x

Tandon, R., Shipley, J. E., Eiser, a S., & Greden, J. F. (1989). Association between abnormal REM sleep and negative symptoms in schizophrenia. *Psychiatry Research*, *27*(3), 359–361. https://doi.org/10.1016/0165-1781(89)90151-0

Tandon, R., Shipley, J. E., Taylor, S., Greden, J. F., Eiser, A., DeQuardo, J., & Goodson, J. (1992). Electroencephalographic sleep abnormalities in schizophrenia: relationship to positive/negative symptoms and prior neuroleptic treatment. *Archives of General Psychiatry*, *49*(3), 185–194. https://doi.org/10.1001/archpsyc.1992.01820030017003

Taylor, M. J., Gregory, A. M., Freeman, D., & Ronald, A. (2015). Do sleep disturbances and psychotic-like experiences in adolescence share genetic and environmental influences? *Journal of Abnormal Psychology*, *124*(3), 674–684. https://doi.org/10.1037/abn0000057

Taylor, S. F., Tandon, R., Shipley, J. E., Eiser, A. S., & Goodson, J. (1991). Sleep onset REM Periods in Schizophrenic Patients. *Biological Psychiatry*, *30*, 205–209.

Taylor, S., Tandon, R., Shipley, J. E., & Eiser, A. (1991). Effect of neuroleptic treatment on polysomnographic measures in schizophrenia. *Biological Psychiatry*, *30*(9), 904–912. https://doi.org/10.1016/0006-3223(91)90004-6

Tek, C., Palmese, L. B., Krystal, A. D., Srihari, V. H., DeGeorge, P. C., Reutenauer, E. L., & Guloksuz, S. (2014). The impact of eszopiclone on sleep and cognition in patients with schizophrenia and insomnia: A double-blind, randomized, placebo-controlled trial. *Schizophrenia Research*, *160*(1–3), 180–185. https://doi.org/10.1016/j.schres.2014.10.002

Tekell, J. L., Hoffmann, R., Hendrickse, W., Greene, R. W., Rush, a. J., & Armitage, R. (2005). High Frequency EEG Activity During Sleep : Characteristics in Schizophrenia and Depression. *Clinical EEG and Neuroscience*, *36*(1), 25–35. https://doi.org/doi: 10.1177/155005940503600107

Tesler, N., Gerstenberg, M., Franscini, M., Jenni, O. G., Walitza, S., & Huber, R. (2015). Reduced sleep spindle density in early onset schizophrenia: A preliminary finding. *Schizophrenia Research*. https://doi.org/10.1016/j.schres.2015.04.042

Thompson, A., Lereya, S., Lewis, G., Zammit, S., Fisher, H., & Wolke, D. (2015). Childhood sleep disturbance and risk of psychotic experiences at 18: UK birth cohort. *The British Journal of Psychiatry*, 23–29. https://doi.org/10.1192/bjp.bp.113.144089

Tononi, G., & Cirelli, C. (2014). Sleep and the price of plasticity: from synaptic and cellular homeostasis to memory consolidation and integration. *Neuron*, *81*(1), 12–34. https://doi.org/10.1016/j.neuron.2013.12.025

van Os, J., Linscott, R. J., Myin-Germeys, I., Delespaul, P., & Krabbendam, L. (2009). A systematic review and meta-analysis of the psychosis continuum: evidence for a psychosis proneness-persistence-impairment model of psychotic disorder. *Psychological Medicine*, *39*(2), 179–95. https://doi.org/10.1017/S0033291708003814

Vazquez-Barquero, J., Lastra, I., Nu, M., Castanedo, S., & Dunn, G. (1996). Patterns of positive and negative symptoms in first episode schizophrenia. *The British Journal of Psychiatry*.

Waite, F., Evans, N., Myers, E., Startup, H., Lister, R., Harvey, A., & Freeman, D. (2016). The patient experience of sleep problems and their treatment in the context of current delusions and hallucinations. *Psychology and Psychotherapy: Theory, Research and Practice*, *89*(2), 181–193. https://doi.org/10.1111/papt.12073

Waite, F., Myers, E., Harvey, A., Espie, C., Startup, H., Sheaves, B., & Freeman, D. (2016). Treating Sleep Problems in Patients with Schizophrenia. *Behavioural and Cognitive Psychotherapy*, *44*(3), 273–87. https://doi.org/10.1017/S1352465815000430

Wamsley, E. J. (2014). Dreaming and offline memory consolidation. *Current Neurology and Neuroscience Reports*, *14*(3), 433. https://doi.org/10.1007/s11910-013-0433-5

Wamsley, E. J., Tucker, M. a, Shinn, A. K., Ono, K. E., McKinley, S. K., Ely, A. V, … Manoach, D. S. (2012). Reduced sleep spindles and spindle coherence in schizophrenia: mechanisms of impaired memory consolidation? *Biological Psychiatry*, *71*(2), 154–61. https://doi.org/10.1016/j.biopsych.2011.08.008

Waters, F., Allen, P., Aleman, A., Fernyhough, C., Woodward, T. S., Badcock, J. C., … Larøi, F. (2012). Auditory hallucinations in schizophrenia and nonschizophrenia populations: a review and integrated model of cognitive mechanisms. *Schizophrenia Bulletin*, *38*(4), 683–93. https://doi.org/10.1093/schbul/sbs045

Waters, F., & Manoach, D. (2012). Sleep dysfunctions in schizophrenia: A practical review. *Open Journal of Psychiatry*, *2*(4), 384–392. https://doi.org/10.4236/ojpsych.2012.224054

Waters, F., Sinclair, C., Rock, D., Jablensky, A., Foster, R., & Wulff, K. (2011). Daily variations in sleep-wake patterns and severity of psychopathology: a pilot study in community-dwelling

individuals with chronic schizophrenia. *Psychiatry Research*, *187*(1–2), 304–6. https://doi.org/10.1016/j.psychres.2011.01.006

West, L., & Janszen, H. (1962). The Psychosis of Sleep Deprivation. *Annals of the New York Academy of Sciences*, 66–70.

Wichniak, A., Skowerska, A., Chojnacka-Wójtowicz, J., Tafliński, T., Wierzbicka, A., Jernajczyk, W., & Jarema, M. (2011). Actigraphic monitoring of activity and rest in schizophrenic patients treated with olanzapine or risperidone. *Journal of Psychiatric Research*, *45*(10), 1381–6. https://doi.org/10.1016/j.jpsychires.2011.05.009

Wigman, J. T. W., Vollebergh, W. A. M., Raaijmakers, Q. A. W., Iedema, J., van Dorsselaer, S., Ormel, J., … van Os, J. (2011). The structure of the extended psychosis phenotype in early adolescence--a cross-sample replication. *Schizophrenia Bulletin*, *37*(4), 850–60. https://doi.org/10.1093/schbul/sbp154

Wilson, S., & Argyropoulos, S. (2012). Sleep in schizophrenia: time for closer attention. *The British Journal of Psychiatry*, *200*(4), 273–4. https://doi.org/10.1192/bjp.bp.111.104091

Winkelman, J. W. (2001). Schizophrenia, Obesity, and Obstructive Sleep Apnea. *The Journal of Clinical Psychiatry*, *62*(1), 8–11. https://doi.org/10.4088/JCP.v62n0103

Wulff, K., Dijk, D. J., Middleton, B., Foster, R., & Joyce, E. M. (2012). Sleep and circadian rhythm disruption in schizophrenia. *British Journal of Psychiatry*, *200*(4), 308–316. https://doi.org/10.1192/bjp.bp.111.096321

Xiang, Y.-T., Weng, Y.-Z., Leung, C.-M., Tang, W.-K., Lai, K. Y. C., & Ungvari, G. S. (2009). Prevalence and correlates of insomnia and its impact on quality of life in Chinese schizophrenia patients. *Sleep*, *32*(1), 105–9.

Yamashita, H., Mori, K., Nagao, M., Okamoto, Y., Morinobu, S., & Yamawaki, S. (2004). Effects of changing from typical to atypical antipsychotic drugs on subjective sleep quality in patients with schizophrenia in a Japanese population. *The Journal of Clinical Psychiatry*, *65*(11), 1525–30.

Yamashita, H., Mori, K., Nagao, M., Okamoto, Y., Morinobu, S., & Yamawaki, S. (2005). Influence of Aging on the Improvement of Subjective Sleep Quality by Atypical Antipsychotic Drugs in Patients With Schizophrenia: Comparison of Middle-Aged and Older Adults. *The American Journal of Geriatric Psychiatry*, *13*(5), 377–384. https://doi.org/10.1097/00019442-200505000-00006

Yang, C., & Winkelman, J. W. (2006). Clinical significance of sleep EEG abnormalities in chronic schizophrenia. *Schizophrenia Research*, *82*(2–3), 251–60. https://doi.org/10.1016/j.schres.2005.10.021

Zanini, M., Castro, J., Coakley, D., Bittencourt, L., Bressan, R., Tufik, S., & Brietzke, E. (2013). Do sleep abnormalities and misaligned sleep/circadian rhythm patterns represent early clinical characteristics for developing psychosis in high risk populations? *Neuroscience and Biobehavioral Reviews*, *37*(10 Pt 2), 2631–7. https://doi.org/10.1016/j.neubiorev.2013.08.012

Zhang, Z.-J., Chen, Y.-C., Wang, H.-N., Wang, H.-H., Xue, Y.-Y., Feng, S.-F., & Tan, Q.-R. (2012). Electroconvulsive therapy improves antipsychotic and somnographic responses in adolescents with first-episode psychosis--a case-control study. *Schizophrenia Research*, *137*(1–3), 97–103. https://doi.org/10.1016/j.schres.2012.01.037

## 8.2 Chapter 2 References

Alhola, P., & Polo-Kantola, P. (2007, January 1). Sleep deprivation: Impact on cognitive performance. *Neuropsychiatric Disease and Treatment*. Dove Press. https://doi.org/10.1016/j.smrv.2012.06.007

Balkin, T. J., Bliese, P. D., Belenky, G., Sing, H., Thorne, D. R., Thomas, M., … Wesensten, N. J. (2004). Comparative utility of instruments for monitoring sleepiness-related performance decrements in the operational environment. *Journal of Sleep Research*, *13*(3), 219–27. https://doi.org/10.1111/j.1365-2869.2004.00407.x

Banks, S., & Dinges, D. F. (2007). Behavioral and physiological consequences of sleep restriction. *Journal of Clinical Sleep Medicine : JCSM : Official Publication of the American Academy of Sleep Medicine*, *3*(5), 519–28. https://doi.org/10.1055/s-0029-1237117.Neurocognitive

Banks, S., Van Dongen, H. P. A., Maislin, G., & Dinges, D. F. (2010). Neurobehavioral dynamics following chronic sleep restriction: dose-response effects of one night for recovery. *Sleep*, *33*(8), 1013–1026.

Baron, R. M., & Kenny, D. a. (1986). The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *Journal of Personality and Social Psychology*, *51*(6), 1173–1182. https://doi.org/10.1037/0022-3514.51.6.1173

Beards, S., & Fisher, H. (2014). The journey to psychosis: an exploration of specific psychological pathways. *Social Psychiatry and Psychiatric Epidemiology*, *49*(10), 1541–4. https://doi.org/10.1007/s00127-014-0953-6

Beck, A. T., Guth, D., Steer, R. A., & Ball, R. (1997). Screening for major depression disorders in medical inpatients with the Beck Depression Inventory for Primary Care. *Behaviour Research and Therapy*, *35*(8), 785–791. https://doi.org/10.1016/S0005-7967(97)00025-9

Belenky, G., Wesensten, N. J., Thorne, D. R., Thomas, M. L., Sing, H. C., Redmond, D. P., … Balkin, T. J. (2003). Patterns of performance degradation and restoration during sleep restriction and subsequent recovery: a sleep dose-response study. *Journal of Sleep Research*, *12*(1), 1–12. https://doi.org/10.1046/j.1365-2869.2003.00337.x

Buysse, D. J., Reynolds, C. F. 3Rd, Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The Pittsburgh Sleep Quality Index: A New Instrument for Psychiatric Practice and Research. *Psychiatry Research*, *28*, 193–213. https://doi.org/10.1016/0165-1781(89)90047-4

Carney, C. E., Buysse, D. J., Ancoli-Israel, S., Edinger, J. D., Krystal, A. D., Lichstein, K. L., & Morin, C. M. (2012). The Consensus Sleep Diary: Standardizing Prospective Sleep Self-Monitoring. *Sleep*. https://doi.org/10.5665/sleep.1642

Doherty, M. J., Campbell, N. M., Tsuji, H., & Phillips, W. A. (2010). The Ebbinghaus illusion deceives adults but not young children. *Developmental Science*, *13*(5), 714–21. https://doi.org/10.1111/j.1467-7687.2009.00931.x

Drake, C. L., Roehrs, T. A., Burduvali, E., Bonahoom, A., Rosekind, M., & Roth, T. (2001). Effects of rapid versus slow accumulation of eight hours of sleep loss. *Psychophysiology*, *38*(6), 979–987. https://doi.org/10.1111/1469-8986.3860979

Duffy, J. F., Zitting, K.-M., & Chinoy, E. D. (2015). Aging and Circadian Rhythms. *Sleep Medicine Clinics*, *10*(4), 423–434. https://doi.org/10.1016/j.jsmc.2015.08.002

Emsley, R., Dunn, G., & White, I. R. (2010). Mediation and moderation of treatment effects in randomised controlled trials of complex interventions. *Statistical Methods in Medical Research*, *19*(3), 237–70. https://doi.org/10.1177/0962280209105014

Feingold, A. (2009). Effect sizes for growth-modeling analysis for controlled clinical trials in the same metric as for classical analysis. *Psychological Methods*, *14*(1), 43–53. https://doi.org/10.1037/a0014699

Finan, P. H., Quartana, P. J., & Smith, M. T. (2015). The Effects of Sleep Continuity Disruption on Positive Mood and Sleep Architecture in Healthy Adults. *Sleep*, *38*(11), 1735–1742. https://doi.org/10.5665/sleep.5154

Fortier-Brochu, E., Beaulieu-Bonneau, S., Ivers, H., & Morin, C. M. (2012). Insomnia and daytime cognitive performance: a meta-analysis. *Sleep Medicine Reviews*, *16*(1), 83–94. https://doi.org/10.1016/j.smrv.2011.03.008

Foster, C., Startup, H., Potts, L., & Freeman, D. (2010). A randomised controlled trial of a worry intervention for individuals with persistent persecutory delusions. *Journal of Behavior Therapy and Experimental Psychiatry*, *41*(1), 45–51. https://doi.org/10.1016/j.jbtep.2009.09.001

Fowler, D., Freeman, D., Smith, B., Kuipers, E., Bebbington, P., Bashforth, H., … Garety, P. (2006). The Brief Core Schema Scales (BCSS): psychometric properties and associations with paranoia and grandiosity in non-clinical and psychosis samples. *Psychological Medicine*, *36*(6), 749. https://doi.org/10.1017/S0033291706007355

Freeman, D. (2016). Persecutory delusions: a cognitive perspective on understanding and treatment. *The Lancet Psychiatry*, *3*(7), 685–692. https://doi.org/10.1016/S2215-0366(16)00066-3

Freeman, D., Dunn, G., Murray, R. M., Evans, N., Lister, R., Antley, A., … Morrison, P. D. (2015). How Cannabis Causes Paranoia: Using the Intravenous Administration of Δ9-Tetrahydrocannabinol (THC) to Identify Key Cognitive Mechanisms Leading to Paranoia. *Schizophrenia Bulletin*, *41*(2), 391–399. https://doi.org/10.1093/schbul/sbu098

Freeman, D., Dunn, G., Startup, H., Pugh, K., Cordwell, J., Mander, H., … Kingdon, D. (2015). Effects of cognitive behaviour therapy for worry on persecutory delusions in patients with psychosis (WIT): a parallel, single-blind, randomised controlled trial with a mediation analysis. *The Lancet Psychiatry*, *2*(4), 305–313. https://doi.org/10.1016/S2215-0366(15)00039-5

Freeman, D., & Garety, P. (2003). Connecting neurosis and psychosis: the direct influence of emotion on delusions and hallucinations. *Behaviour Research and Therapy*, *41*(8), 923–947. https://doi.org/10.1016/S0005-7967(02)00104-3

Freeman, D., Pugh, K., Dunn, G., Evans, N., Sheaves, B., Waite, F., … Fowler, D. (2014). An early Phase II randomised controlled trial testing the effect on persecutory delusions of using CBT to reduce negative cognitions about the self: The potential benefits of enhancing self confidence. *Schizophrenia Research*, *160*(1), 186–192. https://doi.org/10.1016/j.schres.2014.10.038

Freeman, D., Sheaves, B., Goodwin, G., Yu, L.-M., Harrison, P., Emsley, R., … Espie, C. (2015). A randomised controlled trial testing the effects of cognitive behavioural therapy for insomnia on the mental health of university students. *Trials*, *16*(236). https://doi.org/10.1186/s13063-015-0756-4.

Freeman, D., Waite, F., Startup, H., Myers, E., Lister, R., McInerney, J., … Yu, L.-M. M. (2015). Efficacy of cognitive behavioural therapy for sleep improvement in patients with persistent delusions and hallucinations (BEST): A prospective, assessor-blind, randomised controlled pilot trial. *The Lancet Psychiatry*, *2*(11), 975–983. https://doi.org/10.1016/S2215-0366(15)00314-4

Garety, P., & Freeman, D. (1999). Cognitive approaches to delusions: A critical review of theories and evidence. *British Journal of Clinical Psychology*, *38*(2), 113–154. https://doi.org/10.1348/014466599162700

Garety, P., Joyce, E., Jolley, S., Emsley, R., Waller, H., Kuipers, E., … Freeman, D. (2013). Neuropsychological functioning and jumping to conclusions in delusions. *Schizophrenia Research*, *150*(2–3), 570–4. https://doi.org/10.1016/j.schres.2013.08.035

Garety, P., Kuipers, E., Fowler, D., Freeman, D., & Bebbington, P. (2001). A cognitive model of the positive symptoms of psychosis. *Psychological Medicine*, *31*(2), 189–95. https://doi.org/10.1017/S0033291701003312

Hirschfeld, R. M. A., Holzer, C., Calabrese, J. R., Weissman, M., Reed, M., Davies, M., … Hazard, E. (2003). Validity of the mood disorder questionnaire: A general population study. *American Journal of Psychiatry*, *160*(1), 178–180. https://doi.org/10.1176/appi.ajp.160.1.178

Hurdiel, R., Pezé, T., Daugherty, J., Girard, J., Poussel, M., Poletti, L., … Theunynck, D. (2014). Combined effects of sleep deprivation and strenuous exercise on cognitive performances during The North Face® Ultra Trail du Mont Blanc® (UTMB®). *Journal of Sports Sciences*, *33*(7), 670–674. https://doi.org/10.1080/02640414.2014.960883

IBM Corp. Released. (2011). IBM SPSS Statistics for Windows, Version 22.0. *2011*.

Inquisit 4.0.7.4 [Computer software]. (2014). Seattle, WA, WA: Millisecond Software.

Kahn-Greene, E. T., Killgore, D. B., Kamimori, G. H., Balkin, T. J., & Killgore, W. D. S. (2007). The effects of sleep deprivation on symptoms of psychopathology in healthy adults. *Sleep Medicine*, *8*(3), 215–21. https://doi.org/10.1016/j.sleep.2006.08.007

Kahn, M., Fridenson, S., Lerer, R., Bar-Haim, Y., & Sadeh, A. (2014). Effects of one night of induced night-wakings versus sleep restriction on sustained attention and mood: a pilot study. *Sleep Medicine*, *15*(7), 825–32. https://doi.org/10.1016/j.sleep.2014.03.016

Lovibond, S. H., & Lovibond, P. F. (1995). *Manual for the Depression Anxiety Stress Scales. Psychology Foundation of Australia* (Vol. 56). https://doi.org/DOI: 10.1016/0005-7967(94)00075-U

Mason, O., Morgan, C. J. M., Stefanovic, A., & Curran, H. V. (2008). The psychotomimetic states inventory (PSI): measuring psychotic-type experiences from ketamine and cannabis. *Schizophrenia Research*, *103*(1–3), 138–42. https://doi.org/10.1016/j.schres.2008.02.020

Morey, L. (2016). *Personality Assessment Inventory*. Psychological Assessment Resources.

Notredame, C.-E., Pins, D., Deneve, S., & Jardri, R. (2014). What visual illusions teach us about schizophrenia. *Frontiers in Integrative Neuroscience*, *8*, 63. https://doi.org/10.3389/fnint.2014.00063

Pearl, J. (2000). *Causality. New York: Cambridge*.

Petrovsky, N., Ettinger, U., Hill, A., Frenzel, L., Meyhöfer, I., Wagner, M., … Kumari, V. (2014). Sleep deprivation disrupts prepulse inhibition and induces psychosis-like symptoms in healthy humans. *The Journal of Neuroscience*, *34*(27), 9134–40. https://doi.org/10.1523/JNEUROSCI.0904-14.2014

Ragland, J. D., Turetsky, B. I., Gur, R. C., Gunning-Dixon, F., Turner, T., Schroeder, L., … Gur, R. E. (2002). Working memory for complex figures: An fMRI comparison of letter and fractal n-back tasks. *Neuropsychology*, *16*(3), 370–379. https://doi.org/10.1037/0894-4105.16.3.370

Rehman, A., Waite, F., Sheaves, B., Biello, S., Freeman, D., & Gumley, A. (2016). Clinician perceptions of sleep problems, and their treatment, in patients with non-affective psychosis. *Psychosis*, 1–11. https://doi.org/10.1080/17522439.2016.1206955

Ronald, A., Sieradzka, D., Cardno, A. G., Haworth, C. M. a, McGuire, P., & Freeman, D. (2014). Characterization of psychotic experiences in adolescence using the specific psychotic experiences questionnaire: Findings from a study of 5000 16-Year-Old Twins. *Schizophrenia Bulletin*, *40*(4), 868–877. https://doi.org/10.1093/schbul/sbt106

Rupp, T. L., Wesensten, N. J., Bliese, P. D., & Balkin, T. J. (2009). Banking sleep: realization of benefits during subsequent sleep restriction and recovery. *Sleep*, *32*(3), 311–321. https://doi.org/10.1111/j.1365-2869.2009.00800.x

Sadeh, A., Dan, O., & Bar-Haim, Y. (2011). Online assessment of sustained attention following sleep restriction. *Sleep Medicine*, *12*(3), 257–261. https://doi.org/10.1016/j.sleep.2010.02.001

Smith, B., Fowler, D., Freeman, D., Bebbington, P., Bashforth, H., Garety, P., … Kuipers, E. (2006). Emotion and psychosis: links between depression, self-esteem, negative schematic beliefs and delusions and hallucinations. *Schizophrenia Research*, *86*(1–3), 181–8. https://doi.org/10.1016/j.schres.2006.06.018

Smith, N., Freeman, D., & Kuipers, E. (2005). Grandiose delusions: an experimental investigation of the delusion as defense. *The Journal of Nervous and Mental Disease*, *193*(7), 480–7. https://doi.org/DOI 10.1097/01.nmd.0000168235.60469.cc

StataCorp. (2015). Stata Statistical Software: Release 14. *2015*. https://doi.org/10.2307/2234838

Sternemann, U., Schneider, U., Leweke, F. M., Bevilacqua, C. M., Dietrich, D. E., & Emrich, H. M. (1997). [Pro-psychotic change of binocular depth inversion by sleep deprivation]. *Der Nervenarzt*, *68*(7), 593–6.

Van Dongen, H. P., Maislin, G., Mullington, J. M., & Dinges, D. F. (2003). The Cumulative Cost of Additional Wakefulness: Dose-Response Effects on Neurobehavioral Functions and Sleep Physiology From Chronic Sleep Restriction and Total Sleep Deprivation. *Sleep*, *26*(2), 117–126. https://doi.org/10.1093/sleep/26.2.117

van Os, J. (2009). "Salience syndrome" replaces "schizophrenia" in DSM-V and ICD-11: psychiatry's evidence-based entry into the 21st century? *Acta Psychiatrica Scandinavica*, *120*(5), 363–72. https://doi.org/10.1111/j.1600-0447.2009.01456.x

Vorontsova, N., Garety, P., & Freeman, D. (2013). Cognitive factors maintaining persecutory delusions in psychosis: the contribution of depression. *Journal of Abnormal Psychology*, *122*(4), 1121–31. https://doi.org/10.1037/a0034952

Waite, F., Evans, N., Myers, E., Startup, H., Lister, R., Harvey, A., & Freeman, D. (2016). The patient experience of sleep problems and their treatment in the context of current delusions and hallucinations. *Psychology and Psychotherapy: Theory, Research and Practice*, *89*(2), 181–193. https://doi.org/10.1111/papt.12073

Waters, F., Allen, P., Aleman, A., Fernyhough, C., Woodward, T. S., Badcock, J. C., … Larøi, F. (2012). Auditory hallucinations in schizophrenia and nonschizophrenia populations: a review and integrated model of cognitive mechanisms. *Schizophrenia Bulletin*, *38*(4), 683–93. https://doi.org/10.1093/schbul/sbs045

Wigman, J. T. W., Vollebergh, W. A. M., Raaijmakers, Q. A. W., Iedema, J., van Dorsselaer, S., Ormel, J., … van Os, J. (2011). The structure of the extended psychosis phenotype in early adolescence--a cross-sample replication. *Schizophrenia Bulletin*, *37*(4), 850–60. https://doi.org/10.1093/schbul/sbp154

Wittmann, M., Dinich, J., Merrow, M., & Roenneberg, T. (2006). Social jetlag: misalignment of biological and social time. *Chronobiology International*, *23*(1–2), 497–509. https://doi.org/10.1080/07420520500545979

## 8.3 Chapter 3 References

Afonso, P., Brissos, S., Figueira, M. L., & Paiva, T. (2011). Schizophrenia patients with predominantly positive symptoms have more disturbed sleep-wake cycles measured by actigraphy. *Psychiatry Research*, *189*(1), 62–6. https://doi.org/10.1016/j.psychres.2010.12.031

Beck, A. T., Guth, D., Steer, R. A., & Ball, R. (1997). Screening for major depression disorders in medical inpatients with the Beck Depression Inventory for Primary Care. *Behaviour Research and Therapy*, *35*(8), 785–91.

Bradley, J., Freeman, D., Chadwick, E., Harvey, A. G., Mullins, B., Johns, L., … Waite, F. (2017). Treating Sleep Problems in Young People at Ultra-High Risk of Psychosis: A Feasibility Case Series. *Behavioural and Cognitive Psychotherapy*, 1–16. https://doi.org/10.1017/S1352465817000601

Broome, M. R., Day, F., Valli, I., Valmaggia, L., Johns, L. C., Howes, O., … McGuire, P. K. (2012). Delusional ideation, manic symptomatology and working memory in a cohort at clinical high-risk for psychosis: A longitudinal study. *European Psychiatry*, *27*(4), 258–263. https://doi.org/10.1016/j.eurpsy.2010.07.008

Castro, J., Zanini, M., Gonçalves, B., Coelho, F. M., Bressan, R., Bittencourt, L., … Tufik, S. (2015). Circadian rest-activity rhythm in individuals at risk for psychosis and bipolar disorder. *Schizophrenia Research*, *168*(1–2), 50–5. https://doi.org/10.1016/j.schres.2015.07.024

Davies, G., Haddock, G., Yung, A., Mulligan, L. D., & Kyle, S. (2016). A systematic review of the nature and correlates of sleep disturbance in early psychosis. *Sleep Medicine Reviews*. https://doi.org/10.1016/j.smrv.2016.01.001

Feise, R. J. (2002). Do multiple outcome measures require p-value adjustment? *BMC Medical Research Methodology*, *2*(1), 8. https://doi.org/10.1186/1471-2288-2-8

Garety, P., Gittins, M., Jolley, S., Bebbington, P., Dunn, G., Kuipers, E., … Freeman, D. (2013). Differences in cognitive and emotional processes between persecutory and grandiose delusions. *Schizophrenia Bulletin*, *39*(3), 629–39. https://doi.org/10.1093/schbul/sbs059

Garety, P., Kuipers, E., Fowler, D., Freeman, D., & Bebbington, P. (2001). A cognitive model of the positive symptoms of psychosis. *Psychological Medicine*, *31*(2), 189–95.

Hartmann, J. A., Yuen, H. P., McGorry, P. D., Yung, A., Lin, A., Wood, S. J., … Nelson, B. (2016). Declining transition rates to psychotic disorder in "ultra-high risk" clients: Investigation of a

dilution effect. *Schizophrenia Research*, *170*(1), 130–6. https://doi.org/10.1016/j.schres.2015.11.026

IBM Corp. (2015). IBM SPSS Statistics.

Kirkbride, J. B., Stubbins, C., & Jones, P. B. (2012). Psychosis incidence through the prism of early intervention services. *British Journal of Psychiatry*. https://doi.org/10.1192/bjp.bp.111.094896

Kyle, S., Espie, C., & Morgan, K. (2010). "...Not just a minor thing, it is something major, which stops you from functioning daily": quality of life and daytime functioning in insomnia. *Behavioral Sleep Medicine*, *8*(3), 123–140. https://doi.org/10.1080/15402002.2010.487450

Kyle, S., Morgan, K., & Espie, C. (2010). Insomnia and health-related quality of life. *Sleep Medicine Reviews*, *14*(1), 69–82. https://doi.org/10.1016/j.smrv.2009.07.004

Lunsford-Avery, J. R., Gonçalves, B. da S. B., Brietzke, E., Bressan, R., Gadelha, A., Auerbach, R. P., & Mittal, V. A. (2016). Adolescents at clinical-high risk for psychosis: Circadian rhythm disturbances predict worsened prognosis at 1-year follow-up. *Schizophrenia Research*. https://doi.org/10.1016/j.schres.2017.01.051

Lunsford-Avery, J. R., LeBourgeois, M. K., Gupta, T., & Mittal, V. A. (2015). Actigraphic-measured sleep disturbance predicts increased positive symptoms in adolescents at ultra high-risk for psychosis: A longitudinal study. *Schizophrenia Research*. https://doi.org/10.1016/j.schres.2015.03.013

Lunsford-Avery, J. R., & Mittal, V. A. (2013). Sleep Dysfunction Prior to the Onset of Schizophrenia: A Review and Neurodevelopmental Diathesis–Stress Conceptualization. *Clinical Psychology: Science and Practice*, *20*(3), 291–320. https://doi.org/10.1111/cpsp.12041

Lunsford-Avery, J. R., Orr, J. M., Gupta, T., Pelletier-Baldelli, A., Dean, D. J., Smith Watts, A. K., … Mittal, V. a. (2013). Sleep dysfunction and thalamic abnormalities in adolescents at ultra high-risk for psychosis. *Schizophrenia Research*, *151*(1–3), 148–53. https://doi.org/10.1016/j.schres.2013.09.015

Miller, T. J., Mcqlashan, T. H., Rosen, J. L., Cadenhead, K., Ventura, J., Mcfarlane, W., … Woods, S. W. (2003). Prodromal Assessment With the Structured Interview for Prodromal Syndromes and the Scale of Prodromal Symptoms: Predictive Validity, Interrater Reliability, and Training to Reliability. *Schizophrenia Bulletin*, *29*(4), 703–715. https://doi.org/10.1093/oxfordjournals.schbul.a007040

Miller, T. J., Zipursky, R. B., Perkins, D., Addington, J., Woods, S. W., Hawkins, K. A., … McGlashan, T. H. (2003). The PRIME North America randomized double-blind clinical trial of olanzapine versus placebo in patients at risk of being prodromally symptomatic for psychosis. *Schizophrenia Research*, *61*(1), 19–30. https://doi.org/10.1016/S0920-9964(02)00440-1

Morrison, A., French, P., Stewart, S. L. K., Birchwood, M., Fowler, D., Gumley, A. I., … Dunn, G. (2012). Early detection and intervention evaluation for people at risk of psychosis: multisite randomised controlled trial. *BMJ*, *344*(apr05 1), e2233–e2233. https://doi.org/10.1136/bmj.e2233

Morrison, A., Stewart, S. L. K., French, P., Bentall, R. P., Birchwood, M., Byrne, R., … Dunn, G. (2011). Early detection and intervention evaluation for people at high-risk of psychosis-2 (EDIE-2): trial rationale, design and baseline characteristics. *Early Intervention in Psychiatry*, *5*(1), 24–32. https://doi.org/10.1111/j.1751-7893.2010.00254.x

Nutt, D., Wilson, S., & Paterson, L. (2008). Sleep disorders as core symptoms of depression. *Dialogues in Clinical Neuroscience*, *10*(3), 329–36.

Pearl, J. (2000). Causality. *New York: Cambridge*.

Phillips, L. J., Leicester, S. B., O'Dwyer, L. E., Francey, S., Koutsogiannis, J., Abdel-Baki, A., … Mcgorry, P. D. (2002). The PACE Clinic: Identification and Management of Young People at "Ultra" High Risk of Psychosis. *Journal of Psychiatric Practice*, *8*(5), 255–269. https://doi.org/10.1097/00131746-200209000-00002

Poe, S.-L., Brucato, G., Bruno, N., Arndt, L. Y., Ben-David, S., Gill, K. E., … Girgis, R. R. (2017). *Sleep disturbances in individuals at clinical high risk for psychosis*. *Psychiatry Research* (Vol. 249). https://doi.org/10.1016/j.psychres.2016.12.029

Priebe, S., Huxley, P., Knight, S., & Evans, S. (1999). Application and results of the Manchester Short Assessment of Quality of Life (MANSA). *The International Journal of Social Psychiatry*, *45*(1), 7–12. https://doi.org/10.1177/002076409904500102

Ronald, A. (2015). Recent quantitative genetic research on psychotic experiences: New approaches to old questions. *Current Opinion in Behavioral Sciences*. Elsevier Ltd. https://doi.org/10.1016/j.cobeha.2014.10.001

Ruhrmann, S., Schultze-Lutter, F., Salokangas, R., Heinimaa, M., Linszen, D., Dingemans, P., … Klosterkötter, J. (2010). Prediction of Psychosis in Adolescents and Young Adults at High Risk: results from the prospective european prediction of psychosis study. *Archives of General*

*Psychiatry*, *67*(3), 241–251. https://doi.org/10.1001/archgenpsychiatry.2009.206

Schmidt, A., Cappucciati, M., Radua, J., Rutigliano, G., Rocchetti, M., Dell'Osso, L., … Fusar-Poli, P. (2017). Improving Prognostic Accuracy in Subjects at Clinical High Risk for Psychosis: Systematic Review of Predictive Models and Meta-analytical Sequential Testing Simulation. *Schizophrenia Bulletin*, *43*(2), 375–388. https://doi.org/10.1093/schbul/sbw098

Scott, E. M., Robillard, R. R., Hermens, D. F., Naismith, S. L., Rogers, N. L., Ip, T. K. C., … Hickie, I. B. (2016). Dysregulated sleep-wake cycles in young people are associated with emerging stages of major mental disorders. *Early Intervention in Psychiatry*, *10*(1), 63–70. https://doi.org/10.1111/eip.12143

Short, S. (2006). Review of the UK 2000 Time Use Survey, (July).

Taylor, H. E., Stewart, S. L. K., Dunn, G., Parker, S., Fowler, D., & Morrison, A. P. (2014). Core Schemas across the Continuum of Psychosis: A Comparison of Clinical and Non-Clinical Groups. *Behavioural and Cognitive Psychotherapy*, *42*(6), 718–730. https://doi.org/10.1017/S1352465813000593

van Os, J. (2014). The many continua of psychosis. *JAMA Psychiatry*, *71*(9), 985–6. https://doi.org/10.1001/jamapsychiatry.2014.1068

Waters, F., Naik, N., & Rock, D. (2013). Sleep, fatigue, and functional health in psychotic patients. *Schizophrenia Research and …*, *2013*, 425826. https://doi.org/10.1155/2013/425826

Waters, F., Sinclair, C., Rock, D., Jablensky, A., Foster, R., & Wulff, K. (2011). Daily variations in sleep-wake patterns and severity of psychopathology: a pilot study in community-dwelling individuals with chronic schizophrenia. *Psychiatry Research*, *187*(1–2), 304–6. https://doi.org/10.1016/j.psychres.2011.01.006

Wulff, K., Dijk, D. J., Middleton, B., Foster, R., & Joyce, E. M. (2012). Sleep and circadian rhythm disruption in schizophrenia. *British Journal of Psychiatry*, *200*(4), 308–316. https://doi.org/10.1192/bjp.bp.111.096321

Yung, A.., & McGorry, P. D. (1996). The Prodromal Phase of First-episode Psychosis: Past and Current Conceptualizations. *Schizophrenia Bulletin*, *22*(2), 353–70. https://doi.org/10.1093/schbul/22.2.353

Yung, A., Phillips, L. J., Yuen, H., Francey, S., McFarlane, C. A., Hallgren, M., & McGorry, P. D. (2003). Psychosis prediction: 12-month follow up of a high-risk ("prodromal") group.

*Schizophrenia Research*, *60*(1), 21–32. https://doi.org/10.1016/S0920-9964(02)00167-6

Yung, A., Yuen, H. P., Phillips, L. J., Francey, S., & McGorry, P. D. (2003). Mapping the onset of psychosis: The comprehensive assessment of at risk mental states (CAARMS). *Schizophrenia Research*, *60*(1), 30–31. https://doi.org/10.1016/S0920-9964(03)80090-7

Yung, A., Phillips, L., Yuen, H., & McGorry, P. (2004). Risk factors for psychosis in an ultra high-risk group: psychopathology and clinical features. *Schizophrenia Research*, *67*(2–3), 131–42. https://doi.org/10.1016/S0920-9964(03)00192-0

Zanini, M. A., Castro, J., Cunha, G. R., Asevedo, E., Pan, P. M., Bittencourt, L., … Brietzke, E. (2015). Abnormalities in sleep patterns in individuals at risk for psychosis and bipolar disorder. *Schizophrenia Research*. https://doi.org/10.1016/j.schres.2015.08.023

Zanini, M., Castro, J., Coakley, D., Bittencourt, L., Bressan, R., Tufik, S., & Brietzke, E. (2013). Do sleep abnormalities and misaligned sleep/circadian rhythm patterns represent early clinical characteristics for developing psychosis in high risk populations? *Neuroscience and Biobehavioral Reviews*, *37*(10 Pt 2), 2631–7. https://doi.org/10.1016/j.neubiorev.2013.08.012

Zavos, H. M. S., Freeman, D., Haworth, C. M. A., McGuire, P., Plomin, R., Cardno, A. G., & Ronald, A. (2014). Consistent etiology of severe, frequent psychotic experiences and milder, less frequent manifestations: a twin study of specific psychotic experiences in adolescence. *JAMA Psychiatry*, *71*(9), 1049–57. https://doi.org/10.1001/jamapsychiatry.2014.994

## 8.4 Chapter 4 References

AASS. (2014). *International Classification of Sleep Disorders* (3rd ed.).

Antony, M., Bieling, P., & Cox, B. (1998). Psychometric properties of the 42-item and 21-item versions of the Depression Anxiety Stress Scales in clinical groups and a community sample. *Psychological Assessment*, *10*(2), 176–181.

APA. (2013). *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5). Diagnostic and Statistical Manual of Mental Disorders 4th edition TR.* https://doi.org/10.1176/appi.books.9780890425596.744053

Aurora, R. N., Zak, R. S., Auerbach, S. H., Casey, K. R., Chowdhuri, S., Karippot, A., … Tracy, S. L. (2010, August 15). Best practice guide for the treatment of nightmare disorder in adults. *Journal of Clinical Sleep Medicine*. American Academy of Sleep Medicine.

Auslander, L. A., & Jeste, D. V. (2002). Perceptions of problems and needs for service among middle-aged and elderly outpatients with schizophrenia and related psychotic disorders. *Community Mental Health Journal*, *38*(5), 391–402.

Carney, C. E., Buysse, D. J., Ancoli-Israel, S., Edinger, J. D., Krystal, A. D., Lichstein, K. L., & Morin, C. M. (2012). The Consensus Sleep Diary: Standardizing Prospective Sleep Self-Monitoring. *Sleep*. https://doi.org/10.5665/sleep.1642

Freeman, D., Pugh, K., Vorontsova, N., & Southgate, L. (2009). Insomnia and paranoia. *Schizophrenia Research*, *108*(1–3), 280–4. https://doi.org/10.1016/j.schres.2008.12.001

Freeman, D., Sheaves, B., Goodwin, G. M., Yu, L.-M., Nickless, A., Harrison, P. J., … Espie, C. A. (2017). The effects of improving sleep on mental health (OASIS): a randomised controlled trial with mediation analysis. *The Lancet Psychiatry*, *4*(10), 749–758. https://doi.org/10.1016/S2215-0366(17)30328-0

Freeman, D., Waite, F., Startup, H., Myers, E., Lister, R., McInerney, J., … Yu, L.-M. M. (2015). Efficacy of cognitive behavioural therapy for sleep improvement in patients with persistent delusions and hallucinations (BEST): A prospective, assessor-blind, randomised controlled pilot trial. *The Lancet Psychiatry*, *2*(11), 975–983. https://doi.org/10.1016/S2215-0366(15)00314-4

Hansen, K., Höfling, V., Kröner-Borowik, T., Stangier, U., & Steil, R. (2013). Efficacy of psychological interventions aiming to reduce chronic nightmares: A meta-analysis. *Clinical Psychology Review*, *33*(1), 146–155. https://doi.org/10.1016/j.cpr.2012.10.012

Herdman, M., Gudex, C., Lloyd, A., Janssen, M., Kind, P., Parkin, D., … Badia, X. (2011). Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Quality of Life Research : An International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation*, *20*(10), 1727–36. https://doi.org/10.1007/s11136-011-9903-x

IBM Corp. (2015). IBM SPSS Statistics.

Jolley, S., Garety, P., Ellett, L., Kuipers, E., Freeman, D., Bebbington, P., … Dunn, G. (2006). A validation of a new measure of activity in psychosis. *Schizophrenia Research*, *85*(1–3), 288–295. https://doi.org/10.1016/j.schres.2006.03.012

Kalucy, M. J., Grunstein, R., Lambert, T., & Glozier, N. (2013). Obstructive sleep apnoea and schizophrenia - A research agenda. *Sleep Medicine Reviews*, *17*(5), 357–365. https://doi.org/10.1016/j.smrv.2012.10.003

Kirkbride, J. B., Stubbins, C., & Jones, P. B. (2012). Psychosis incidence through the prism of early intervention services. *British Journal of Psychiatry*. https://doi.org/10.1192/bjp.bp.111.094896

Krakow, B. J., Melendrez, D. C., Johnston, L. G., Clark, J. O., Santana, E. M., Warner, T. D., … Lee, S. A. (2002). Sleep dynamic therapy for Cerro Grande fire evacuees with posttraumatic stress symptoms: A preliminary report. *Journal of Clinical Psychiatry*, *63*(8), 673–684. https://doi.org/10.4088/JCP.v63n0804

Li, S. X., Lam, S. P., Zhang, J., Yu, M. W. M., Chan, J. W. Y., Chan, C. S. Y., … Wing, Y.-K. (2016). Sleep Disturbances and Suicide Risk in an 8-Year Longitudinal Study of Schizophrenia-Spectrum Disorders. *Sleep*, *39*(6), 1275–82. https://doi.org/10.5665/sleep.5852

Lovibond, S. H., & Lovibond, P. F. (1995). *Manual for the Depression Anxiety Stress Scales. Psychology Foundation of Australia* (Vol. 56). https://doi.org/DOI: 10.1016/0005-7967(94)00075-U

Mayers, A. G., & Baldwin, D. S. (2005). Antidepressants and their effect on sleep. *Human Psychopharmacology: Clinical and Experimental*, *20*(8), 533–559. https://doi.org/10.1002/hup.726

Merikangas, K. R., Zhang, J., Emsellem, H., Swanson, S. A., Vgontzas, A., Belouad, F., … Mignot, E. (2014). The structured diagnostic interview for sleep patterns and disorders: rationale and initial evaluation. *Sleep Medicine*, *15*(5), 530–5. https://doi.org/10.1016/j.sleep.2013.10.011

Monti, J. M., & Monti, D. (2004). Sleep in schizophrenia patients and the effects of antipsychotic

drugs. *Sleep Medicine Reviews*, *8*(2), 133–48. https://doi.org/10.1016/S1087-0792(02)00158-2

Morin, C. M., Belleville, G., Bélanger, L., & Ivers, H. (2011). The Insomnia Severity Index: psychometric indicators to detect insomnia cases and evaluate treatment response. *Sleep*, *34*(5), 601–8.

Moturi, S., & Ivanenko, A. (2009). Complex diagnostic and treatment issues in psychotic symptoms associated with narcolepsy. *Psychiatry (Edgmont (Pa. : Township))*, *6*(6), 38–44.

Nadorff, M. R., Nadorff, D. K., & Germain, A. (2015). Nightmares: Under-Reported, Undetected, and Therefore Untreated. *Journal of Clinical Sleep Medicine*, *11*(7), 747–50. https://doi.org/10.5664/jcsm.4850

Nagappa, M., Liao, P., Wong, J., Auckley, D., Ramachandran, S. K., Memtsoudis, S., … Chung, F. (2015). Validation of the stop-bang questionnaire as a screening tool for obstructive sleep apnea among different populations: A systematic review and meta-Analysis. *PLoS ONE*, *10*(12). https://doi.org/10.1371/journal.pone.0143697

National Institute for Health and Clinical Excellence (NICE). (2015). Managing long-term insomnia (>4 weeks).

Ohayon, M. M., Priest, R. G., Caulet, M., & Guilleminault, C. (1996). Hypnagogic and hypnopompic hallucinations: pathological phenomena? *The British Journal of Psychiatry*, *169*(4), 459–467. https://doi.org/10.1192/bjp.169.4.459

Qaseem, A., Kansagara, D., Forciea, M. A., Cooke, M., Denberg, T. D., CH, K., & J, L. (2016). Management of Chronic Insomnia Disorder in Adults: A Clinical Practice Guideline From the American College of Physicians. *Annals of Internal Medicine*, *165*(2), 125. https://doi.org/10.7326/M15-2175

Rehman, A., Waite, F., Sheaves, B., Biello, S., Freeman, D., & Gumley, A. (2016). Clinician perceptions of sleep problems, and their treatment, in patients with non-affective psychosis. *Psychosis*, 1–11. https://doi.org/10.1080/17522439.2016.1206955

Ronald, A., Sieradzka, D., Cardno, A. G., Haworth, C. M. a, McGuire, P., & Freeman, D. (2014). Characterization of psychotic experiences in adolescence using the specific psychotic experiences questionnaire: Findings from a study of 5000 16-Year-Old Twins. *Schizophrenia Bulletin*, *40*(4), 868–877. https://doi.org/10.1093/schbul/sbt106

Schutte-Rodin, S., Broch, L., Buysse, D., Dorsey, C., & Sateia, M. (2008). Clinical guideline for the

evaluation and management of chronic insomnia in adults. *Journal of Clinical Sleep Medicine : JCSM : Official Publication of the American Academy of Sleep Medicine*, *4*(5), 487–504.

Sheaves, B. (2015). The nightmare intervention study (trial protocol). *International Standard Randomised Controlled Trial Number Registry*, (ISRCTN12668007). https://doi.org/DOI 10.1186/ISRCTN12668007

Sheaves, B., Freeman, D., Isham, L., Mcinerney, J., Nickless, A., Yu, L., … Barrera, A. (2017). Stabilising sleep for patients admitted at acute crisis to a psychiatric hospital (OWLS): an assessor-blind, pilot randomised controlled trial. *Psychological Medicine*

Sheaves, B., Onwumere, J., Keen, N., Stahl, D., & Kuipers, E. (2014). Nightmares in patients with psychosis: the relationship with sleep, psychotic, affective and cognitive symptoms. *Canadian Journal of Psychiatry*, (8), 354–61. https://doi.org/10.1177/070674371506000804

Smets, E. M., Garssen, B., Bonke, B., & De Haes, J. C. (1995). The Multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. *Journal of Psychosomatic Research*, *39*(3), 315–325. https://doi.org/10.1016/0022-3999(94)00125-O

Spoormaker, V. I., Verbeek, I., van den Bout, J., & Klip, E. C. (2005). Initial validation of the SLEEP-50 questionnaire. *Behavioral Sleep Medicine*, *3*(4), 227–246. https://doi.org/10.1207/s15402010bsm0304_4

Stein, K. D., Jacobsen, P. B., Blanchard, C. M., & Thors, C. (2004). Further validation of the multidimensional fatigue symptom inventory-short form. *Journal of Pain and Symptom Management*, *27*(1), 14–23. https://doi.org/10.1016/j.jpainsymman.2003.06.003

Waite, F., Evans, N., Myers, E., Startup, H., Lister, R., Harvey, A., & Freeman, D. (2016). The patient experience of sleep problems and their treatment in the context of current delusions and hallucinations. *Psychology and Psychotherapy: Theory, Research and Practice*, *89*(2), 181–193. https://doi.org/10.1111/papt.12073

Waite, F., Myers, E., Harvey, A., Espie, C., Startup, H., Sheaves, B., & Freeman, D. (2016). Treating Sleep Problems in Patients with Schizophrenia. *Behavioural and Cognitive Psychotherapy*, *44*(3), 273–87. https://doi.org/10.1017/S1352465815000430

Waters, F., Blom, J. D., Dang-Vu, T. T., Cheyne, A. J., Alderson-Day, B., Woodruff, P., & Collerton, D. (2016). What Is the Link Between Hallucinations, Dreams, and Hypnagogic-Hypnopompic Experiences? *Schizophrenia Bulletin*, *42*(5), 1098–109. https://doi.org/10.1093/schbul/sbw076

Waters, F., Faulkner, D., Naik, N., & Rock, D. (2012). Effects of polypharmacy on sleep in psychiatric inpatients. *Schizophrenia Research*, *139*(1–3), 225–8. https://doi.org/10.1016/j.schres.2012.05.013

Wulff, K., Dijk, D. J., Middleton, B., Foster, R., & Joyce, E. M. (2012). Sleep and circadian rhythm disruption in schizophrenia. *British Journal of Psychiatry*, *200*(4), 308–316. https://doi.org/10.1192/bjp.bp.111.096321

## 8.5 Chapter 5 References

Baron, R. M., & Kenny, D. a. (1986). The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *Journal of Personality and Social Psychology*, *51*(6), 1173–1182. https://doi.org/10.1037/0022-3514.51.6.1173

Benoit, K. (2011). Linear Regression Models with Logarithmic Transformations. *London School of Economics*, 1–8.

Box, G. E. P., Cox, D. R., Society, S., & Methodological, S. B. (1964). An Analysis of Transformations. *Analysis*, *26*(2), 211–252. https://doi.org/10.1177/0022427810397950

Christensen, H., Batterham, P. J., Gosling, J. A., Ritterband, L. M., Griffiths, K. M., Thorndike, F. P., … Mackinnon, A. J. (2016). Effectiveness of an online insomnia program (SHUTi) for prevention of depressive episodes (the GoodNight Study): a randomised controlled trial. *The Lancet Psychiatry*, *3*(4), 333–341. https://doi.org/10.1016/S2215-0366(15)00536-2

Espie, C. (1991). *The Psychological Treatment of Insomnia*. Chichester, UK: Wiley.

Freeman, D., & Garety, P. (2003). Connecting neurosis and psychosis: the direct influence of emotion on delusions and hallucinations. *Behaviour Research and Therapy*, *41*(8), 923–947. https://doi.org/10.1016/S0005-7967(02)00104-3

Freeman, D., Pugh, K., Vorontsova, N., & Southgate, L. (2009). Insomnia and paranoia. *Schizophrenia Research*, *108*(1–3), 280–4. https://doi.org/10.1016/j.schres.2008.12.001

Freeman, D., Sheaves, B., Goodwin, G. M., Yu, L.-M., Nickless, A., Harrison, P. J., … Espie, C. (2017). The effects of improving sleep on mental health (OASIS): a randomised controlled trial with mediation analysis. *The Lancet Psychiatry*, *4*(10), 749–758. https://doi.org/10.1016/S2215-0366(17)30328-0

Freeman, D., Stahl, D., McManus, S., Meltzer, H., Brugha, T., Wiles, N., & Bebbington, P. (2012). Insomnia, worry, anxiety and depression as predictors of the occurrence and persistence of paranoid thinking. *Social Psychiatry and Psychiatric Epidemiology*, *47*(8), 1195–203. https://doi.org/10.1007/s00127-011-0433-1

Freeman, D., Waite, F., Startup, H., Myers, E., Lister, R., McInerney, J., … Yu, L.-M. M. (2015). Efficacy of cognitive behavioural therapy for sleep improvement in patients with persistent delusions and hallucinations (BEST): A prospective, assessor-blind, randomised controlled pilot

trial. *The Lancet Psychiatry*, *2*(11), 975–983. https://doi.org/10.1016/S2215-0366(15)00314-4

Hartley, S., Barrowclough, C., & Haddock, G. (2013). Anxiety and depression in psychosis: A systematic review of associations with positive psychotic symptoms. *Acta Psychiatrica Scandinavica*, *128*, 327–346. https://doi.org/10.1111/acps.12080

Harvey, A. (2002). A cognitive model of insomnia. *Behaviour Research and Therapy*, *40*(8), 869–93.

Harvey, A., & Murray, G. (2011). Sleep disturbance as transdiagnostic: consideration of neurobiological mechanisms. *Clinical Psychology Review*, *31*(2), 225–235. https://doi.org/10.1016/j.cpr.2010.04.003.Sleep

Hennig, T., & Lincoln, T. M. (2017). Sleeping Paranoia Away? An Actigraphy and Experience-Sampling Study with Adolescents. *Child Psychiatry & Human Development*, 1–10. https://doi.org/10.1007/s10578-017-0729-9

Hodgekins, J., French, P., Birchwood, M., Mugford, M., Christopher, R., Marshall, M., … Fowler, D. (2015). Comparing time use in individuals at different stages of psychosis and a non-clinical comparison group. *Schizophrenia Research*, *161*(2–3), 188–93. https://doi.org/10.1016/j.schres.2014.12.011

IBM Corp. (2015). IBM SPSS Statistics.

Jansson-Fröjmark, M., & Lindblom, K. (2008). A bidirectional relationship between anxiety and depression, and insomnia? A prospective study in the general population. *Journal of Psychosomatic Research*, *64*(4), 443–449. https://doi.org/10.1016/j.jpsychores.2007.10.016

Keene, O. N. (1995). The log trasnformation is special. *Statistics in Medicine*, *14*(March 1993), 811–819.

Li, L., Wu, C., Gan, Y., Qu, X., & Lu, Z. (2016). Insomnia and the risk of depression: a meta-analysis of prospective cohort studies. *BMC Psychiatry*, *16*(1), 375. https://doi.org/10.1186/s12888-016-1075-3

Lovibond, S. H., & Lovibond, P. F. (1995). *Manual for the Depression Anxiety Stress Scales. Psychology Foundation of Australia* (Vol. 56). https://doi.org/DOI: 10.1016/0005-7967(94)00075-U

Mulligan, L. D., Haddock, G., Emsley, R., Neil, S. T., & Kyle, S. (2016). High resolution examination of the role of sleep disturbance in predicting functioning and psychotic symptoms in

schizophrenia: A novel experience sampling study. *Journal of Abnormal Psychology*, *125*(6), 788–797. https://doi.org/10.1037/abn0000180

Neckelmann, D., Mykletun, A., & Dahl, A. A. (2007). Chronic insomnia as a risk factor for developing anxiety and depression. *Sleep*, *30*(7), 873–80.

Pilton, M., Varese, F., Berry, K., & Bucci, S. (2015). The relationship between dissociation and voices: A systematic literature review and meta-analysis. *Clinical Psychology Review*, *40*, 138–155. https://doi.org/10.1016/j.cpr.2015.06.004

Ronald, A., Sieradzka, D., Cardno, A. G., Haworth, C. M. a, McGuire, P., & Freeman, D. (2014). Characterization of psychotic experiences in adolescence using the specific psychotic experiences questionnaire: Findings from a study of 5000 16-Year-Old Twins. *Schizophrenia Bulletin*, *40*(4), 868–877. https://doi.org/10.1093/schbul/sbt106

Sheaves, B., Bebbington, P., Guy, M., Harrison, P., Espie, C., Foster, G., … Foster, R. (2016). Insomnia and hallucinations in the general population: Findings from the 2000 and 2007 British Psychiatric Morbidity Surveys. *Psychiatry Research*, *241*, 141–146. https://doi.org/10.1016/j.psychres.2016.03.055

Spoormaker, V. I., Verbeek, I., van den Bout, J., & Klip, E. C. (2005). Initial validation of the SLEEP-50 questionnaire. *Behavioral Sleep Medicine*, *3*(4), 227–246. https://doi.org/10.1207/s15402010bsm0304_4

Stubbs, B., Williams, J., Gaughran, F., & Craig, T. (2016). How sedentary are people with psychosis? A systematic review and meta-analysis. *Schizophrenia Research*. https://doi.org/10.1016/j.schres.2016.01.034

Van Der Kloet, D., Giesbrecht, T., Franck, E., Van Gastel, A., De Volder, I., Van Den Eede, F., … Merckelbach, H. (2013). Dissociative symptoms and sleep parameters - An all-night polysomnography study in patients with insomnia. *Comprehensive Psychiatry*, *54*(6), 658–664. https://doi.org/10.1016/j.comppsych.2012.12.025

Waite, F., Evans, N., Myers, E., Startup, H., Lister, R., Harvey, A., & Freeman, D. (2016). The patient experience of sleep problems and their treatment in the context of current delusions and hallucinations. *Psychology and Psychotherapy: Theory, Research and Practice*, *89*(2), 181–193. https://doi.org/10.1111/papt.12073

Waite, F., Myers, E., Harvey, A., Espie, C., Startup, H., Sheaves, B., & Freeman, D. (2016). Treating

Sleep Problems in Patients with Schizophrenia. *Behavioural and Cognitive Psychotherapy*, *44*(3), 273–87. https://doi.org/10.1017/S1352465815000430

Waters, F., Sinclair, C., Rock, D., Jablensky, A., Foster, R., & Wulff, K. (2011). Daily variations in sleep-wake patterns and severity of psychopathology: a pilot study in community-dwelling individuals with chronic schizophrenia. *Psychiatry Research*, *187*(1–2), 304–6. https://doi.org/10.1016/j.psychres.2011.01.006

Wulff, K., Dijk, D. J., Middleton, B., Foster, R., & Joyce, E. M. (2012). Sleep and circadian rhythm disruption in schizophrenia. *British Journal of Psychiatry*, *200*(4), 308–316. https://doi.org/10.1192/bjp.bp.111.096321

Xiang, Y.-T., Weng, Y.-Z., Leung, C.-M., Tang, W.-K., Lai, K. Y. C., & Ungvari, G. S. (2009). Prevalence and correlates of insomnia and its impact on quality of life in Chinese schizophrenia patients. *Sleep*, *32*(1), 105–9.

## 8.6 Chapter 6 References

AASS. (2014). *International Classification of Sleep Disorders* (3rd ed.).

Afonso, P., Figueira, M. L., & Paiva, T. (2014). Sleep-wake patterns in schizophrenia patients compared to healthy controls. *The World Journal of Biological Psychiatry : The Official Journal of the World Federation of Societies of Biological Psychiatry*, *15*(7), 517–24. https://doi.org/10.3109/15622975.2012.756987

Antony, M., Bieling, P., & Cox, B. (1998). Psychometric properties of the 42-item and 21-item versions of the Depression Anxiety Stress Scales in clinical groups and a community sample. *Psychological Assessment*, *10*(2), 176–181.

APA. (2013). *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5). Diagnostic and Statistical Manual of Mental Disorders 4th edition TR.* https://doi.org/10.1176/appi.books.9780890425596.744053

Billiard, M., Dolenc, L., Aldaz, C., Ondze, B., & Besset, A. (1994). Hypersomnia associated with mood disorders: A new perspective. *Journal of Psychosomatic Research*, *38*(1 SUPPL. 1), 41–47. https://doi.org/10.1016/0022-3999(94)90134-1

Breslau, N., Roth, T., Rosenthal, L., & Andreski, P. (1996). Sleep disturbance and psychiatric disorders: A longitudinal epidemiological study of young Adults. *Biological Psychiatry*, *39*(6), 411–418. https://doi.org/10.1016/0006-3223(95)00188-3

Cappuccio, F. P., D'Elia, L., Strazzullo, P., & Miller, M. a. (2010). Sleep duration and all-cause mortality: a systematic review and meta-analysis of prospective studies. *Sleep*, *33*(5), 585–592.

Carney, C. E., Buysse, D. J., Ancoli-Israel, S., Edinger, J. D., Krystal, A. D., Lichstein, K. L., & Morin, C. M. (2012). The Consensus Sleep Diary: Standardizing Prospective Sleep Self-Monitoring. *Sleep*. https://doi.org/10.5665/sleep.1642

Dauvilliers, Y., Lopez, R., Ohayon, M. M., & Bayard, S. (2013). Hypersomnia and depressive symptoms: methodological and clinical aspects. *BMC Medicine*, *11*, 78. https://doi.org/10.1186/1741-7015-11-78

Fang, F., Sun, H., Wang, Z., Ren, M., Calabrese, J. R., & Gao, K. (2016). Antipsychotic Drug-Induced Somnolence: Incidence, Mechanisms, and Management. *CNS Drugs*. https://doi.org/10.1007/s40263-016-0352-5

Faulkner, S., & Bee, P. (2017). Experiences, perspectives and priorities of people with schizophrenia spectrum disorders regarding sleep disturbance and its treatment: a qualitative study. *BMC Psychiatry*, *17*(1), 158. https://doi.org/10.1186/s12888-017-1329-8

Ford, D. E. (1989). Epidemiologic Study of Sleep Disturbances and Psychiatric Disorders. *JAMA*, *262*(11), 1479. https://doi.org/10.1001/jama.1989.03430110069030

Freeman, D. (2016). Persecutory delusions: a cognitive perspective on understanding and treatment. *The Lancet Psychiatry*, *3*(7), 685–692. https://doi.org/10.1016/S2215-0366(16)00066-3

Globus, G. (1969). A Syndrome Associated with Sleeping Late. *Psychosomatic Medicine*, *31*(6), 528–535. https://doi.org/10.1097/00006842-196911000-00006

Harvey, A. (2002). A cognitive model of insomnia. *Behaviour Research and Therapy*, *40*(8), 869–93.

Herdman, M., Gudex, C., Lloyd, A., Janssen, M., Kind, P., Parkin, D., … Badia, X. (2011). Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Quality of Life Research : An International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation*, *20*(10), 1727–36. https://doi.org/10.1007/s11136-011-9903-x

Hou, C.-L., Zang, Y., Ma, X.-R., Cai, M.-Y., Li, Y., Jia, F.-J., … Xiang, Y.-T. (2016). The Relationship Between Sleep Patterns, Quality of Life, and Social and Clinical Characteristics in Chinese Patients With Schizophrenia. *Perspectives in Psychiatric Care*, *0*, 1–8. https://doi.org/10.1111/ppc.12186

IBM Corp. (2015). IBM SPSS Statistics.

Johns, M. W. (1991). A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep*, *14*(6), 540–545. https://doi.org/10.1016/j.sleep.2007.08.004

Johns, M. W. (2017). About the ESS. Retrieved October 10, 2017, from http://epworthsleepinessscale.com/about-the-ess/

Kaplan, K. A., & Harvey, A. (2009). Hypersomnia across mood disorders: a review and synthesis. *Sleep Medicine Reviews*, *13*(4), 275–85. https://doi.org/10.1016/j.smrv.2008.09.001

Kaplan, K. A., McGlinchey, E. L., Soehner, A., Gershon, A., Talbot, L. S., Eidelman, P., … Harvey, A. (2015). Hypersomnia subtypes, sleep and relapse in bipolar disorder. *Psychological Medicine*, *45*(8), 1751–63. https://doi.org/10.1017/S0033291714002918

Kluge, M., Himmerich, H., Wehmeier, P. M., Rummel-Kluge, C., Dalal, M., Hinze-Selch, D., … Schuld, A. (2012). Sleep propensity at daytime as assessed by Multiple Sleep Latency Tests (MSLT) in patients with schizophrenia increases with clozapine and olanzapine. *Schizophrenia Research*, *135*(1–3), 123–127. https://doi.org/10.1016/j.schres.2011.12.017

Lovibond, S. H., & Lovibond, P. F. (1995). *Manual for the Depression Anxiety Stress Scales. Psychology Foundation of Australia* (Vol. 56). https://doi.org/DOI: 10.1016/0005-7967(94)00075-U

Martin, J., Jeste, D. V., Caliguiri, M. P., Patterson, T., Heaton, R., & Ancoli-Israel, S. (2001). Actigraphic estimates of circadian rhythms and sleep/wake in older schizophrenia patients. *Schizophrenia Research*, *47*(1), 77–86. https://doi.org/10.1016/S0920-9964(00)00029-3

Maslowsky, J., & Ozer, E. J. (2014). Developmental trends in sleep duration in adolescence and young adulthood: evidence from a national United States sample. *The Journal of Adolescent Health : Official Publication of the Society for Adolescent Medicine*, *54*(6), 691–7. https://doi.org/10.1016/j.jadohealth.2013.10.201

Matthews, C. E., Chen, K. Y., Freedson, P. S., Buchowski, M. S., Beech, B. M., Pate, R. R., & Troiano, R. P. (2008). Amount of time spent in sedentary behaviors in the United States, 2003-2004. *American Journal of Epidemiology*, *167*(7), 875–81. https://doi.org/10.1093/aje/kwm390

Merikangas, K. R., Zhang, J., Emsellem, H., Swanson, S. A., Vgontzas, A., Belouad, F., … Mignot, E. (2014). The structured diagnostic interview for sleep patterns and disorders: rationale and initial evaluation. *Sleep Medicine*, *15*(5), 530–5. https://doi.org/10.1016/j.sleep.2013.10.011

Morrison, P., Meehan, T., & Stomski, N. J. (2015). Living with antipsychotic medication side-effects: The experience of Australian mental health consumers. *International Journal of Mental Health Nursing*, *24*(3), 253–261. https://doi.org/10.1111/inm.12110

Nofzinger, E. A., Thase, M. E., Reynolds, C. F., Himmelhoch, J. M., Mallinger, A., Houck, P., & Kupfer, D. J. (1991). Hypersomnia in bipolar depression: a comparison with narcolepsy using the multiple sleep latency test. *American Journal of Psychiatry*, *148*(9), 1177–1181. https://doi.org/10.1176/ajp.148.9.1177

Perdigués, S. R., Quecuti, R. S., Mané, A., Mann, L., Mundell, C., & Fernandez-Egea, E. (2016). An observational study of clozapine induced sedation and its pharmacological management. *European Neuropsychopharmacology*, *26*(1), 156–161. https://doi.org/10.1016/j.euroneuro.2015.11.006

Poulin, J., Chouinard, S., Pampoulova, T., Lecomte, Y., Stip, E., & Godbout, R. (2010). Sleep habits in middle-aged, non-hospitalized men and women with schizophrenia: a comparison with healthy controls. *Psychiatry Research*, *179*(3), 274–8. https://doi.org/10.1016/j.psychres.2009.08.009

Rehman, A., Waite, F., Sheaves, B., Biello, S., Freeman, D., & Gumley, A. (2016). Clinician perceptions of sleep problems, and their treatment, in patients with non-affective psychosis. *Psychosis*, 1–11. https://doi.org/10.1080/17522439.2016.1206955

Ronald, A., Sieradzka, D., Cardno, A. G., Haworth, C. M. a, McGuire, P., & Freeman, D. (2014). Characterization of psychotic experiences in adolescence using the specific psychotic experiences questionnaire: Findings from a study of 5000 16-Year-Old Twins. *Schizophrenia Bulletin*, *40*(4), 868–877. https://doi.org/10.1093/schbul/sbt106

Sateia, M. J. (2014). International classification of sleep disorders-third edition highlights and modifications. *Chest*, *146*(5), 1387–1394. https://doi.org/10.1378/chest.14-0970

Sharma, P., Dikshit, R., Shah, N., Karia, S., & Sousa, A. De. (2016). Excessive Daytime Sleepiness in Schizophrenia : A Naturalistic Clinical Study, 10–12. https://doi.org/10.7860/JCDR/2016/21272.8627

Smets, E. M., Garssen, B., Bonke, B., & De Haes, J. C. (1995). The Multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. *Journal of Psychosomatic Research*, *39*(3), 315–325. https://doi.org/10.1016/0022-3999(94)00125-O

Soehner, A. M., Kaplan, K. A., & Harvey, A. (2014). Prevalence and clinical correlates of co-occurring insomnia and hypersomnia symptoms in depression. *Journal of Affective Disorders*, *167*, 93–7. https://doi.org/10.1016/j.jad.2014.05.060

Stein, K. D., Jacobsen, P. B., Blanchard, C. M., & Thors, C. (2004). Further validation of the multidimensional fatigue symptom inventory-short form. *Journal of Pain and Symptom Management*, *27*(1), 14–23. https://doi.org/10.1016/j.jpainsymman.2003.06.003

Stubbs, B., Williams, J., Gaughran, F., & Craig, T. (2016). How sedentary are people with psychosis? A systematic review and meta-analysis. *Schizophrenia Research*. https://doi.org/10.1016/j.schres.2016.01.034

Trotti, L. M. (2017, October 1). Waking up is the hardest thing I do all day: Sleep inertia and sleep drunkenness. *Sleep Medicine Reviews*. W.B. Saunders. https://doi.org/10.1016/j.smrv.2016.08.005

Vernet, C., & Arnulf, I. (2009). Idiopathic hypersomnia with and without long sleep time: a controlled series of 75 patients. *Sleep*, *32*(6), 753–9.

Vgontzas, A. N., Bixler, E. O., Kales, A., Criley, C., & Vela-Bueno, A. (2000). Differences in nocturnal and daytime sleep between primary and psychiatric hypersomnia: diagnostic and treatment implications. *Psychosomatic Medicine*, *62*(2), 220–226.

Vorontsova, N., Garety, P., & Freeman, D. (2013). Cognitive factors maintaining persecutory delusions in psychosis: the contribution of depression. *Journal of Abnormal Psychology*, *122*(4), 1121–31. https://doi.org/10.1037/a0034952

Wade, M., Tai, S., Awenat, Y., & Haddock, G. (2017). A systematic review of service-user reasons for adherence and nonadherence to neuroleptic medication in psychosis. *Clinical Psychology Review*, *51*, 75–95. https://doi.org/10.1016/j.cpr.2016.10.009

Waite, F., Evans, N., Myers, E., Startup, H., Lister, R., Harvey, A., & Freeman, D. (2016). The patient experience of sleep problems and their treatment in the context of current delusions and hallucinations. *Psychology and Psychotherapy: Theory, Research and Practice*, *89*(2), 181–193. https://doi.org/10.1111/papt.12073

## 8.7 Chapter 7 References

Aurora, R. N., Zak, R. S., Auerbach, S. H., Casey, K. R., Chowdhuri, S., Karippot, A., … Tracy, S. L. (2010, August 15). Best practice guide for the treatment of nightmare disorder in adults. *Journal of Clinical Sleep Medicine*. American Academy of Sleep Medicine.

Becker, P. M., & Novak, M. (2014). Diagnosis, comorbidities, and management of restless legs syndrome. *Current Medical Research and Opinion*, *30*(8), 1441–1460. https://doi.org/10.1185/03007995.2014.918029

Bradley, J., Freeman, D., Chadwick, E., Harvey, A. G., Mullins, B., Johns, L., … Waite, F. (2017). Treating Sleep Problems in Young People at Ultra-High Risk of Psychosis: A Feasibility Case Series. *Behavioural and Cognitive Psychotherapy*, 1–16. https://doi.org/10.1017/S1352465817000601

Christensen, H., Batterham, P. J., Gosling, J. A., Ritterband, L. M., Griffiths, K. M., Thorndike, F. P., … Mackinnon, A. J. (2016). Effectiveness of an online insomnia program (SHUTi) for prevention of depressive episodes (the GoodNight Study): a randomised controlled trial. *The Lancet Psychiatry*, *3*(4), 333–341. https://doi.org/10.1016/S2215-0366(15)00536-2

Espie, C. (1991). *The Psychological Treatment of Insomnia*. Chichester, UK: Wiley.

Espie, C., Kyle, S., Williams, C., Ong, J. C., Douglas, N. J., Hames, P., & Brown, J. S. L. (2012). A Randomized, Placebo-Controlled Trial of Online Cognitive Behavioral Therapy for Chronic Insomnia Disorder Delivered via an Automated Media-Rich Web Application. *Sleep*, *35*(6), 769–781. https://doi.org/10.5665/sleep.1872

Espie, C., Luik, A. I., Cape, J., Drake, C. L., Siriwardena, A. N., Ong, J. C., … Kyle, S. D. (2016). Digital Cognitive Behavioural Therapy for Insomnia versus sleep hygiene education: the impact of improved sleep on functional health, quality of life and psychological well-being. Study protocol for a randomised controlled trial. *Trials*, *17*(1), 257. https://doi.org/10.1186/s13063-016-1364-7

Espie, C., MacMahon, K. M. A., Kelly, H.-L., Broomfield, N. M., Douglas, N. J., Engleman, H. M., … Wilson, P. (2007). Randomized clinical effectiveness trial of nurse-administered small-group cognitive behavior therapy for persistent insomnia in general practice. *Sleep*, *30*(5), 574–84.

Faulkner, S., & Bee, P. (2016). Perspectives on sleep, sleep problems, and their treatment, in people with serious Mental Illnesses: A systematic review. *PLoS ONE*, *11*(9), e0163486. https://doi.org/10.1371/journal.pone.0163486

Faulkner, S., & Bee, P. (2017). Experiences, perspectives and priorities of people with schizophrenia spectrum disorders regarding sleep disturbance and its treatment: a qualitative study. *BMC Psychiatry*, *17*(1), 158. https://doi.org/10.1186/s12888-017-1329-8

Freeman, D. (2016). Persecutory delusions: a cognitive perspective on understanding and treatment. *The Lancet Psychiatry*, *3*(7), 685–692. https://doi.org/10.1016/S2215-0366(16)00066-3

Freeman, D., Sheaves, B., Goodwin, G. M., Yu, L.-M., Nickless, A., Harrison, P. J., … Espie, C. (2017). The effects of improving sleep on mental health (OASIS): a randomised controlled trial with mediation analysis. *The Lancet Psychiatry*, *4*(10), 749–758. https://doi.org/10.1016/S2215-0366(17)30328-0

Freeman, D., Stahl, D., McManus, S., Meltzer, H., Brugha, T., Wiles, N., & Bebbington, P. (2012). Insomnia, worry, anxiety and depression as predictors of the occurrence and persistence of paranoid thinking. Social Psychiatry and Psychiatric Epidemiology, 47(8), 1195–203. https://doi.org/10.1007/s00127-011-0433-1

Freeman, D., Thompson, C., Vorontsova, N., Dunn, G., Carter, L.-A., Garety, P., … Ehlers, A. (2013). Paranoia and post-traumatic stress disorder in the months after a physical assault: a longitudinal study examining shared and differential predictors. *Psychological Medicine*, *43*(12), 2673–84. https://doi.org/10.1017/S003329171300038X

Freeman, D., Waite, F., Startup, H., Myers, E., Lister, R., McInerney, J., … Yu, L.-M. M. (2015). Efficacy of cognitive behavioural therapy for sleep improvement in patients with persistent delusions and hallucinations (BEST): A prospective, assessor-blind, randomised controlled pilot trial. *The Lancet Psychiatry*, *2*(11), 975–983. https://doi.org/10.1016/S2215-0366(15)00314-4

Garety, P., Kuipers, E., Fowler, D., Freeman, D., & Bebbington, P. (2001). A cognitive model of the positive symptoms of psychosis. *Psychological Medicine*, *31*(2), 189–95.

Geddes, G., Ehlers, A., & Freeman, D. (2016). Hallucinations in the months after a trauma: An investigation of the role of cognitive processing of a physical assault in the occurrence of hallucinatory experiences. *Psychiatry Research*. https://doi.org/10.1016/j.psychres.2016.10.081

Grezellschak, S., Jansen, A., & Westermann, S. (2016). Emotion regulation in patients with psychosis: A link between insomnia and paranoid ideation? *Journal of Behavior Therapy and Experimental Psychiatry*. https://doi.org/10.1016/j.jbtep.2016.08.001

Harvey, A. (2002). A cognitive model of insomnia. *Behaviour Research and Therapy*, *40*(8), 869–93.

Hennig, T., & Lincoln, T. M. (2017). Sleeping Paranoia Away? An Actigraphy and Experience-Sampling Study with Adolescents. *Child Psychiatry & Human Development*, 1–10. https://doi.org/10.1007/s10578-017-0729-9

Humpston, C. S., Walsh, E., Oakley, D. A., Mehta, M. A., Bell, V., & Deeley, Q. (2016). The relationship between different types of dissociation and psychosis-like experiences in a non-clinical sample. Consciousness and Cognition, 41, 83–92. https://doi.org/10.1016/j.concog.2016.02.009

Kilicaslan, E. E., Esen, A. T., Kasal, M. I., Ozelci, E., Boysan, M., & Gulec, M. (2017). Childhood trauma, depression, and sleep quality and their association with psychotic symptoms and suicidality in schizophrenia. *Psychiatry Research*. https://doi.org/10.1016/j.psychres.2017.08.081

Knowles, R., McCarthy-Jones, S., & Rowse, G. (2011). Grandiose delusions: a review and theoretical integration of cognitive and affective perspectives. *Clinical Psychology Review*, *31*(4), 684–96. https://doi.org/10.1016/j.cpr.2011.02.009

Koffel, E., & Watson, D. (2009). Unusual sleep experiences, dissociation, and schizotypy: Evidence for a common domain. *Clinical Psychology Review*, *29*(6), 548–59. https://doi.org/10.1016/j.cpr.2009.06.004

McCrae, C. S., Bramoweth, A. D., Williams, J., Roth, A., & Mosti, C. (2014). Impact of brief cognitive behavioral treatment for insomnia on health care utilization and costs. *Journal of Clinical Sleep Medicine : JCSM : Official Publication of the American Academy of Sleep Medicine*, *10*(2), 127–35. https://doi.org/10.5664/jcsm.3436

Meltzer, L. J., Phillips, C., & Mindell, J. A. (2009). Clinical psychology training in sleep and sleep disorders. *Journal of Clinical Psychology*, *65*(3), 305–18. https://doi.org/10.1002/jclp.20545

Monti, J. M., Torterolo, P., & Pandi Perumal, S. R. (2017). The effects of second generation antipsychotic drugs on sleep variables in healthy subjects and patients with schizophrenia. *Sleep Medicine Reviews*, *33*, 51–57. https://doi.org/10.1016/j.smrv.2016.05.002

Morrison, A. P., French, P., Stewart, S. L. K., Birchwood, M., Fowler, D., Gumley, A. I., … Dunn, G. (2012). Early detection and intervention evaluation for people at risk of psychosis: multisite randomised controlled trial. *BMJ*, *344*(apr05 1), e2233–e2233. https://doi.org/10.1136/bmj.e2233

National Institute for Health and Clinical Excellence (NICE). (2015). Managing long-term insomnia (>4 weeks).

Preacher, K. J. (2014). Advances in Mediation Analysis: A Survey and Synthesis of New Developments. *Annual Review of Psychology*, (August), 1–28. https://doi.org/10.1146/annurev-psych-010814-015258

Qaseem, A., Kansagara, D., Forciea, M. A., Cooke, M., Denberg, T. D., CH, K., & J, L. (2016). Management of Chronic Insomnia Disorder in Adults: A Clinical Practice Guideline From the American College of Physicians. *Annals of Internal Medicine*, *165*(2), 125. https://doi.org/10.7326/M15-2175

Rehman, A., Gumley, A., & Biello, S. (2017). Sleep Quality and Paranoia: The role of alexithymia, negative emotions and perceptual anomalies. *Psychiatry Research*. https://doi.org/10.1016/J.PSYCHRES.2017.09.066

Rehman, A., Waite, F., Sheaves, B., Biello, S., Freeman, D., & Gumley, A. (2016). Clinician perceptions of sleep problems, and their treatment, in patients with non-affective psychosis. *Psychosis*, 1–11. https://doi.org/10.1080/17522439.2016.1206955

Rek, S., Sheaves, B., & Freeman, D. (2017). Nightmares in the general population: identifying potential causal factors. *Social Psychiatry and Psychiatric Epidemiology*. https://doi.org/10.1007/s00127-017-1408-7

Sheaves, B. (2015). The nightmare intervention study (trial protocol). *International Standard Randomised Controlled Trial Number Registry*, (ISRCTN12668007). https://doi.org/DOI 10.1186/ISRCTN12668007

Sheaves, B., Freeman, D., Isham, L., Mcinerney, J., Nickless, A., Yu, L., … Barrera, A. (2017). Stabilising sleep for patients admitted at acute crisis to a psychiatric hospital (OWLS): an assessor-blind, pilot randomised controlled trial. *Psychological Medicine*

Sheaves, B., Porcheret, K., Tsanas, A., Espie, C., Foster, R., Freeman, D., … Goodwin, G. (2016). Insomnia, Nightmares, and Chronotype as Markers of Risk for Severe Mental Illness: Results from a Student Population. *Sleep*, *39*(1), 173–81. https://doi.org/10.5665/sleep.5342

Taylor, D. J., Mallory, L. J., Lichstein, K. L., Durrence, H. H., Riedel, B. W., & Bush, A. J. (2007). Comorbidity of Chronic Insomnia With Medical Problems. *Sleep*, *30*(2), 213–218. https://doi.org/10.1093/sleep/30.2.213

Urquhart, D. S., Orme, J. a, & Suresh, S. (2012). Survey of undergraduate sleep medicine teaching in UK medical schools. *Archives of Disease in Childhood*, *97*(1), 90–1.

https://doi.org/10.1136/archdischild-2011-301073

Van Der Kloet, D., Giesbrecht, T., Franck, E., Van Gastel, A., De Volder, I., Van Den Eede, F., … Merckelbach, H. (2013). Dissociative symptoms and sleep parameters - An all-night polysomnography study in patients with insomnia. *Comprehensive Psychiatry*, *54*(6), 658–664. https://doi.org/10.1016/j.comppsych.2012.12.025

Vitiello, M. V., McCurry, S. M., Shortreed, S. M., Balderson, B. H., Baker, L. D., Keefe, F. J., … Von Korff, M. (2013). Cognitive-Behavioral Treatment for Comorbid Insomnia and Osteoarthritis Pain in Primary Care: The Lifestyles Randomized Controlled Trial. *Journal of the American Geriatrics Society*, *61*(6), 947–956. https://doi.org/10.1111/jgs.12275

Waite, F., Evans, N., Myers, E., Startup, H., Lister, R., Harvey, A., & Freeman, D. (2016). The patient experience of sleep problems and their treatment in the context of current delusions and hallucinations. *Psychology and Psychotherapy: Theory, Research and Practice*, *89*(2), 181–193. https://doi.org/10.1111/papt.12073

Waite, F., Myers, E., Harvey, A., Espie, C., Startup, H., Sheaves, B., & Freeman, D. (2016). Treating Sleep Problems in Patients with Schizophrenia. *Behavioural and Cognitive Psychotherapy*, *44*(3), 273–87. https://doi.org/10.1017/S1352465815000430

Waters, F., Chiu, V. W., Janca, A., Atkinson, A., & Ree, M. (2015). Preferences for different insomnia treatment options in people with schizophrenia and related psychoses: a qualitative study. *Frontiers in Psychology*, *6*, 990. https://doi.org/10.3389/fpsyg.2015.00990

Waters, F., Faulkner, D., Naik, N., & Rock, D. (2012). Effects of polypharmacy on sleep in psychiatric inpatients. *Schizophrenia Research*, *139*(1–3), 225–8. https://doi.org/10.1016/j.schres.2012.05.013

# Appendices

# List of Appendices

1.1 Publication 1: The role of sleep dysfunction in the occurrence of delusions and hallucinations: A systematic review 1
2.1 Publication 2: Disrupting sleep the effects of sleep loss on psychotic experiences tested in an experimental study with mediation analysis 21
2.2 Recruitment 31
2.3 Study process 33
2.4 Adherence to sleep conditions 34
2.5 Experimental Task Administration (Inquisit) 36
2.6 Specific Psychotic Experience Questionnaire 37
2.7 Depression Anxiety Stress Scale (DASS) 43
2.8 Worry scale 46
2.9 Brief Core Schema Scale (BCSS) 47
2.10 Ebbinghaus visual illusion task 49
2.11 Perceptual Vigilance Task 52
2.12 Beads task (Jumping to Conclusions) 54
2.13 N-back task 56
2.14 Expanded table of means 60
2.15 Interaction analyses 63
3.1 SPSS example syntax 67
4.1 Diagnostic Interview for Sleep Patterns and Disorders (DISP) 68
4.2 Scoring guidelines (DISP) 90
4.3 Diagnostic and severity scoring guidelines by disorder for DISP 91
4.4 Sleep-50 agreement with diagnostic interview 98
4.5 European 5-dimension 5-level health related quality of life questionnaire (EQ5D5L) 99
4.6 Multi-dimensional Fatigue Symptom Inventory (MFSI) 102
5.1 Sleep-50 Questionnaire 104
5.2 Original objectives and analysis plan for clinical longitudinal study 108
6.1 Epworth Sleepiness Scale (ESS) 112

## 1.1 Publication 1: The role of sleep dysfunction in the occurrence of delusions and hallucinations: A systematic review

The appendix originally presented here cannot be made freely available via ORA because of copyright.

Please see https://doi.org/10.1016/j.cpr.2015.09.001 for the open access paper.

Publication 1: The role of sleep dysfunction in the occurrence of delusions and hallucinations: A systematic review

Publication 1: The role of sleep dysfunction in the occurrence of delusions and hallucinations: A systematic review

Publication 1: The role of sleep dysfunction in the occurrence of delusions and hallucinations: A systematic review

Publication 1: The role of sleep dysfunction in the occurrence of delusions and hallucinations: A systematic review

Publication 1: The role of sleep dysfunction in the occurrence of delusions and hallucinations: A systematic review

Publication 1: The role of sleep dysfunction in the occurrence of delusions and hallucinations: A systematic review

Publication 1: The role of sleep dysfunction in the occurrence of delusions and hallucinations: A systematic review

Publication 1: The role of sleep dysfunction in the occurrence of delusions and hallucinations: A systematic review

Publication 1: The role of sleep dysfunction in the occurrence of delusions and hallucinations: A systematic review

Publication 1: The role of sleep dysfunction in the occurrence of delusions and hallucinations: A systematic review

## 2.1 Publication: Disrupting sleep the effects of sleep loss on psychotic experiences tested in an experimental study with mediation analysis

The appendix originally presented here cannot be made freely available via ORA because of copyright.

Please see https://doi.org/10.1093/schbul/sbx103 for the open access paper.

Publication: Disrupting sleep the effects of sleep loss on psychotic experiences tested in an experimental study with mediation analysis

Publication: Disrupting sleep the effects of sleep loss on psychotic experiences tested in an experimental study with mediation analysis

Publication: Disrupting sleep the effects of sleep loss on psychotic experiences tested in an experimental study with mediation analysis

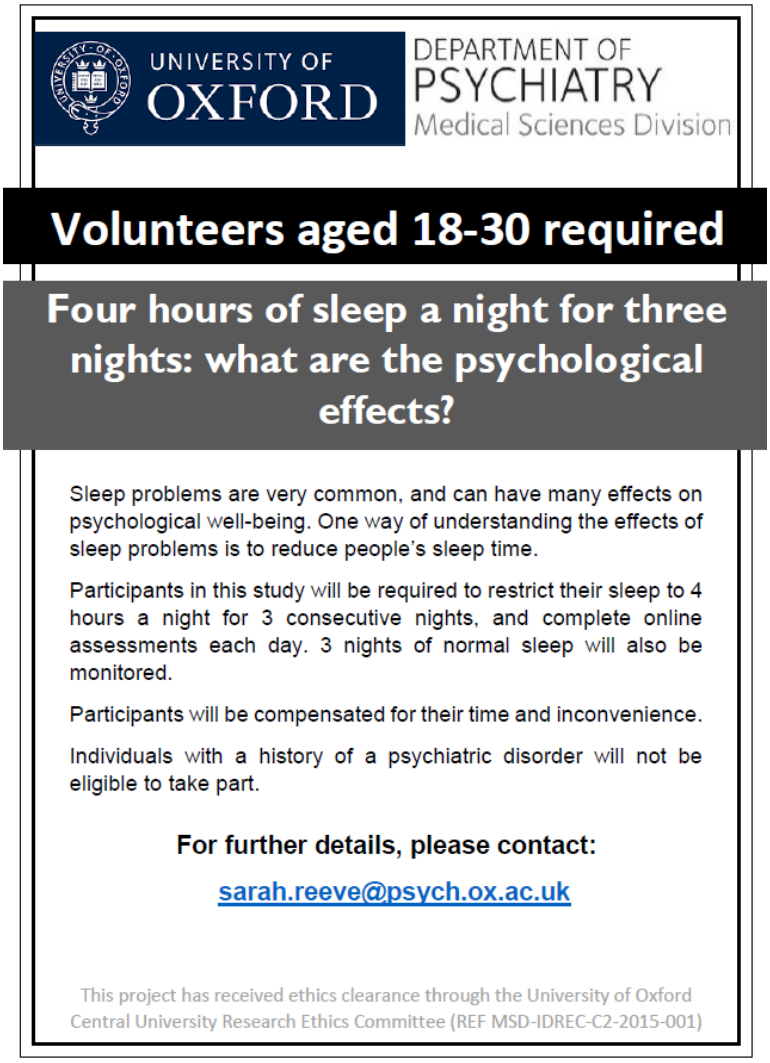
Publication: Disrupting sleep the effects of sleep loss on psychotic experiences tested in an experimental study with mediation analysis

Publication: Disrupting sleep the effects of sleep loss on psychotic experiences tested in an experimental study with mediation analysis

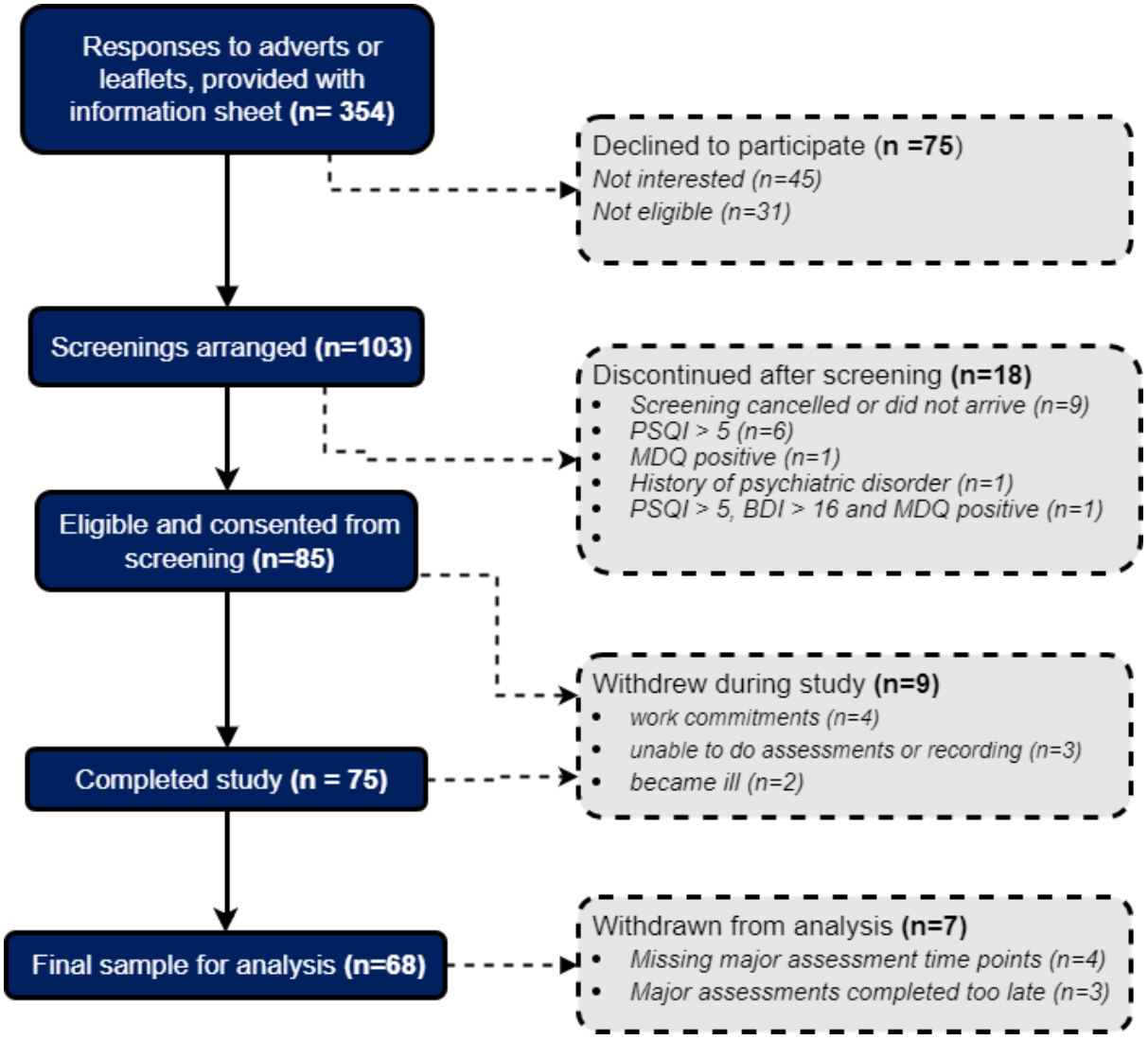
## 2.2 Recruitment

Participants were recruited from the student and wider population of Oxford. Adverts were emailed out on University of Oxford and Oxford Brookes mailing lists, poster adverts were posted in various university buildings, and online advertisements were placed on the Daily Info website (a local Oxford newspaper). Leaflets were posted to 20,000 domestic addresses in the immediate area (OX1, OX3, OX4) in order to boost recruitment near the end of the study. A sample advert and consort diagram for recruitment can be found below. Recruitment was carried out from February to October 2016.

### 2.2.1 Sample recruitment flyer

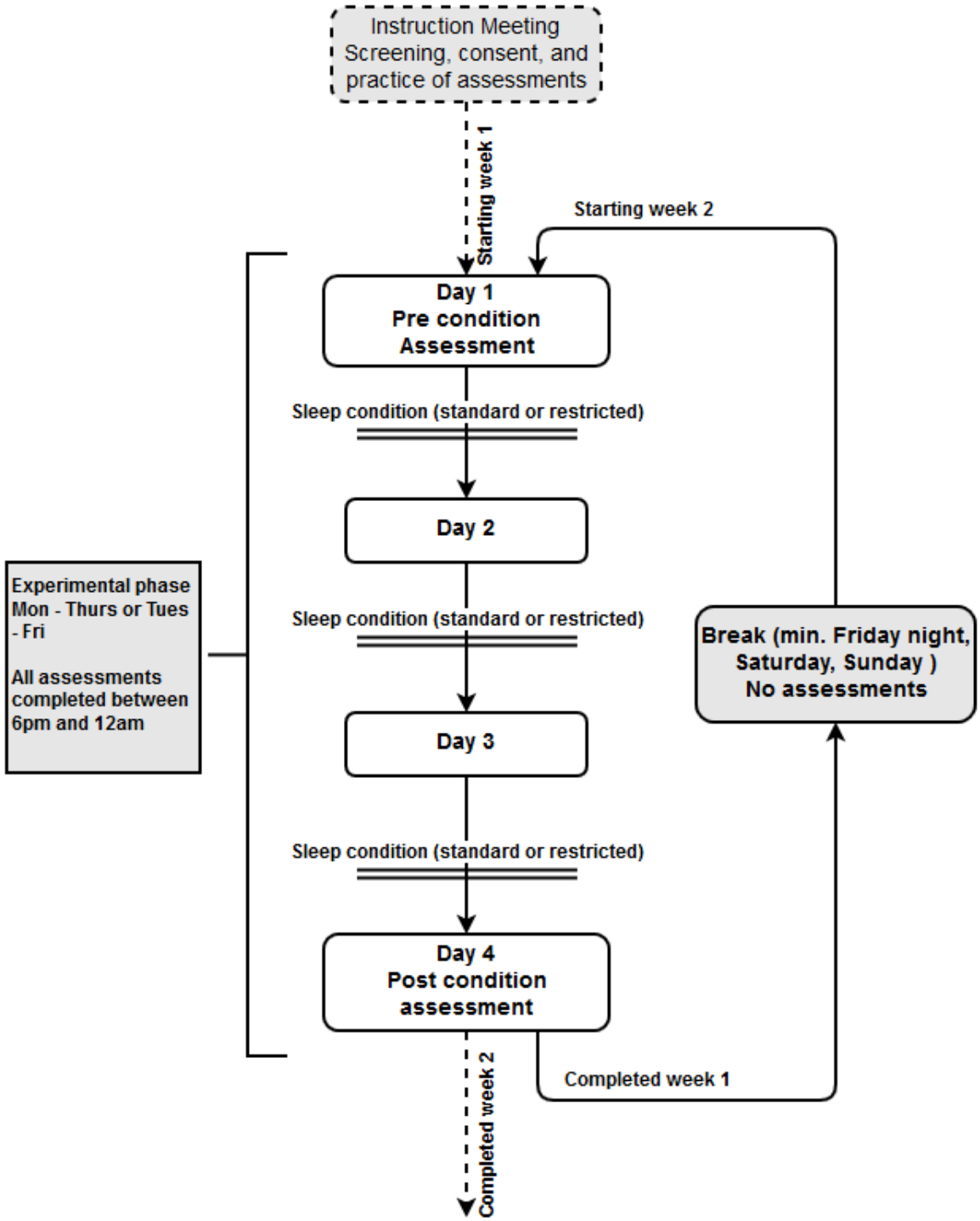


### 2.2.2 Consort diagram for recruitment




*NB "ill" here refers to colds or flu, not to mental health issues.

## 2.3 Study process

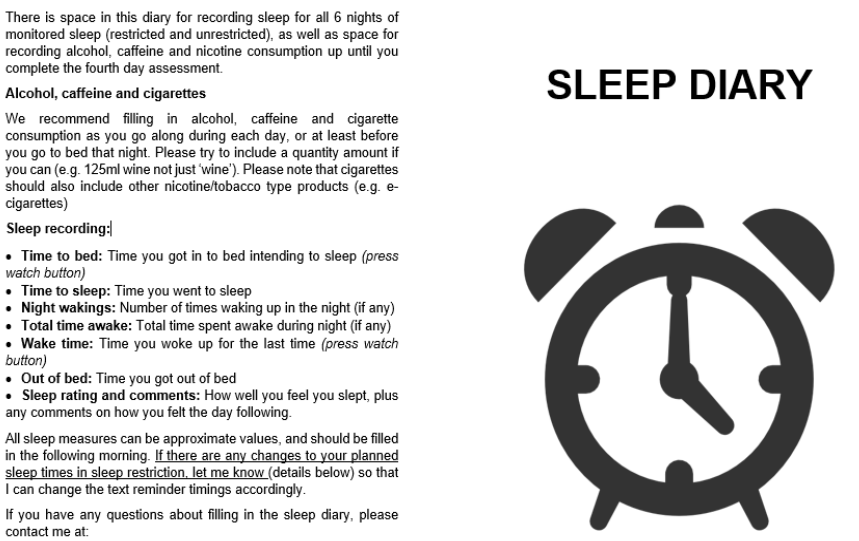


## 2.4 Adherence to sleep conditions

In the sleep restriction study several measures were sued to ensure that participants adhered to the self-enforced sleep condition as instructed. Further details on each measure are provided below

### 2.4.1 Sleep diary

Participants completed a sleep diary (see examples below ) for the normal sleep and restricted sleep condition. This diary was based on the Carney consensus sleep diary (2012), with the addition of a qualitative "Overall feedback" section for both weeks. The sleep diary was used as one adherence validation measure, however clearly as it is self-report it was not itself sufficient.



There is space in this diary for recording sleep for all 6 nights of monitored sleep (restricted and unrestricted), as well as space for recording alcohol, caffeine and nicotine consumption up until you complete the fourth day assessment.

**Alcohol, caffeine and cigarettes**

We recommend filling in alcohol, caffeine and cigarette consumption as you go along during each day, or at least before you go to bed that night. Please try to include a quantity amount if you can (e.g. 125ml wine not just 'wine'). Please note that cigarettes should also include other nicotine/tobacco type products (e.g. e-cigarettes)

**Sleep recording:**

- **Time to bed:** Time you got in to bed intending to sleep *(press watch button)*
- **Time to sleep:** Time you went to sleep
- **Night wakings:** Number of times waking up in the night (if any)
- **Total time awake:** Total time spent awake during night (if any)
- **Wake time:** Time you woke up for the last time *(press watch button)*
- **Out of bed:** Time you got out of bed
- **Sleep rating and comments:** How well you feel you slept, plus any comments on how you felt the day following.

All sleep measures can be approximate values, and should be filled in the following morning. If there are any changes to your planned sleep times in sleep restriction, let me know (details below) so that I can change the text reminder timings accordingly.

If you have any questions about filling in the sleep diary, please contact me at:

**Email**: sarah.reeve@psych.ox.ac.uk
**Mobile**: 07528 513283

**SLEEP DIARY**



Fig 1: front and reverse of sleep diary booklet. Reverse contains instructions on use, and contact details.

| Date | Caffeine? | Alcohol? | Cigarettes? | Time to bed BUTTON | Time to sleep | Night wakings | Total time awake | Wake time BUTTON | Out of bed | Sleep quality rating and comments |
|---|---|---|---|---|---|---|---|---|---|---|
| *12th Jan* | *2 instant coffees* | *1 glass of wine - 125ml* | */* | *2am* | *2.05am* | *1* | *10 minutes* | *6am* | *6.05am* | *Sleep rating: 4/5 Have a headache this morning (13th)* |
| | | | | | | | | | | Sleep rating: /5 |
| | | | | | | | | | | Sleep rating: /5 |
| | | | | | | | | | | Sleep rating: /5 |
| | | | | Overall feedback: | | | | | | |
| | | | | | | | | | | Sleep rating: /5 |
| | | | | | | | | | | Sleep rating: /5 |
| | | | | | | | | | | Sleep rating: /5 |
| | | | | Overall feedback: | | | | | | |

Fig 2: Sleep diary. Participants were instructed in use in initial session in instruction meeting with researcher. Recording was carried out for three days and nights and the 4th day of each condition, up until post- assessment for condition was completed.

### 2.4.2 Actigraphic recording

In the current study the Motionware algorithm was applied across the 24-hour period to find the longest period of inactivity, and assess the proportion of time spent asleep within it. It was not possible to use the sleep diary 'Time to bed' and 'Time out of bed' measures as anchors (as would be used in the standard method) as if participants were under-reporting their sleep these would not have been effective.

### 2.4.3 Text message (SMS) prompts

Participants were required to respond to text messages every hour from 10pm until their chosen sleep time in order to demonstrate they were awake. Text messages had to be responded to within 15 minutes - study compensation was reduced by £5 for each text not responded to within this window.

These text messages were sent from an automated service (www.textanywhere.com) which allows scheduled texts to be sent. One limitation of the programme is that the texts had to be sent at the same minutes past the hour for each prompt in an evening (e.g. at 22:17, 23:17, 00:17 etc.). All prompts were therefore set up to be sent within the first 20 minutes of the hour, and were varied across nights for each participant. Very few participants The message read as follows: "Please confirm that you are still awake by replying to this text.". Text responses were received in the textanywhere online inbox, and were checked for adherence prior to compensation being sent.

### 2.4.4 Caffeine, alcohol and nicotine recording

Participants were asked to record their caffeine, alcohol and nicotine (cigarette , vape, or other nicotine source) intake in their sleep diaries. Caffeine (mg) intake was then estimated using the Mayo Clinics reference tool (https://www.mayoclinic.org/healthy-lifestyle/nutrition-and-healthy-eating/in-depth/caffeine/art-20049372). Alcohol unit intake was estimated using the NHS online unit tool: https://www.nhs.uk/Livewell/alcohol/Pages/alcohol-units.aspx. Nicotine intake was estimated at 2mg per cigarette smoked. No participants used vapes or any other nicotine source.

## 2.5 Experimental Task Administration (Inquisit)

### 2.5.1 Assessments online

The Inquisit 4 software package allows reliable administration of questionnaires and psychometric tasks over the internet. Presentation of stimuli (e.g. resolution, timing) are standardised across different media (e.g. laptop, monitor, tablet) and systems (e.g. Mac OSX, Windows). The software prevents other tasks being undertaken during the experimental window, preventing distraction.

Participants were sent a link via email at 1800h on each day an assessment was due – this was managed via the MailChimp (www.mailchimp.com) email distribution service. Participants were instructed to start the assessment before midnight (0000h) – the timestamps of all assessments were checked to ensure they were completed within this window.

Once the assessment is complete the data are securely uploaded to the millisecond website, from where they can be downloaded in .sav (SPSS) format.

### 2.5.2 Programming of experimental tasks

The N-back task (working memory), Ebbinghaus task (illusion response), Beads task (Jumping to Conclusions; JTC), and Perceptual Vigilance Task (PVT; reaction time) were all programmed by myself in the Inquisit code language, in some cases based on existing task code in the Millisecond Test Library (http://www.millisecond.com/download/library/) – for details see the relevant appendices below

## 2.6 Specific Psychotic Experience Questionnaire

The SPEQ is a self-report measure for psychotic experiences developed for use with adolescents and younger adult samples. It is comprised of several subscales which are adapted from previously existing measures for individual psychotic experiences, in order to provide a multidimensional psychotic experience scale. The paranoia subscale is based on the Paranoia Checklist (Freeman et al., 2005), the hallucinations subscale is based on the Cardiff Anomalous Perceptions Scale (Bell et al., 2006), the cognitive disorganisation subscale is based on the Oxford-Liverpool Inventory of Feelings and Experiences (Mason & Claridge, 2006), and the grandiosity subscale is based on the 'myself' subscale of from the cognition checklist for mania revised (Beck et al., 2006). Each of these original questionnaires have been widely used in clinical and non-clinical populations.

The SPEQ subscales all have high internal consistency (Cronbach's alphas between 0.77–0.90). The SPEQ has been used in clinical and non-clinical groups (Ronald et al., 2014, Zavos et al., 2014). The applicability to a range of populations is a strength of the SPEQ for this thesis, as it allowed the same psychotic experience measure to be used in each chapter of the thesis.

## Paranoia subscale

| **Please read each statement and select the number that best indicates how often you have had each thought or feeling. There are no right or wrong answers. Try not to spend too much time on any statement.** | | | | | |
|---|---|---|---|---|---|
| ***(not at all)*** | ***(rarely)*** | ***(sometimes)*** | ***(often)*** | ***(frequently)*** | ***(nearly all the time)*** |
| *0* | *1* | *2* | *3* | *4* | *5* |
| 1. Someone has bad intentions towards me | | | | | |
| *0* | *1* | *2* | *3* | *4* | *5* |
| 2. Bad things are being said behind my back | | | | | |
| *0* | *1* | *2* | *3* | *4* | *5* |
| 3. People are being hostile towards me | | | | | |
| *0* | *1* | *2* | *3* | *4* | *5* |
| 4. People are trying to upset me | | | | | |
| *0* | *1* | *2* | *3* | *4* | *5* |
| 5. Someone has it in for me | | | | | |
| *0* | *1* | *2* | *3* | *4* | *5* |
| 6. People are looking at me in an unfriendly way | | | | | |
| *0* | *1* | *2* | *3* | *4* | *5* |
| 7. There might be negative comments being spread about me | | | | | |
| *0* | *1* | *2* | *3* | *4* | *5* |
| 8. People might be conspiring against me | | | | | |
| *0* | *1* | *2* | *3* | *4* | *5* |
| 9. I am under threat from others | | | | | |
| *0* | *1* | *2* | *3* | *4* | *5* |
| 10. People are laughing at me | | | | | |
| *0* | *1* | *2* | *3* | *4* | *5* |
| 11. People would harm me if given an opportunity | | | | | |
| *0* | *1* | *2* | *3* | *4* | *5* |
| 12. People are deliberately trying to irritate me | | | | | |
| *0* | *1* | *2* | *3* | *4* | *5* |
| 13. I need to be on my guard against others | | | | | |
| *0* | *1* | *2* | *3* | *4* | *5* |
| 14. I might be being observed or followed | | | | | |
| *0* | *1* | *2* | *3* | *4* | *5* |
| 15. I can detect coded messages about me in the press/TV/internet | | | | | |
| *0* | *1* | *2* | *3* | *4* | *5* |
| ***Overall, how distressed are you by these experiences?*** | | | | | |

| | | | |
|---|---|---|---|
| ***0 (not distressed)*** | ***1 (a bit distressed)*** | ***2 (quite distressed)*** | ***3 (very distressed)*** |

## Hallucinations subscale

| **Please read each statement and select the number that best indicates how frequently you have each of these experiences. There are no right or wrong answers. Try not to spend too much time on any statement.** | | | | | |
|---|---|---|---|---|---|
| ***Not at all*** | ***Rarely*** | ***Once a month*** | ***Once a week*** | ***Several times a week*** | ***Daily*** |
| *0* | *1* | *2* | *3* | *4* | *5* |
| 1. Hear sounds or music that people near you don't hear? | | | | | |
| *0* | *1* | *2* | *3* | *4* | *5* |
| 2. See things that other people cannot? | | | | | |
| *0* | *1* | *2* | *3* | *4* | *5* |
| 3. Feel that someone is touching you, but when you look nobody is there? | | | | | |
| *0* | *1* | *2* | *3* | *4* | *5* |
| 4. Hear noises or sounds when there is nothing around to explain them? | | | | | |
| *0* | *1* | *2* | *3* | *4* | *5* |
| 5. Detect smells which don't seem to come from your surroundings? | | | | | |
| *0* | *1* | *2* | *3* | *4* | *5* |
| 6. See shapes, lights, or colours even though there is nothing really there? | | | | | |
| *0* | *1* | *2* | *3* | *4* | *5* |
| 7. Notice smells or odours that people next to you seem unaware of? | | | | | |
| *0* | *1* | *2* | *3* | *4* | *5* |
| 8. Experience unusual burning sensations or other strange feelings in or on your body that can't be explained? | | | | | |
| *0* | *1* | *2* | *3* | *4* | *5* |
| 9. Hear voices commenting on what you're thinking or doing? | | | | | |
| *0* | *1* | *2* | *3* | *4* | *5* |
| ***Overall, how distressed are you by these experiences?*** | | | | | |
| ***0 (not distressed)*** | ***1 (a bit distressed)*** | ***2 (quite distressed)*** | ***3 (very distressed)*** | | |

## Cognitive Disorganisation subscale

| **Please read each statement and select the number that best matches your feelings over the last month.** |
|---|
| 1. Are you easily confused if too much happens at the same time?<br>*Yes* *No* |
| 2. Are you easily distracted when you read or talk to someone?<br>*Yes* *No* |
| 3. Do you currently have difficulty in starting to do things?<br>*Yes* *No* |
| 4. Are you finding it difficult to keep interested in the same thing for a long time?<br>*Yes* *No* |
| 5. Are you easily distracted from work by daydreams?<br>*Yes* *No* |
| 6. When in a crowded room, do you currently have difficulty in following a conversation?<br>*Yes* *No* |
| 7. Is it hard for you to make decisions?<br>*Yes* *No* |
| 8. Do you currently have difficulties in controlling your thoughts?<br>*Yes* *No* |
| 9. Do you feel that your speech is currently difficult to understand because the words are all mixed up and don't make sense?<br>*Yes* *No* |
| 10. Are you a person whose mood goes up and down easily?<br>*Yes* *No* |
| 11. Do you dread going into a room by yourself where other people have already gathered and are talking?<br>*Yes* *No* |
| ***Overall, how distressed are you by these experiences?*** |
| ***0 (not distressed)*** ***1 (a bit distressed)*** ***2 (quite distressed)*** ***3 (very distressed)*** |

## Grandiosity subscale

| **Please read each statement and select the number that best how much you agree with each statement, based on your thoughts and feelings over the last month.** | | | |
|---|---|---|---|
| ***Not at all*** | ***Somewhat*** | ***A great deal*** | ***Completely*** |
| *0* | *1* | *2* | *3* |
| 1. I am, or am destined to be, someone very important | | | |
| *0* | *1* | *2* | *3* |
| 2. Everyone is going to know about me because of my greatness | | | |
| *0* | *1* | *2* | *3* |
| 3. I am a very special or unusual person | | | |
| *0* | *1* | *2* | *3* |
| 4. I am much more unique than anyone else | | | |
| *0* | *1* | *2* | *3* |
| 5. I have special abilities that others do not | | | |
| *0* | *1* | *2* | *3* |
| 6. Everything I do is great | | | |
| *0* | *1* | *2* | *3* |
| 7. I have many great ideas | | | |
| *0* | *1* | *2* | *3* |
| 8. I have a special mission | | | |
| *0* | *1* | *2* | *3* |
| ***Overall, how distressed are you by these experiences?*** | | | |
| ***0 (not distressed)*** | ***1 (a bit distressed)*** | ***2 (quite distressed)*** | ***3 (very distressed)*** |

## 2.7 Depression Anxiety Stress Scale (DASS)

The appendix originally presented here cannot be made freely available via ORA because of copyright.

## 2.8 Worry scale

The appendix originally presented here cannot be made freely available via ORA because of copyright.

## 2.9 Brief Core Schema Scale (BCSS)

The BCSS is a self-report measure for core beliefs about self (positive and negative) and others (positive and negative). The scale was developed and validated in non-clinical and clinical groups, The Cronbach's alphas for positive and negative self-schema scales for non-clinical (and clinical) participants were 0.78 (0.79) and 0.86 (0.84), and, for the positive and negative-other schema scales: 0.88 (0.84) and 0.88 (0.87) respectively (Fowler et al., 2006).

Items 1-6 are negative self, 7-12 positive self, 13-18 negative other, 19-24 positive other.

| **Please indicate whether you currently hold each belief, and if you do, how strongly you hold the belief.** | | | | |
|---|---|---|---|---|
| ***Do not have this belief*** | | ***Believe it moderately*** | ***Believe it very much*** | |
| ***0*** | ***Believe it slightly 1*** | ***2*** | ***3*** | ***Believe it totally 4*** |
| 1. I am unloved | | | | |
| *0* | *1* | *2* | *3* | *4* |
| 2. I am worthless | | | | |
| *0* | *1* | *2* | *3* | *4* |
| 3. I am weak | | | | |
| *0* | *1* | *2* | *3* | *4* |
| 4. I am vulnerable | | | | |
| *0* | *1* | *2* | *3* | *4* |
| 5. I am bad | | | | |
| *0* | *1* | *2* | *3* | *4* |
| 6. I am a failure | | | | |
| *0* | *1* | *2* | *3* | *4* |
| 7. I am respected | | | | |
| *0* | *1* | *2* | *3* | *4* |
| 8. I am valuable | | | | |
| *0* | *1* | *2* | *3* | *4* |
| 9. I am talented | | | | |
| *0* | *1* | *2* | *3* | *4* |
| 10. I am successful | | | | |
| *0* | *1* | *2* | *3* | *4* |
| 11. I am good | | | | |
| *0* | *1* | *2* | *3* | *4* |
| 12. I am interesting | | | | |
| *0* | *1* | *2* | *3* | *4* |
| 13. Others are hostile | | | | |
| *0* | *1* | *2* | *3* | *4* |
| 14. Others are harsh | | | | |
| *0* | *1* | *2* | *3* | *4* |

| **Please indicate whether you currently hold each belief, and if you do, how strongly you hold the belief.** | | | | |
|---|---|---|---|---|
| ***Do not have this belief*** | | ***Believe it moderately*** | ***Believe it very much*** | |
| ***0*** | ***Believe it slightly 1*** | ***2*** | ***3*** | ***Believe it totally 4*** |
| 15. Others are unforgiving | | | | |
| *0* | *1* | *2* | *3* | *4* |
| 16. Others are bad | | | | |
| *0* | *1* | *2* | *3* | *4* |
| 17. Others are devious | | | | |
| *0* | *1* | *2* | *3* | *4* |
| 18. Others are nasty | | | | |
| *0* | *1* | *2* | *3* | *4* |
| 19. Others are fair | | | | |
| *0* | *1* | *2* | *3* | *4* |
| 20. Others are good | | | | |
| *0* | *1* | *2* | *3* | *4* |
| 21. Others are trustworthy | | | | |
| *0* | *1* | *2* | *3* | *4* |
| 22. Others are accepting | | | | |
| *0* | *1* | *2* | *3* | *4* |
| 23. Others are supportive | | | | |
| *0* | *1* | *2* | *3* | *4* |
| 24. Others are truthful | | | | |
| *0* | *1* | *2* | *3* | *4* |

## 2.10 Ebbinghaus visual illusion task

The Ebbinghaus visual illusion task requires participants to select which of two presented circles is larger. In the illusory conditions these primary (orange) circles are surrounded by larger or smaller secondary (grey) circles which introduce an illusory effect, distorting the perception of the sizes of the primary circles. make the size difference between the primary circles easier ('Helpful' condition) or more difficult ('Misleading' condition) to determine. There is a control condition where no secondary circles are present. The difficulty of discriminating within the conditions is also manipulated by varying the magnitude of difference in size between the correct (larger) and incorrect (smaller) primary circles.

The individual stimuli were created in Drawio (https://www.draw.io/) an online service which allows precise design of visual objects. This was used to create the below stimuli:

1. Primary circles: 90pt, 94pt, 98pt, 100pt, 102pt, 106pt, 110pt orange circles (100pt is reference, difficulty of discrimination decreases with increasing size difference between reference and primary circle)
2. Secondary circles: A square formation of 8 grey circles, either 75pt (small surround) or 125 pt (large surround) in size. The small surround makes the primary circle seem bigger, whereas the large surround makes it appear smaller.

These were combined to create the following stimuli groups

1. No surround (control):
    a. 100pt orange circle accompanied by 90pt, 94pt, 98pt orange circle (no surrounds)
    b. 100pt orange circle accompanied by 102pt, 106pt, or 110pt orange circle (no surrounds)
2. Helpful illusion:
    a. 100pt orange circle (with small surround) accompanied by a 90pt, 94pt, 98pt orange circle (with large surround)

    AND

    b. 100pt orange circle (with large surround) accompanied by a 102, 106, 110pt orange circle (with small surround)
3. Misleading illusion:

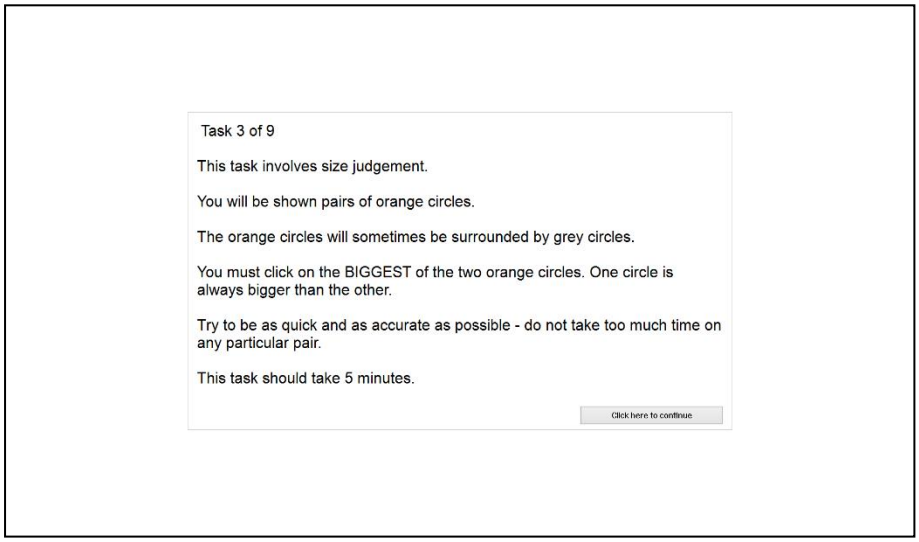
a. 100pt orange circle (with large surround) accompanied by a 90pt, 94pt, 98pt orange circle (with small surround)

   AND

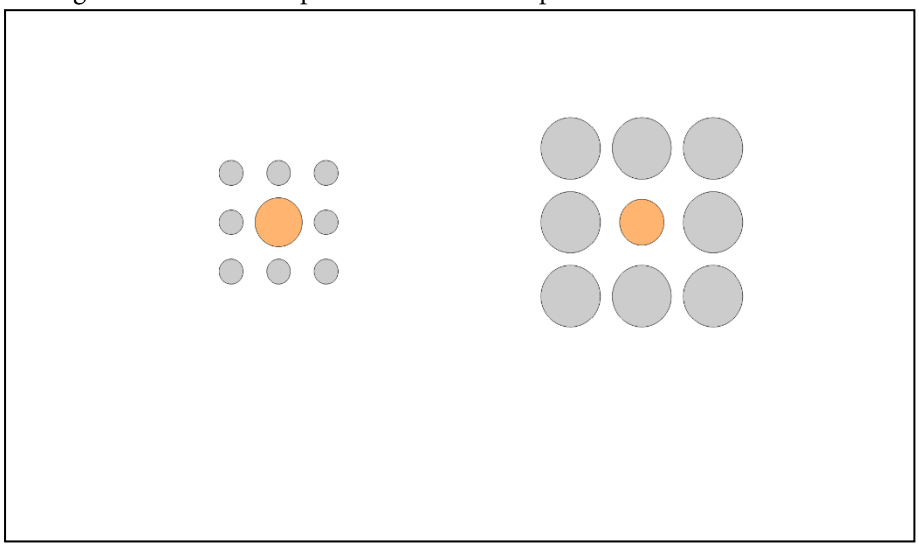
b. 100pt orange circle (with small surround) accompanied by a 102, 106, 110pt orange circle (with large surround).

In all cases the correct stimuli to select is the larger of the two orange circles presented (i.e. the 100pt orange circle in the a) conditions, or the accompanying circle in the b) conditions). The side that the correct stimulus was presented on was counterbalanced within each condition group. Example screenshots can be seen below:

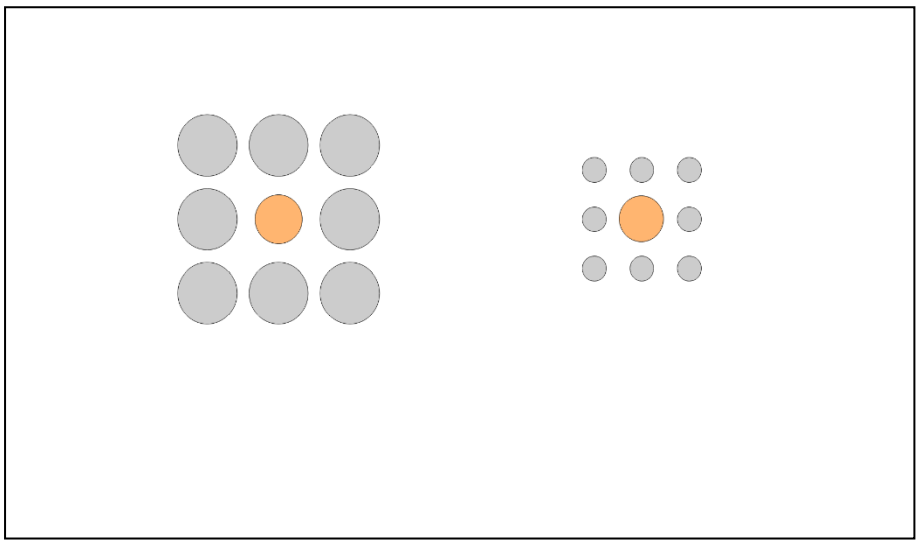
Ebbinghaus screen 1: Task introduction



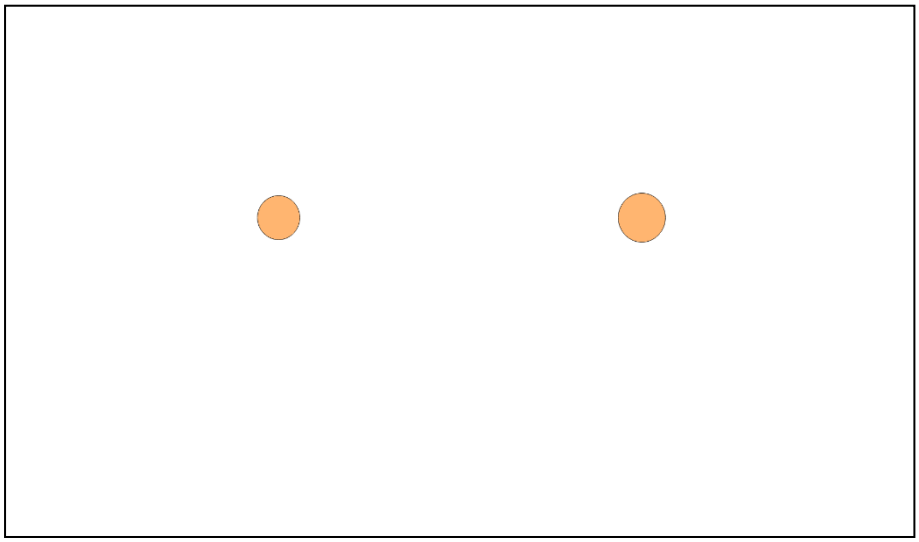

Ebbinghaus screen 2: Helpful condition example – correct circle is on left



Ebbinghaus screen 3: Misleading condition – correct circle is on left



Ebbinghaus screen 4: Control condition – correct circle is on right



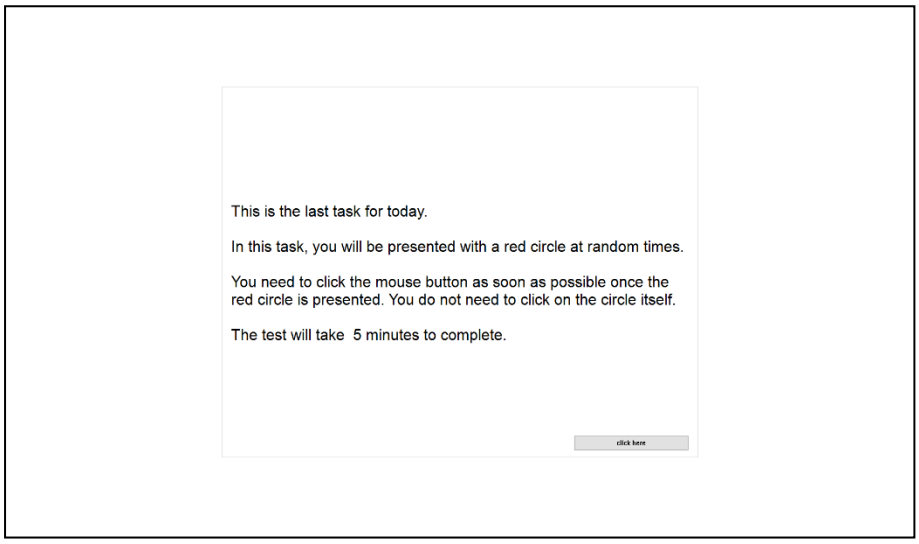
## 2.11 Perceptual Vigilance Task

The perceptual vigilance task was based on the code from the following source:

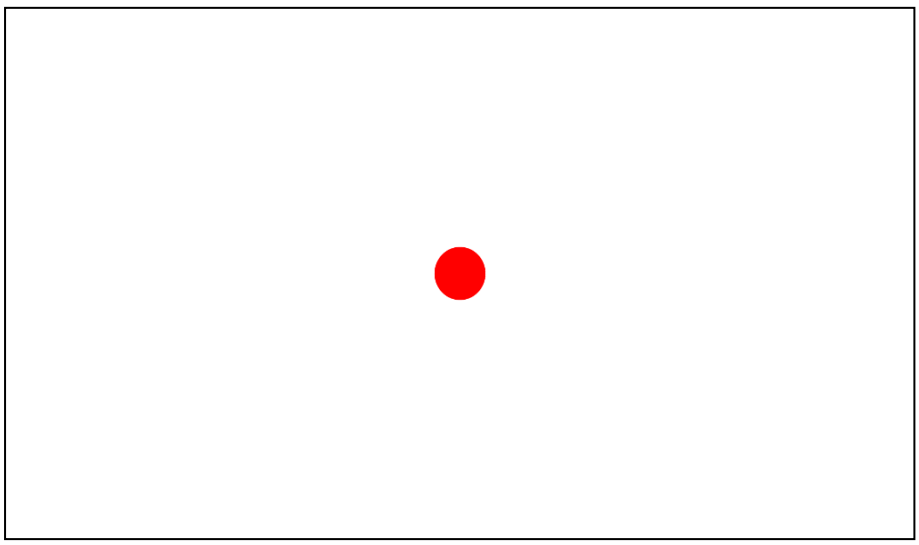
http://www.millisecond.com/download/library/perceptualvigilancetask/

In this task participants are required to react (by clicking) as soon as possible after a red dot appears on the screen. The dot appears in one of 9 locations (within a 3x3 grid in the centre of the screen) at intervals randomly chosen from 1 to 10 seconds. The dot remains present until a response is made, once the response is made the next trial starts immediately. This task duration is 5 minutes. Example screenshots are below:

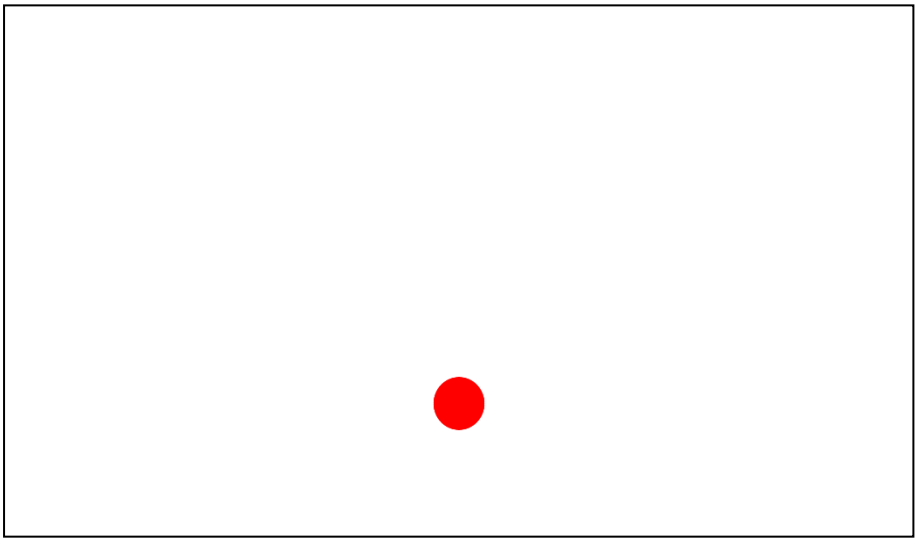
Perceptual vigilance screen 1: instructions




Perceptual vigliance screen 2: example trial 1



Perceptual vigliance screen 3: example trial 2



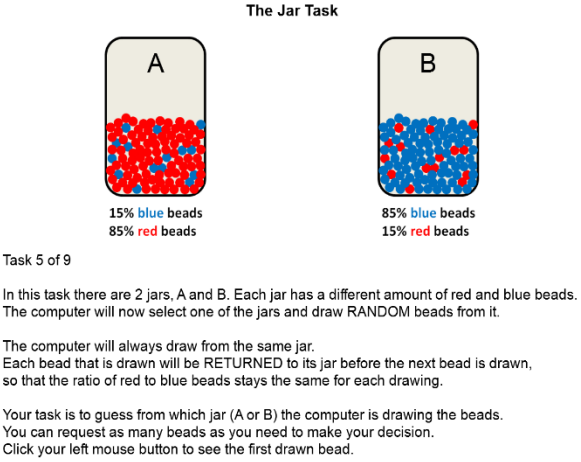
## 2.12 Beads task (Jumping to Conclusions)

The task programming was based on the code at

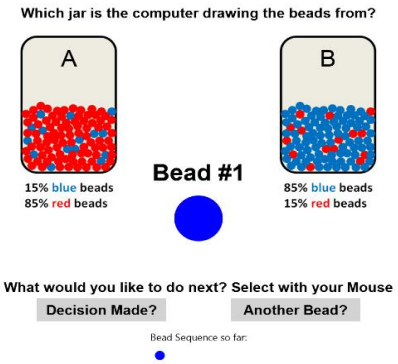
https://www.millisecond.com/download/library/jtc_beadstask/

In this task participants are presented with two jars – the jars are filled with blue and red beads (one 85:15 blue to red, the other 85:15 red to blue). They are told that one of the jars will be chosen randomly, and beads taken one at a time from it (with replacement). From the beads presented they are asked to decide which jar has been chosen. Participants can ask for a maximum of 20 beads, with a response after 2 beads or fewer judged as demonstrating the jumping to conclusions bias.

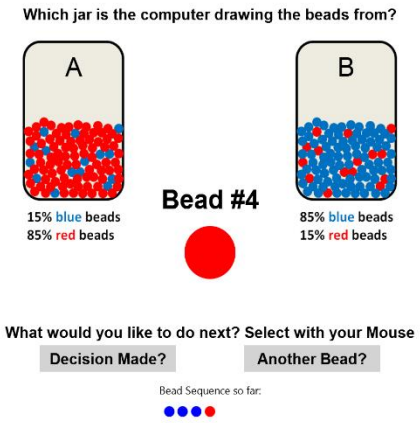
Beads task screen 1: instructions



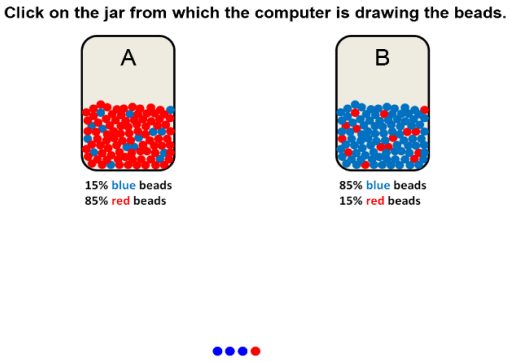

Beads task screen 2: first bead drawn, choices are to receive another bead or click on decision made



Beads task screen 3: if "Another Bead?" button is clicked, another bead is shown (note sequence is tracked at bottom of screen)




Beads task screen 4: Once "Decision Made?" button is clicked, the participant selects the jar they think the beads have been coming from (no feedback is given). The task then ends.



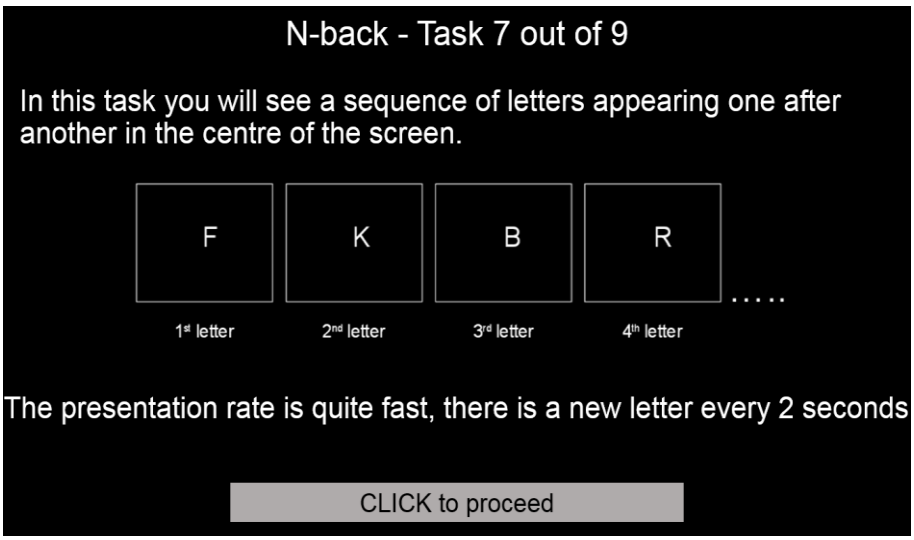
## 2.13 N-back task

In the N-back participants are presented with a series of letters (a new letter every two seconds), and asked to click whenever the sequence matches a particular rule. The rule can be a 1 back (is the current letter the same as the previous letter?), a 2-back (is the current letter the same as the letter two positions back in the sequence?), or a 3-back (is the current letter the same as the letter three positions back in the sequence?). Screenshots from the instructions for the task can be seen below.

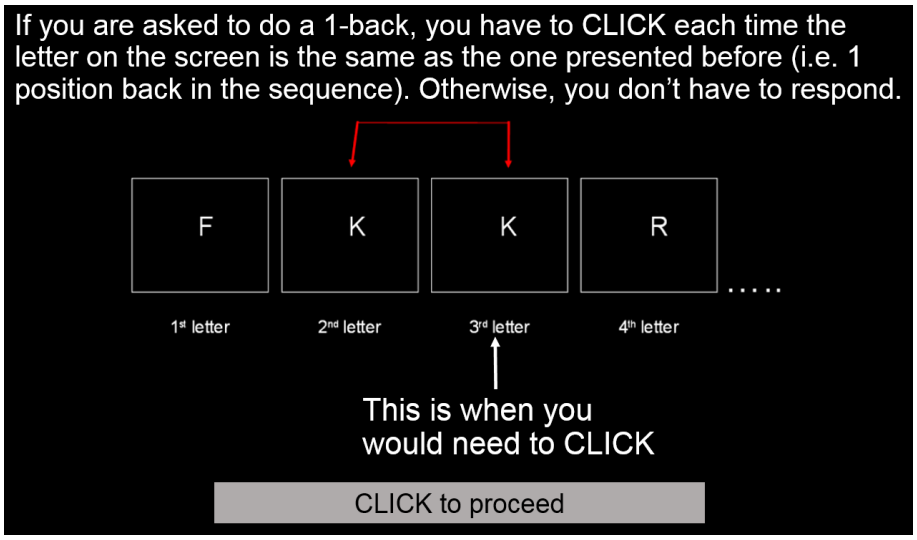
The task code was based on http://www.millisecond.com/download/library/nback/ with the following adjustments

1. Stimuli were changed from images to letters (consonants only)
2. The adaptive changes to task based on performance option was not used
3. A practice set of blocks was added (1, 2, and 3-back in ascending order) to be run in the initial participant meeting
4. Number of blocks and stimuli were changed to 2 blocks of each task, with 20 letters presented in each block. One third of letters matched the rule for that block. The 6 blocks were presented randomly
5. Response mode was altered to single click (left mouse button) in order to allow task to be completed on any media
6. Feedback on performance was removed

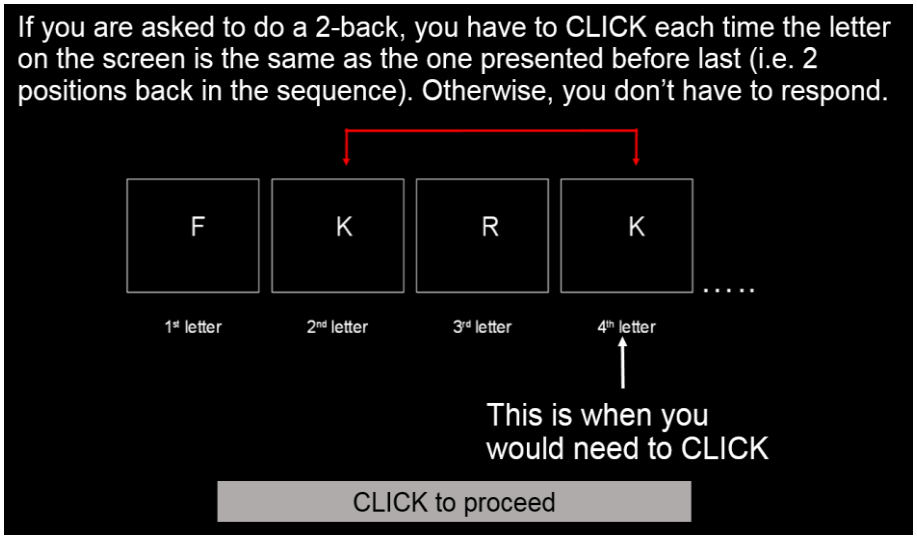
N-back screen 1: Introduction



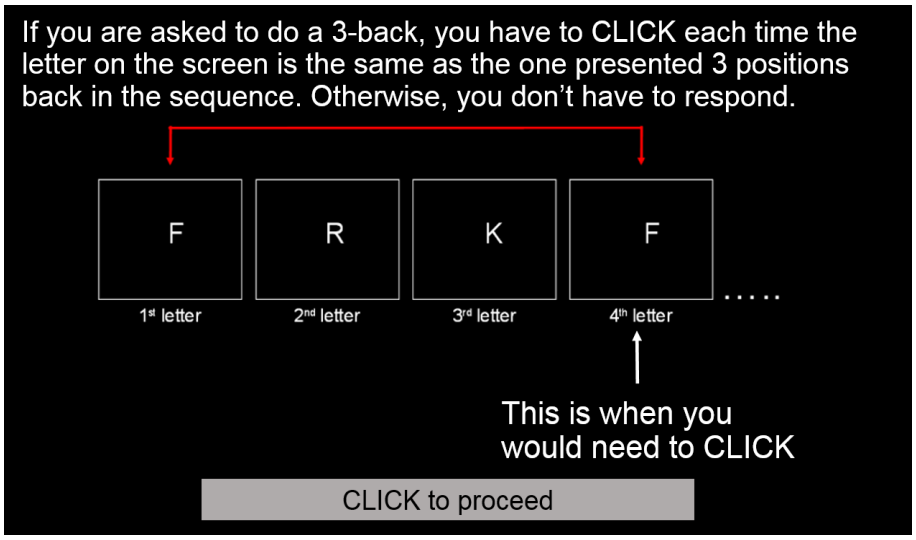

N-back screen 2: 1-back instructions



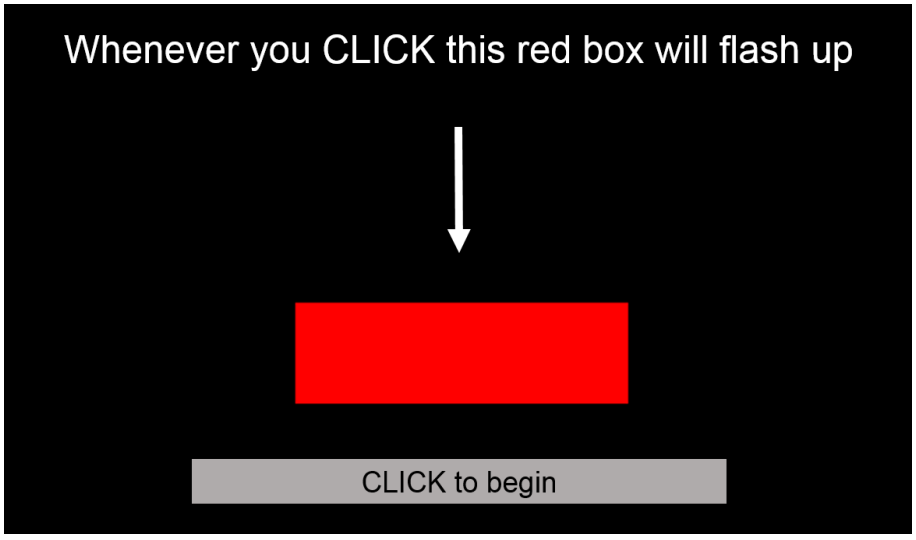

N-back screen 3: 2-back instructions



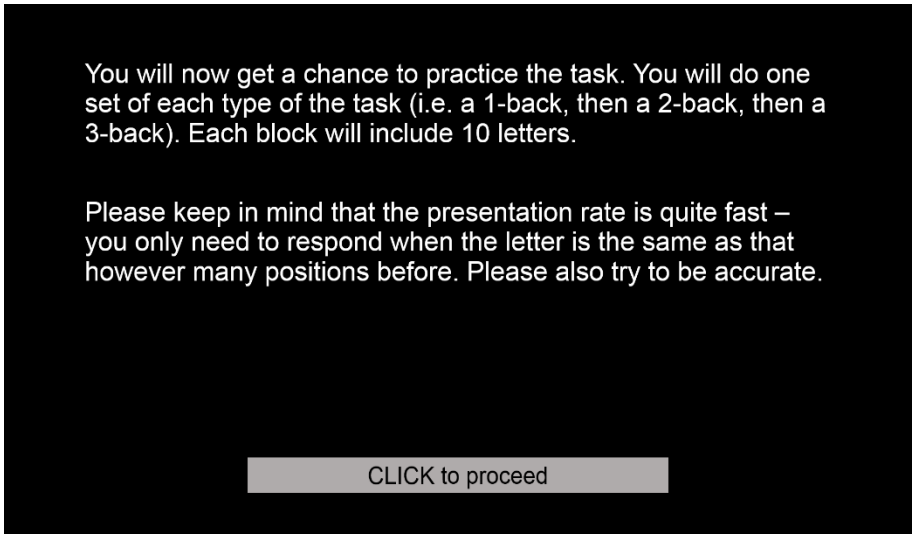
N-back screen 4: 3-back instructions



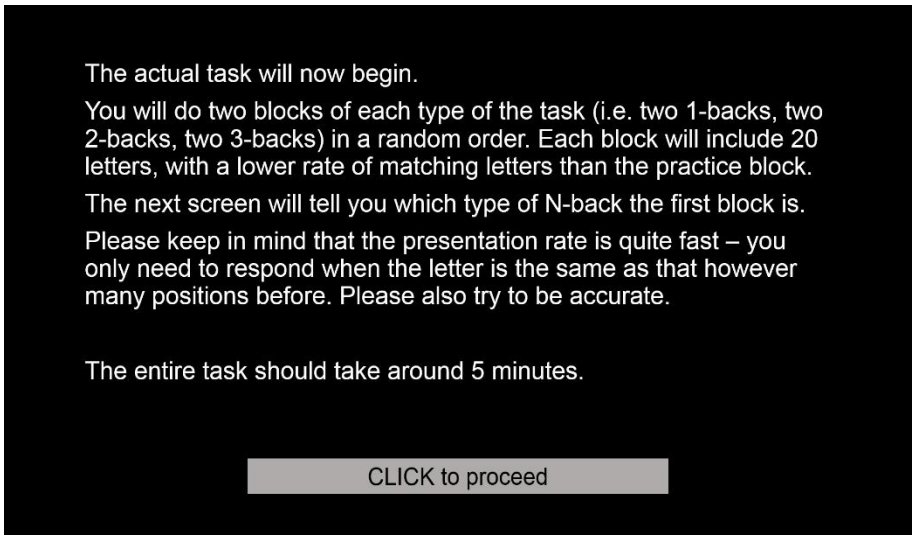

N-back instruction screen 5: response feedback box



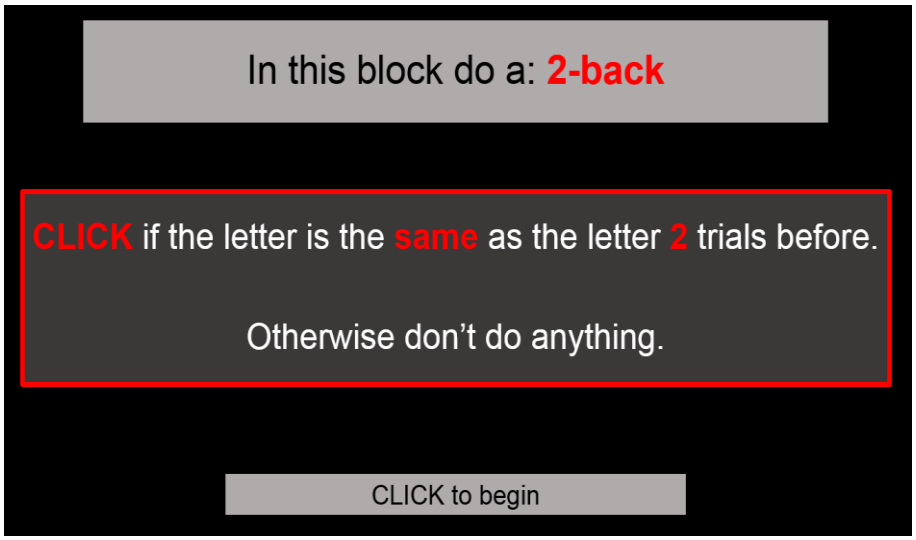

N-back instruction screen 6: Practice introduction (on run through with experimenter only)



N-back instruction screen 7: Main task introduction




N-back instruction screen 8: Block introduction (example here is for 2-back, similar screens shown for 1-back and 3-back )



## 2.14 Expanded table of means

| Outcome variable | Condition | Order | Mean (SD) pre | Mean (SD) post |
|---|---|---|---|---|
| Paranoia (SPEQ) | Restricted | Restricted then standard | 2.2 (2.7) | 3.5 (5.2) |
| | | Standard then restricted | 2.5 (3.9) | 4.1 (5.6) |
| | | **Total** | **2.3 (3.4)** | **3.8 (5.4)** |
| | Standard | Restricted then standard | 1.5 (2.4) | 2.6 (6.7) |
| | | Standard then restricted | 4.0 (6.0) | 2.5 (3.9) |
| | | **Total** | **2.8 (4.7)** | **2.5 (5.4)** |
| Hallucinations (SPEQ) | Restricted | Restricted then standard | .5 (.9) | 1.0 (1.8) |
| | | Standard then restricted | 2 (.6) | 1.4 (2.9) |
| | | **Total** | **.4 (.8)** | **1.2 (2.4)** |
| | Standard | Restricted then standard | .2 (.6) | .2 (.4) |
| | | Standard then restricted | 1.4 (2.9) | .1 (.8) |
| | | **Total** | **.3 (1.5)** | **.1 (.7)** |
| Cognitive Disorganisation (SPEQ) | Restricted | Restricted then standard | 2.4 (3.5) | 4.5 (3.6) |
| | | Standard then restricted | 2.7 (4.2) | 5.2 (4.7) |
| | | **Total** | **2.6 (3.9)** | **4.8 (4.2)** |
| | Standard | Restricted then standard | 2.3 (3.6) | 2.2 (2.8) |
| | | Standard then restricted | 5.2 (4.7) | 2.6 (4.1) |
| | | **Total** | **2.7 (3.8)** | **2.5 (3.5)** |
| Grandiosity (SPEQ) | Restricted | Restricted then standard | 6.7 (6.1) | 6.7 (6.1) |
| | | Standard then restricted | 6.6 (7.4) | 6.7 (7.2) |
| | | **Total** | **6.6 (6.7)** | **6.7 (6.6)** |
| | Standard | Restricted then standard | 7.0 (6.6) | 6.5 (6.2) |
| | | Standard then restricted | 6.7 (7.2) | 6.3 (6.8) |
| | | **Total** | **6.4 (6.1)** | **6.4 (6.5)** |
| Psychotic experience distress (SPEQ) | Restricted | Restricted then standard | .3 (.6) | .7 (1.0) |
| | | Standard then restricted | .4 (.9) | .7 (1.3) |
| | | **Total** | **.3 (.8)** | **.7 (1.1)** |
| | Standard | Restricted then standard | .3 (.8) | .2 (.7) |
| | | Standard then restricted | .5 (.9) | .3 (.7) |
| | | **Total** | **.4 (.8)** | **.3 (.7)** |
| Depression (DASS) | Restricted | Restricted then Standard | 2.0 (3.4) | 4.5 (5.4) |
| | | Standard then restricted | 2.1 (4.5) | 3.7 (6.7) |
| | | **Total** | **2.0 (3.9)** | **4.6 (6.1)** |
| | Standard | Restricted then Standard | 1.5 (3.1) | 1.7 (4.8) |
| | | Standard then restricted | 2.1 (3.4) | 1.5 (2.9) |
| | | **Total** | **1.8 (3.2)** | **1.6 (3.9)** |

| Outcome variable | Condition | Order | Mean (SD) pre | Mean (SD) post |
|---|---|---|---|---|
| Anxiety (DASS) | Restricted | Restricted then Standard | 2.6 (3.1) | 5.6 (5.7) |
| | | Standard then restricted | 1.9 (3.3) | 4.9 (4.7) |
| | | **Total** | **2.2 (3.2)** | **5.2 (5.2)** |
| | Standard | Restricted then Standard | 2.4 (3.1) | 2.5 (5.0) |
| | | Standard then restricted | 3,4 (4.3) | 1.7 (2.4) |
| | | **Total** | **3.0 (3.8)** | **2.1 (3.9)** |
| Stress (DASS) | Restricted | Restricted then Standard | 3.2 (3.6) | 8.4 (8.6) |
| | | Standard then restricted | 4.2 (8.0) | 7.1 (7.2) |
| | | **Total** | **3.8 (6.2)** | **7.8 (7.8)** |
| | Standard | Restricted then Standard | 3.1 (4.4) | 2.8 (5.0) |
| | | Standard then restricted | 4.9 (5.9) | 3.8 (4.2) |
| | | **Total** | **4.0 (5.3)** | **3.3 (4.6)** |
| Negative self beliefs (BCSS) | Restricted | Restricted then Standard | 1.7 (2.0) | 2.4 (3.1) |
| | | Standard then restricted | 1.8 (2.6) | 2.8 (3.3) |
| | | **Total** | **1.8 (2.2)** | **2.6 (3.2)** |
| | Standard | Restricted then Standard | 1.5 (2.2) | 1.4 (2.0) |
| | | Standard then restricted | 2.2 (2.3) | 1.8 (2.3) |
| | | **Total** | **1.9 (2.3)** | **1.6 (2.1)** |
| Positive self beliefs (BCSS) | Restricted | Restricted then Standard | 15.1 (4.4) | 13.7 (4.2) |
| | | Standard then restricted | 11.3 (5.6) | 10.5 (5.4) |
| | | **Total** | **13.1 (5.3)** | **12.0 (5.1)** |
| | Standard | Restricted then Standard | 14.6 (4.6) | 14.0 (5.4) |
| | | Standard then restricted | 12.8 (4.0) | 11.9 (5.0) |
| | | **Total** | **13.7 (4.4)** | **13.0 (5.3)** |
| Negative beliefs about others (BCSS) | Restricted | Restricted then Standard | 1.4 (2.0) | 2 (3.1) |
| | | Standard then restricted | 2.5 (3.1) | 3.3 (4.1) |
| | | **Total** | **1.9 (2.7)** | **2.6 (3.7)** |
| | Standard | Restricted then Standard | 1.7 (2.1) | 1.7 (2.2) |
| | | Standard then restricted | 2.3 (3.3) | 1.7 (2.6) |
| | | **Total** | **2.0 (2.8)** | **1.7 (2.4)** |
| Positive beliefs about others (BCSS) | Restricted | Restricted then Standard | 13.6 (4.2) | 13.5 (3.3) |
| | | Standard then restricted | 10.5 (5.1) | 10.1 (5.6) |
| | | **Total** | **12 (5.0)** | **11.8 (4.9)** |
| | Standard | Restricted then Standard | 13.2 (2.5) | 13.2 (4.3) |
| | | Standard then restricted | 12.5 (3.8) | 10.9 (5.4) |
| | | **Total** | **12.9 (3.7)** | **12.1 (5.0)** |

Expanded table of means

| Outcome variable | Condition | Order | Mean (SD) pre | Mean (SD) post |
|---|---|---|---|---|
| Worry | Restricted | Restricted then Standard | 5.7 (6.0) | 6.7 (6.9) |
| | | Standard then restricted | 6.1 (6.8) | 8.4 (7.7) |
| | | **Total** | **5.9 (6.4)** | **7.6 (7.3)** |
| | Standard | Restricted then Standard | 4.4 (5.1) | 3.5 (5.1) |
| | | Standard then restricted | 7.6 (7.5) | 6.5 (6.4) |
| | | **Total** | **6.0 (6.6)** | **5.0 (6.0)** |
| Ebbinghaus-difference | Restricted | Restricted then Standard | 79.8 (19.6) | 81.6 (18.3) |
| | | Standard then restricted | 81.4 (17.9) | 76.8 (26.1) |
| | | **Total** | **80.6 (18.6)** | **79.1 (22.6)** |
| | Standard | Restricted then Standard | 80.9 (19.8) | 75.4 (21.2) |
| | | Standard then restricted | 81.9 (17.5) | 81.0 (21.4) |
| | | **Total** | **81.4 (18.5)** | **78.2 (21.3)** |
| Perceptual vigilance – average RT | Restricted | Restricted then Standard | 425.1 (93.0) | 478.9 (153.1) |
| | | Standard then restricted | 771.7 (1344.0) | 739.7 (524.4) |
| | | **Total** | **603.5 (975.3)** | **613.2 (409.9)** |
| | Standard | Restricted then Standard | 520.1 (354.6) | 515.5 (252.4) |
| | | Standard then restricted | 501.7 (242.7) | 561.2 (312.5) |
| | | **Total** | **510.7 (300.8)** | **539.0 (283.7)** |
| Perceptual vigilance – no. of lapses (RT <=500ms) | Restricted | Restricted then Standard | 8.4 (9.7) | 13.8 (12.5) |
| | | Standard then restricted | 15.4 (14.7) | 22.2 (17.1) |
| | | **Total** | **12.0 (12.9)** | **18.1 (15.5)** |
| | Standard | Restricted then Standard | 10.8 (9.1) | 13.2 (9.3) |
| | | Standard then restricted | 12.7 (13.9) | 17.4 (14.6) |
| | | **Total** | **11.1 (11.8)** | **15.4 (12.4)** |
| Decision Value (N-back) | Restricted | Restricted then Standard | .2 (.1) | .2 (.1) |
| | | Standard then restricted | .2 (.1) | .2 (.1) |
| | | **Total** | **.2 (.1)** | **.2 (.1)** |
| | Standard | Restricted then Standard | .2 (.0) | .2 (.1) |
| | | Standard then restricted | .2 (.1) | .2 (.1) |
| | | **Total** | **.2 (.0)** | **.2 (.1)** |
| No of beads – jumping to conclusions | Restricted | Restricted then Standard | 4.4 (3.8) | 4.2 (3.8) |
| | | Standard then restricted | 4.7 (4.4) | 4.9 (5.2) |
| | | **Total** | **3.5 (4.1)** | **4.6 (4.5)** |
| | Standard | Restricted then Standard | 4.4 (4.4) | 4.3 (3.9) |
| | | Standard then restricted | 4.0 (2.7) | 4.3 (3.2) |
| | | **Total** | **4.2 (3.6)** | **4.3 (3.5)** |

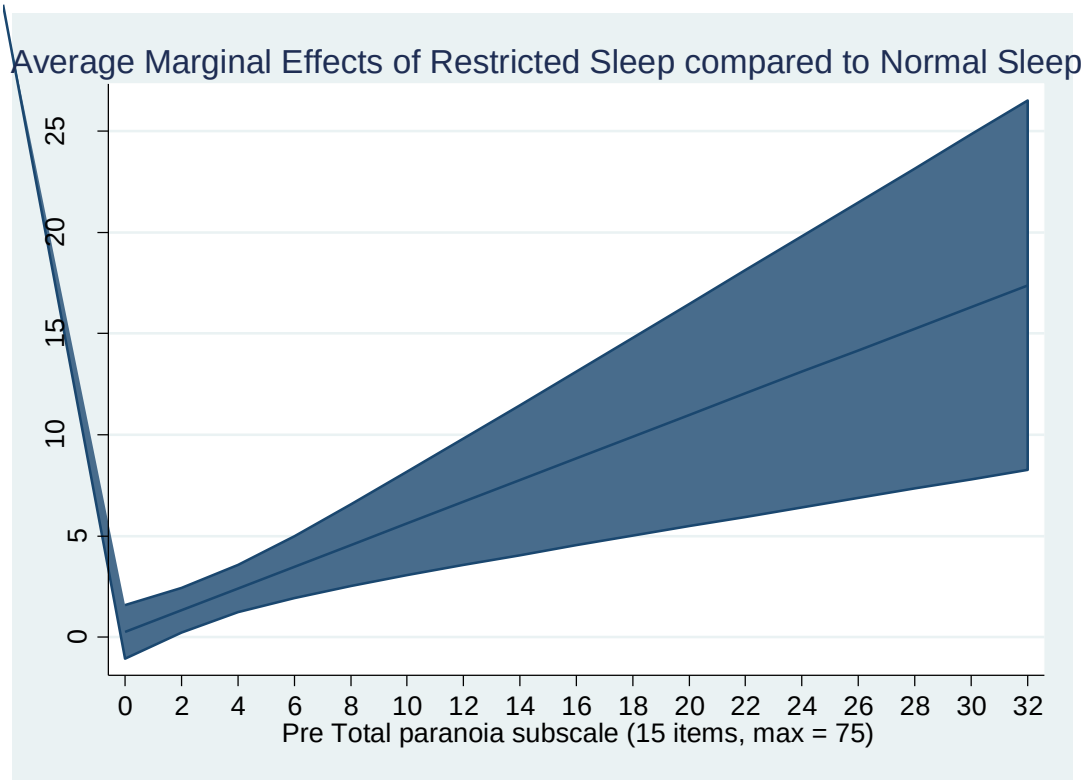
## 2.15 Interaction analyses

Checking whether interactions between baseline (i.e. at the start of each respective experimental condition) and condition are significant.

### 2.15.1 SPEQ Paranoia

Interaction term between condition and paranoia = 0.535 (0.156), p=0.001

The graph shows the effect of the interaction and 95% confidence interval across levels of paranoia (x-axis). The y-axis shows the treatment effect on paranoia (comparing restricted sleep to normal sleep).

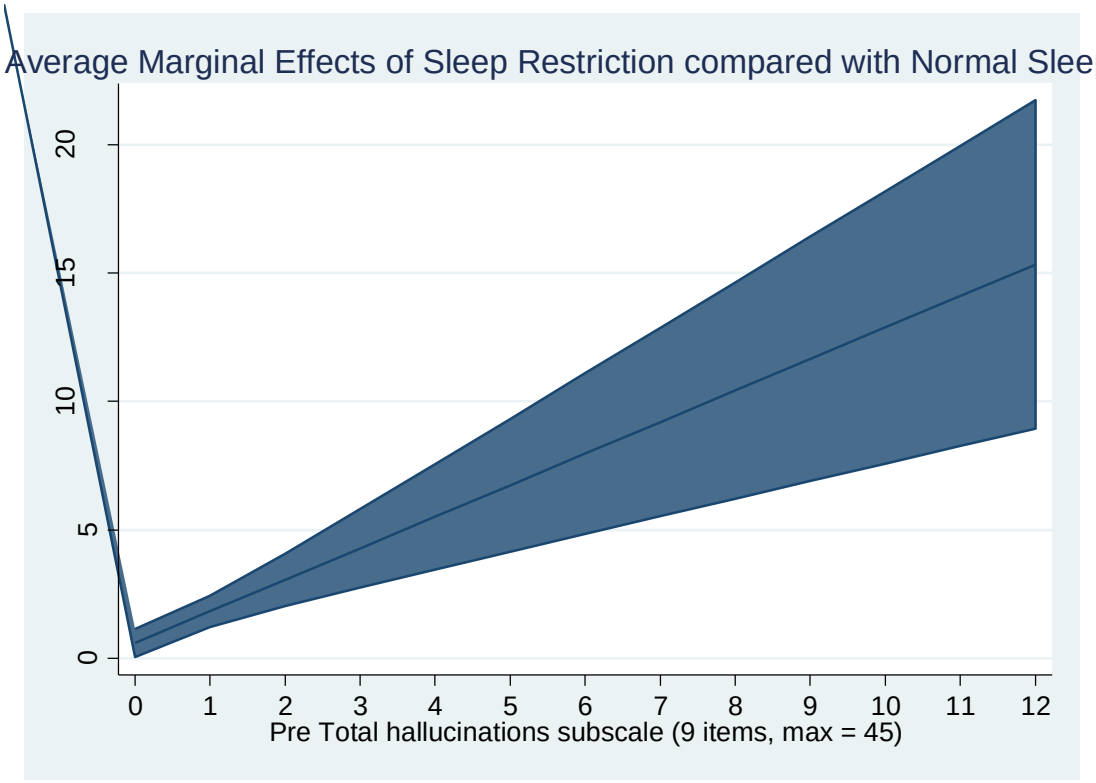



The interpretation of this is that there is a significant increase in paranoia under restricted sleep compared to normal sleep (because of the positive coefficient). This increase in paranoia is greater as the baseline level of paranoia is higher.

## 2.15.2 SPEQ Hallucinations

Interaction term between condition and hallucinations = 1.228 (0.280), p<0.001

The graph shows the effect of the interaction and 95% confidence interval across levels of hallucinations (x-axis). The y-axis shows the treatment effect on hallucinations (comparing restricted sleep to normal sleep).

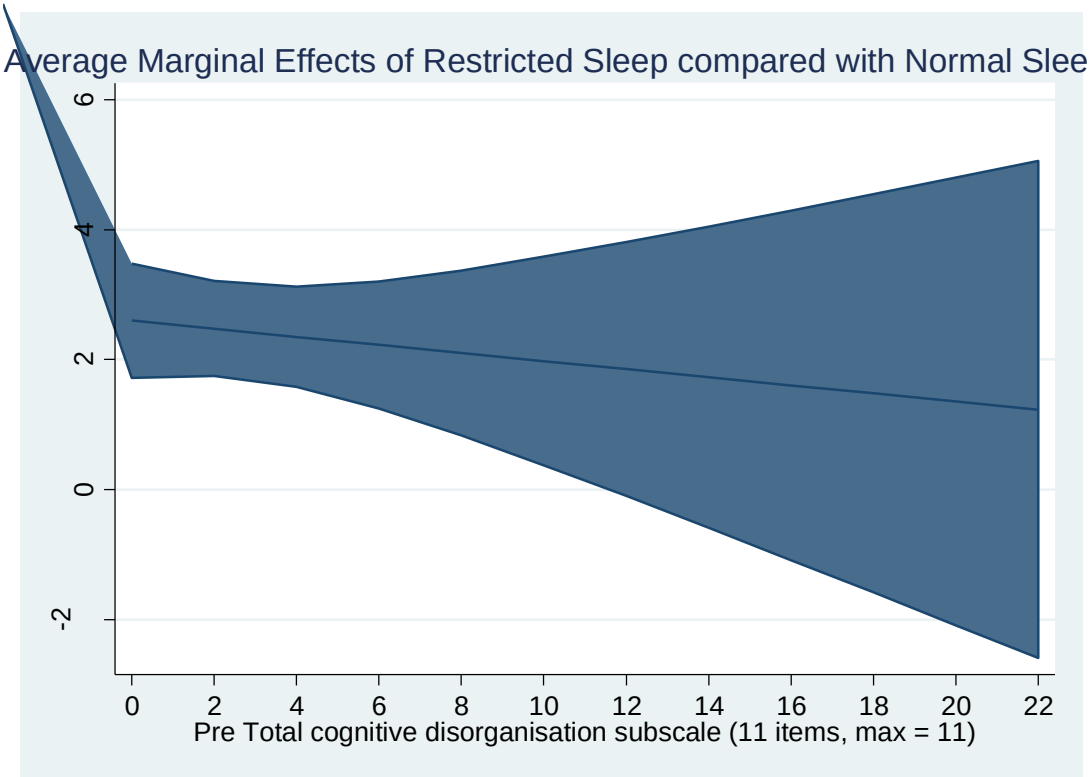



The interpretation of this is that there is a significant increase in hallucinations under restricted sleep compared to normal sleep (because of the positive coefficient). This increase in hallucinations is greater as the baseline level of hallucinations is higher.

## 2.15.3 SPEQ Cognitive Disorganisation

Interaction term between condition and cognitive disorganisation = -0.06 (0.10), p=0.528

The graph shows the effect of the interaction and 95% confidence interval across levels of cognitive disorganisation (x-axis). The y-axis shows the treatment effect on cognitive disorganisation (comparing restricted sleep to normal sleep).

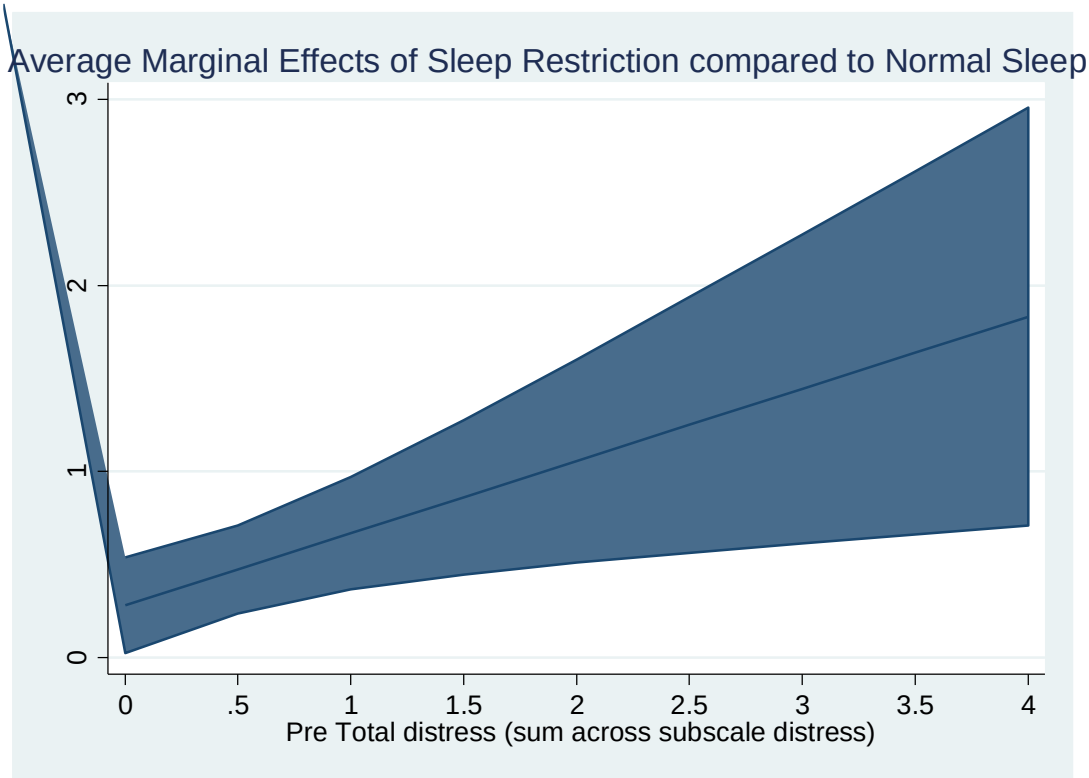



The interpretation of this is that there is a significant increase in cognitive disorganisation under restricted sleep compared to normal sleep. This increase in cognitive disorganisation is less as the baseline level of cognitive disorganisation is higher.

## 2.15.4 SPEQ Total Distress

Interaction term between condition and distress = 0.388 (0.154), p=0.012

The graph shows the effect of the interaction and 95% confidence interval across levels of distress (x-axis). The y-axis shows the treatment effect on distress (comparing restricted sleep to normal sleep).




The interpretation of this is that there is a significant increase in distress under restricted sleep compared to normal sleep (because of the positive coefficient). This increase in distress is greater as the baseline level of distress is higher

## 3.1 SPSS example syntax

```
DATASET ACTIVATE DataSet1.
MIXED utcsev BY rgroup SiteCode WITH BadDur Range
 /CRITERIA=CIN(95) MXITER(100) MXSTEP(10) SCORING(1) SINGULAR(0.000000000001)
HCONVERGE(0,
 ABSOLUTE) LCONVERGE(0, ABSOLUTE) PCONVERGE(0.000001, ABSOLUTE)
 /FIXED=rgroup SiteCode BadDur Range | SSTYPE(3)
 /METHOD=REML
 /PRINT=SOLUTION
 /REPEATED=timepoint | SUBJECT(Number) COVTYPE(DIAG).

MIXED utcsev BY rgroup SiteCode WITH BadDurPrev RangePrev
 /CRITERIA=CIN(95) MXITER(100) MXSTEP(10) SCORING(1) SINGULAR(0.000000000001)
HCONVERGE(0,
 ABSOLUTE) LCONVERGE(0, ABSOLUTE) PCONVERGE(0.000001, ABSOLUTE)
 /FIXED=rgroup SiteCode BadDurPrev RangePrev | SSTYPE(3)
 /METHOD=REML
 /PRINT=SOLUTION
 /REPEATED=timepoint | SUBJECT(Number) COVTYPE(DIAG).

MIXED utcsev BY rgroup SiteCode WITH BadDur Range BadDurPrev RangePrev
 /CRITERIA=CIN(95) MXITER(100) MXSTEP(10) SCORING(1) SINGULAR(0.000000000001)
HCONVERGE(0,
 ABSOLUTE) LCONVERGE(0, ABSOLUTE) PCONVERGE(0.000001, ABSOLUTE)
 /FIXED=rgroup SiteCode BadDur Range BadDurPrev RangePrev | SSTYPE(3)
 /METHOD=REML
 /PRINT=SOLUTION
 /REPEATED=timepoint | SUBJECT(Number) COVTYPE(DIAG).

MIXED utcsev BY rgroup SiteCode WITH BadDur Range BadDurPrev RangePrev utcsevPrev
 /CRITERIA=CIN(95) MXITER(100) MXSTEP(10) SCORING(1) SINGULAR(0.000000000001)
HCONVERGE(0,
 ABSOLUTE) LCONVERGE(0, ABSOLUTE) PCONVERGE(0.000001, ABSOLUTE)
 /FIXED=rgroup SiteCode BadDur Range BadDurPrev RangePrev utcsevPrev | SSTYPE(3)
 /METHOD=REML
 /PRINT=SOLUTION
 /REPEATED=timepoint | SUBJECT(Number) COVTYPE(DIAG).
```

## 4.1 Diagnostic Interview for Sleep Patterns and Disorders (DISP)

The appendix originally presented here cannot be made freely available via ORA because of copyright.

## 4.2 Scoring guidelines for the Diagnostic Interview for Sleep Patterns and Disorders (DISP)

| Variable | Coding | Notes on coding |
|---|---|---|
| Diagnosis | 0 = No Diagnosis<br>1 = Diagnosis<br>-99 = Unknown/Missing<br>All diagnostic criteria to be satisfied for a 1<br><br>Exceptions (where not possible to tell diagnosis without polysomnography or other tests). PSG criteria shaded in grey in table below<br>**PLMS**: only have presence/absence of kicking<br>**REM** sleep behaviour disorder: only have reports of activity during night<br>**Narcolepsy** (with or without cataplexy): requires multiple sleep onset latency test (MSLT) with polysomnography (PSG) to confirm sleepiness, or hypocretin tests for narcolepsy with cataplexy<br>**Hypersomnia**: requires multiple sleep onset latency test with polysomnography to confirm sleepiness<br>**Apnoea**: PSG required for diagnosis, therefore number of indicators (based on supplementary symptoms) is reported<br>NB **Bruxism**: some supplementary criteria require PSG, but diagnosis possible without | DISP originally has 0-3 coding (0 =not present, 1= symptoms only, 2= subclinical, 3=diagnosis), but this was changed to 0(no diagnosis)/1 (diagnosis) to simplify reporting.<br><br>Diagnostic criteria are derived from ICSD-2, DSM-5, and ICSD-3 in order to encompass maximum information<br><br>Only current sleep disorders were included in scoring. |
| Severity | Severity coded on 1-3 scale (1=mild, 2=moderate, 3=severe) composed individually for each disorder based on below characteristics:<br>1) symptom counts (where extra indicators beyond diagnosis are available)<br>2) frequency of symptoms (where threshold from diagnostic criteria is available)<br>3) duration of symptoms (where threshold from diagnostic criteria is available)<br>4) distress/impairment rated on 1-10 scale, highest used – rated to severity as following: mild = 1-3; moderate = 4-6; severe =>7<br>Overall coding is based on average of these four characteristics – where indicators are split across two levels, round down e.g. D/I and frequency is 3, duration and symptom counts are 2, score would be 2 | DISP originally requires 1-3 scoring based on hospitalisations and occupational/functional issues, but this requirement is unrealistic for psychosis where individuals are often unemployed, and where hospitalisations that have occurred are difficult to place on sleep issues. Therefore, the severity coding described was developed based on diagnostic criteria guidelines. |
| Treatment | 0 = None<br>1 = Recommended treatment (e.g. for insomnia: Cognitive Behavioural Therapy for Insomnia or hypnotic medication)<br>2 = Non-recommended treatment e.g. antipsychotics, sleep hygiene sheet, non-specific sleep advice)<br>3 = self-treated | For each disorder where screening questions passed, participant is asked if they have mentioned the problem to their care team, and then if they are receiving treatment for it. |

| | | |
|---|---|---|
| | -99 = unknown | |
| **Other notes:** If > or <, anchor number was used (e.g. >10, used 10); If range given average was used. | | |

## 4.3 Diagnostic and severity scoring guidelines by disorder for DISP

| Disorder | Diagnostic criteria – from ICSD2 unless labelled otherwise | Scoring - Diagnosis | Scoring - Severity |
|---|---|---|---|
| **Circadian = Delayed or Advanced sleep phase syndrome** | | | |
| Delayed sleep phase syndrome | A. There is a delay in the phase of the major sleep period in relation to the desired sleep time and wake-up time, as evidenced by a chronic or recurrent complaint of inability to fall asleep at a desired conventional clock time together with the inability to awaken at a desired and socially acceptable time.<br>B. When allowed to choose their preferred schedule, patients will exhibit normal sleep quality and duration for age and maintain a delayed, but stable, phase of entrainment to the 24-hour sleep-wake pattern.<br>C. Sleep log or actigraphy monitoring (including sleep diary) for at least seven days demonstrates a stable delay in the timing of the habitual sleep period.<br>D (from ICSD3) difficulty causes sleepiness, insomnia, or both | A: Y to "strong night owl", regularly asleep later than 1am AND difficulty falling asleep at earlier times<br>B: unable to assess due to high level of sleep disorder co-morbidity in the group<br>C: sleep diary indicates consistent late sleep time i.e. post 1am sleep, actigraph confirms<br>D: having great difficulty waking up in the morning (sometimes/always) OR feeling awake and refreshed after sleeping (never/sometimes) | 1) 2hr out (i.e. 1am); mild distress/impairment<br>2) 4hr out (i.e. 3am); moderate distress/impairment<br>3) 6hr out (i.e. 5am); severe distress/impairment |
| Advanced sleep phase syndrome | A. There is an advance in the phase of the major sleep period in relation to the desired sleep time and wake-up time, as evidenced by a chronic or recurrent complaint of inability to stay awake until the desired conventional clock time, together with an inability to remain asleep until the desired and socially acceptable time for awakening.<br>B. When patients are allowed to choose their preferred schedule, sleep quality and duration are normal for age with an advanced, but stable, phase of entrainment to the 24-hour sleep-wake pattern.<br>C. Sleep logs or actigraphy monitoring (including sleep diaries) for at least seven days demonstrates a stable advance in the timing of the habitual sleep period.<br>D (from ICSD3) difficulty causes sleepiness, insomnia, or both | A: Y to "strong early bird", regularly asleep before 9pm AND difficulty staying awake at later times<br>B: unable to assess due to high level of sleep disorder co-morbidity in the group<br>C: sleep diary indicates consistent early sleep time i.e. pre 9pm, actigraph confirms<br>D: having difficulty waking too early and unable to get back to sleep (yes/no) OR feeling awake and refreshed after sleeping (never/sometimes) | 1) 2hr out (i.e. 9pm); mild distress/impairment<br>2) 4hr out (ie. 7pm); moderate distress/impairment<br>3) 6hr out (i.e. 5pm); severe distress/impairment |

Diagnostic and severity scoring guidelines by disorder for DISP

| Disorder | Diagnostic criteria – from ICSD2 unless labelled otherwise | Scoring - Diagnosis | Scoring - Severity |
|---|---|---|---|
| Insomnia | A. Difficulty initiating sleep, difficulty maintaining sleep, or waking up too early or sleep that is chronically nonrestorative or poor in quality.<br>B. The above sleep difficulty occurs despite adequate opportunity and circumstances for sleep.<br>C. At least one of the following forms of daytime impairment related to the night time sleep difficulty is reported by the patient:<br>1. Fatigue or malaise<br>2. Attention, concentration, or memory impairment<br>3. Social or vocational dysfunction or poor school performance<br>4. Mood disturbance or irritability<br>5. Daytime sleepiness<br>6. Motivation, energy, or initiative reduction<br>7. Proneness for errors or accidents at work or while driving<br>8. Tension, headaches, or gastrointestinal symptoms in response to sleep loss<br>9. Concerns or worries about sleep<br>D: (from DSM-5) Trouble sleeping has occurred at least 3 times a week for the last 3 months | A: Y to difficulty initiating sleep OR staying asleep OR falling back to sleep OR waking too early in morning (DASLP103-106)<br>B: From routine sleep section there is adequate time in bed, plus no other obvious reason for lack of sleep, e.g. shift work or children.<br>C: One of consequences (fatigue, attention impairment, social dysfunction etc. – DASLP113-123)) endorsed OR distress and dmpairment > 0<br>D: Occurs >=3/wk, lasted >=3 months | 1) 1 of A; 3/wk; =3 mo; mild distress/impairment<br>2) 2 of A; >=4/wk; <= 1 year; moderate distress/impairment<br>3) 3-4 of A; >=6/wk; >1 year; severe distress/impairment |
| Obstructive Sleep Apnoea | OSA may be diagnosed if the AHI (apnoea-hypopnoea index) or REI (respirator index event) from PSG is ≥5 episodes/hour with evidence of respiratory effort during all respiratory events; diagnosis is not better explained by another sleep, medical, or neurological disorder, or medication or drug use; and at least 1 of the following is present:<br>1. Complaints of daytime sleepiness, unrefreshing sleep, fatigue, insomnia, or unintentional sleep episodes during wakefulness<br>2. Waking with breath holding, gasping, or choking<br>3. Bed partner reports loud snoring, breathing interruptions, or both, during patient's sleep | Not possible to assess, additional criteria from screening questionnaires (e.g. STOP-bang) not possible to assess.<br>Number of the 6 indicators (DASLP172-177) endorsed to be reported instead of a screen or diagnosis result | Not scored |

| Disorder | Diagnostic criteria – from ICSD2 unless labelled otherwise | Scoring - Diagnosis | Scoring - Severity |
|---|---|---|---|
| Restless leg syndrome | A. The patient reports an urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations in the legs.<br>B. The urge to move or the unpleasant sensations begin or worsen during periods of rest or inactivity such as lying or sitting.<br>C. The urge to move or the unpleasant sensations are partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues.<br>D. The urge to move or the unpleasant sensations are worse, or only occur, in the evening or night.<br>E. The condition is not better explained by another current sleep disorder, medical or neurological disorder, mental disorder, medication use, or substance use disorder.<br>F: (from ICSD-3) Must cause disruption to sleep, distress, or disturbance<br>G: (From DSM-5) Has to occur at least 3/week for at least last three months | A: Y to repeated urge to move legs (strange or uncomfortable feelings optional) (DASLP256)<br>B: Y to sensations occur mostly at rest (DASLP259)<br>C: Y to relieved by standing or walking around (DASLP260)<br>D: Y to worse late in day or in evening (DASLP261)<br>F: Disturbs sleep (DASLP262) OR distress OR impairment > 0<br>G:Onset >=3mo ago, Frequency >=3 wk | 1) =3/week; <=3 months; cause some difficulty getting to sleep (DASLP262); mild distress/impairment<br>2) <=5/week; <=1yr; cause great difficulty getting to sleep(DASLP262); moderate distress/impairment<br>3) >6week; >1yr; caused great difficulty getting to sleep(DASLP262); severe distress/impairment |
| Periodic limb movement | A. Polysomnography demonstrates repetitive, highly stereotyped, limb movements that are:<br>1. 0.5 to five seconds in duration<br>2. Of amplitude greater than or equal to 25% of toe dorsiflexion during calibration<br>3. In a sequence of four or more movements<br>4. Separated by an interval of more than five seconds (from limb-movement onset to limb-movement onset) and less than 90 seconds (typically there is an interval of 20 to 40 seconds)<br>B. The PLMS Index exceeds five per hour in children and 15 per hour in most adult cases.<br>C. There is clinical sleep disturbance or a complaint of daytime fatigue.<br>D. The PLMS are not better explained by another current sleep disorder, medical or neurological disorder, mental disorder, medication use, or substance use disorder. | Y to kicking at night (DASLP313) | All criteria require PSG therefore not scorable beyond report of kicking |

Diagnostic and severity scoring guidelines by disorder for DISP

| Disorder | Diagnostic criteria – from ICSD2 unless labelled otherwise | Scoring - Diagnosis | Scoring - Severity |
|---|---|---|---|
| Bruxism | A. The patient reports or is aware of tooth-grinding or tooth clenching during sleep.<br>B. One or more of the following is present:<br>1. Abnormal wear of the teeth.<br>2. Jaw muscle discomfort, fatigue, or pain and jaw lock upon awakening<br>3. Masseter muscle hypertrophy upon voluntary forceful clenching.<br>4. Sounds associated with bruxism.<br>C. The jaw muscle activity is not better explained by another current sleep disorder, medical or neurological disorder, medication use, or substance use disorder. | A: Y to grinding/clenching teeth at night (DASLP228)<br>B: Y to dentist noticing teeth worn down OR waking in morning with headache and sore jaw (DASLP229-230) | 1) 2 of DASLP228-230; no dental problems (DASLP236); mild distress or impairment<br>2) 3 of DASLP228-230; dental problems (DASLP236236); moderate distress or impairment<br>2) 3 of DASLP228-230; dental problems (DASLP236236); severe distress or impairment |
| Sleep walking | A. Ambulation occurs during sleep.<br>B. Persistence of sleep, an altered state of consciousness, or impaired judgement during ambulation is demonstrated by:<br>1. Difficulty in arousing the person<br>2. Mental confusion when awakened from an episode<br>3. Amnesia (complete or partial) for the episode<br>4. Routine behaviours that occur at inappropriate times<br>5. Inappropriate or nonsensical behaviours<br>6. Dangerous or potentially dangerous behaviours<br>C. The disturbance is not better explained by another sleep disorder, medical or neurological disorder, mental disorder, medication use, or substance use disorder. | A: Y to reporting sleep walking (DASLP437)<br>B: Y to all NREM indicators (e.g. no memory, difficult to wake, inappropriate behaviours -DASLP438-543) | Unable to rate:<br>No frequency/duration criteria<br>Distress/impairment not included as part of questionnaire |
| Night terrors | A. A sudden episode of terror occurs during sleep, usually initiated by a cry or loud scream that is accompanied by autonomic nervous system and behavioural manifestations of intense fear.<br>9<br>B. At least one of the following associated features is present:<br>1. Difficulty in arousing the person<br>2. Mental confusion when awakened from an episode<br>3. Amnesia (complete or partial) for the episode<br>4. Dangerous or potentially dangerous behaviours<br>C. The disturbance is not better explained by another sleep disorder, medical or neurological disorder, mental disorder, medication use, or substance use disorder. | A: Y to episodes of strong feelings of fear while sleeping (DASLP549) AND increase in heart rate/breathing etc. during episode (DASLP550);<br>B Y to all NREM indicators (DASLP551-553) | 1) <1wk; <1mo; mild distress/impairment<br>2) <7wk; <6mo; moderate distress/impairment<br>3) 7/wk; >=6mo; severe distress/impairment<br><br>*Severity and frequency based on nightmares |

| Disorder | Diagnostic criteria – from ICSD2 unless labelled otherwise | Scoring - Diagnosis | Scoring - Severity |
|---|---|---|---|
| Enuresis | A. The patient is older than five years of age<br>B. The patient exhibits recurrent involuntary voiding during sleep, occurring at least twice a week.<br>C: the condition has been present for at least three months<br>D The patient has never been consistently dry during sleep (for primary)<br>OR the patient has previously been consistently dry during sleep for at least six months (for secondary) | A: all sample >18, all satisfied<br>B: Y to current problem with bedwetting (DASLP579 AND DASLP589), occurring >= 2 times a week<br>C: duration >= 3 months<br>D: not discriminating primary/secondary | 1) frequency 2/wk*; duration <6mo; mild distress/impairment<br>2) 3-4/wk; 6mo-1yr; moderate distress/impairment<br>3) >=5/wk; >=1yr; severe distress/impairment<br>*Frequency anchored on diagnostic criteria |
| REM sleep behaviour disorder | A. Presence of REM sleep without atonia: the EMG finding of excessive amounts of sustained or intermittent elevation of submental EMG tone or excessive phasic submental or (upper or lower) limb EMG twitching.<br>B. At least one of the following is present:<br>1. Sleep related injurious, potentially injurious, or disruptive behaviours by history<br>2. Abnormal REM sleep behaviours documented during polysomnographic<br>C. Absence of EEG epileptic form activity during REM sleep unless RBD can be clearly distinguished from any concurrent REM sleep related seizure disorder.<br>D. The sleep disturbance is not better explained by another sleep disorder, medical or neurological disorder, mental disorder, medication use, or substance use disorder. | Diagnosis:<br>A: Y to acting out dreams (DASLP450) AND move so much that could cause damage to self or partner (DASLP454) OR movements disrupt sleep (DASLP456) | 1) mild distress/impairment<br>2) moderate distress/impairment<br>3) severe distress/impairment<br>No frequency/duration criteria available in diagnostic manuals |
| Nightmares | A. Recurrent episodes of awakenings from sleep with recall of intensely disturbing dream mentation, usually involving fear or anxiety but also anger, sadness, disgust, and other dysphoric emotions.<br>B. Full alertness on awakening with little confusion or disorientation; recall of sleep mentation is immediate and clear.<br>C. At least one of the following associated features is present:<br>1. Delayed return to sleep after the episodes.<br>2. Occurrence of episodes in the latter half of the habitual sleep period<br>3. ICSD3 – causes clinical significant distress or impairment | A: Y to often having nightmares (DASLP612) AND feel frightened/angry/uneasy (DASLP613) OR make feel distressed (DASLP614)<br>B: Y to clearly recall (DASLP615)<br>C: Y difficulty falling back to sleep (DASLP616) OR >0 distress/impairment | 1) frequency <1wk; duration <=1mo; mild distress/impairment<br>2) >=1/wk; <6mo; moderate distress/impairment<br>3) 7/wk; =>6mo; severe distress/impairment<br><br>Severity based on DSM-5 guidelines |

Diagnostic and severity scoring guidelines by disorder for DISP

| Disorder | Diagnostic criteria – from ICSD2 unless labelled otherwise | Scoring - Diagnosis | Scoring - Severity |
|---|---|---|---|
| Sleep-related hallucinations | A: There is a complaint of recurrent hallucinations that are experienced just prior to sleep onset or upon awakening during the night or in the morning.<br>B. The hallucinations are predominantly visual.<br>C. The disturbance is not better explained by another sleep disorder (especially narcolepsy), mental disorder, medical disorder, medication, or substance use. | A Y to seeing or hearing things when falling asleep or waking up currently (DASLP399 AND DASLP409)<br>B: unknown | Indicators = unusual or bizarre; frightening; occurring on waking or after naps; see/hear when drowsy (DASLP400-403)<br>1) 1 indicator; frequency <=1/mo; mild distress/impairment<br>2) 2 indicators; <1/wk; moderate distress/impairment<br>3) 3-4 indicators; >=1wk; severe distress/impairment |
| Sleep paralysis | All ICSD3<br>A. A recurrent inability to move the trunk and all of the limbs at sleep onset or upon awakening from sleep.<br>B. Each episode lasts seconds to a few minutes.<br>C. The episodes cause clinically significant distress including bedtime anxiety or fear of sleep.<br>D. The disturbance is not better explained by another sleep disorder (especially narcolepsy), mental disorder, medical condition, medication, or substance use. | A Y to wake up unable to move as if paralysed (DASLP412) AND greater than 1 occurrence in last year (DASLP419)<br>B unknown<br>C >0 distress or impairment | 1) frequency <=1/mo; mild distress/impairment<br>2) < 1/wk; moderate distress/impairment<br>3) >=1/wk; severe distress/impairment<br>Frequency boundaries based on Sharpless et al 2010 |
| **Excessive sleepiness disorders = hypersomnia OR narcolepsy with OR without cataplexy** | | | |
| Narcolepsy with cataplexy | A. The patient has a complaint of excessive sleepiness occurring almost daily for at least three months.<br>B. A definite history of cataplexy, defined as sudden and transient episodes of loss of muscle tone<br>triggered by emotions, is present<br>C. The diagnosis of narcolepsy with cataplexy should be confirmed by nocturnal polysomnography followed by an MSLT. Alternatively, hypocretin-1 levels in the CSF are less than or equal to 110pg/ mL or one third of mean normal control values.<br>D. The hypersomnia is not better explained by another sleep disorder, medical or neurological disorder, mental disorder, medication use, or substance use disorder. | A: Y to excessive sleepiness >=4/wk (DASLP341) AND Y to sleep attacks >= 4/wk (DASLP348)<br>B: Y to cataplexy reports (DASLP365-394) | 1) mild distress/impairment<br>2) moderate distress/impairment<br>3) severe distress/impairment |

| Disorder | Diagnostic criteria – from ICSD2 unless labelled otherwise | Scoring - Diagnosis | Scoring - Severity |
|---|---|---|---|
| Narcolepsy without cataplexy | A. The patient has a complaint of excessive sleepiness occurring almost daily for at least three months.<br>B. Typical cataplexy is not present, although doubtful or atypical cataplexy-like episodes may be reported.<br>C. The diagnosis of narcolepsy without cataplexy must be confirmed by nocturnal polysomnography followed by an MSLT.<br>D. The hypersomnia is not better explained by another sleep disorder, medical or neurological disorder, mental disorder, medication use, or substance use disorder | A: Y to excessive sleepiness >=4/wk (DASLP341) AND Y to sleep attacks >= 4/wk (DASLP348)<br>B: N to cataplexy reports (DASLP365-394) | 1) mild distress/impairment<br>2) moderate distress/impairment<br>3) severe distress/impairment |
| Hypersomnia | A: Extreme daytime sleepiness (>5/wk for >=3 mo)<br>B: no cataplexy<br>C: An MSLT performed according to standard techniques shows fewer than two sleep onset REM periods or no sleep onset REM periods if the REM latency on the preceding polysomnogram was less than or equal to 15 minutes.<br>D: one of<br>1. The MSLT shows a mean sleep latency of ≤ 8 minutes. OR<br>2. (ICSD3) >=11hr in 24hr sleep period as demonstrated by sleep log and confirmed by actigraphy | A = Y to excessive sleepiness >=4/wk (DASLP341)<br>B: N to cataplexy reports (DASLP365-394)<br>D = >=11hr sleep in 24 hours average reported in sleep diary, confirmed by actigraphy | indicators = always experiencing difficulty waking up (DASLP480c), never feeling awake and refreshed from sleeping (DASLP480d), feeling that sleeping too long (DASLP482)<br>1) duration 3-6mo; 1 of indicators; mild distress/impairment<br>2) >6mo; 2 of indicators; moderate distress/impairment<br>3) >=1yr; 3 indicators; severe distress/impairment |

## 4.4 Sleep-50 agreement with diagnostic interview

| Disorder | Diagnosis % | Diagnosis N | Sleep-50 Average subscale scores (SD) | | |
|---|---|---|---|---|---|
| | | | No diagnosis | Diagnosis | p- value[a] |
| Insomnia | 50.0 | 30 | 15.0 (3.8) | 23.13 (5.7) | .003 |
| Nightmare Disorder | 46.7 | 29 | 6.33 (5.4) | 15.56 (2.6) | .001 |
| Sleep-related hallucinations | 41.7 | 25 | | | |
| Excessive sleepiness | 23.3 | 14 | | | |
| RLS | 23.3 | 14 | 6.60 (2.21) | 7.88 (2.4) | .191 |
| PLM | 20.0 | 12 | | | |
| Bruxism | 18.3 | 11 | | | |
| Sleep paralysis | 15.0 | 9 | | | |
| Night terror | 8.3 | 5 | | | |
| Circadian (Delay/Advance) | 8.3 | 5 | 6.22 (2.4) | 8.0 (2.8) | .326 |
| Sleep walking | 5.0 | 3 | 3.59 (1.0) | 5.0 (1.4) | .082 |
| REMSBD | 3.3 | 2 | | | |
| Enuresis | 1.7 | 1 | | | |

[a]independent sample t-tests

## 4.5 European 5-dimension 5-level health related quality of life questionnaire (EQ5D5L)

The appendix originally presented here cannot be made freely available via ORA because of copyright.

## 4.6 Multi-dimensional Fatigue Symptom Inventory (MFSI)

The appendix originally presented here cannot be made freely available via ORA because of copyright.

## 5.1 Sleep-50 Questionnaire

The appendix originally presented here cannot be made freely available via ORA because of copyright.

## 5.2 Original objectives and analysis plan for clinical longitudinal study

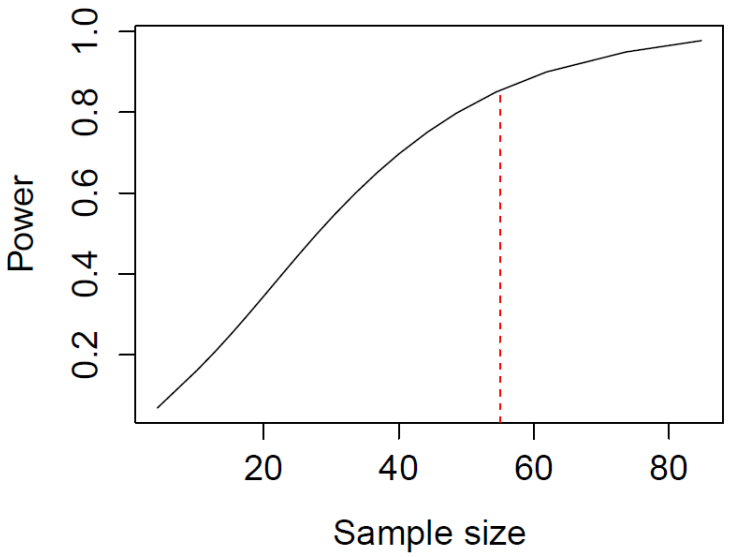
### 5.2.1 Objectives table

| Objectives | Outcome Measures |
|---|---|
| Primary<br>1. Investigate the cross-sectional and longitudinal relationship between insomnia severity and individual psychotic experiences (i.e. paranoia, hallucinations, grandiosity, anhedonia, and cognitive disorganisation) among individuals with non-affective psychosis. [a] | Insomnia severity: Sleep-50<br>Psychotic experiences: SPEQ |
| Secondary<br>2. Investigate the (cross-sectional and longitudinal) relationships between sleep variables (sleep efficiency and total sleep time, as measured by self-report and objective monitoring) and psychotic experiences [a]<br><br>3. Explore whether the relationship between sleep disturbance (insomnia severity, sleep efficiency, sleep time) and psychotic experience is mediated/moderated by mood (depression, anxiety, worry), cognition (jumping to conclusions reasoning bias, working memory) and perception (top down processing) among individuals with non-affective psychosis [a]<br><br>4. Investigate the relationship between sleep duration and psychotic experiences [b] | Sleep efficiency and sleep time: Sleep diary (self report), wristwatch actigraphy (objective activity recording)<br>Psychotic experiences: SPEQ<br><br>Insomnia severity: DISP; Sleep-50;<br>Sleep efficiency and sleep time: Sleep diary, wristwatch actigraphy<br>Psychotic experiences: SPEQ<br>Mood: DASS, Worry scale<br>Cognition: Beads task, N-back task<br>Perception: White noise task, Ebbinghaus task<br><br>Sleep duration: DISP<br>Psychotic experiences: SPEQ |
| Tertiary<br>5. Investigate the (cross-sectional and longitudinal) impact of insomnia symptoms on quality of life (QOL) among individuals with non-affective psychosis [a] | Sleep dysfunction DISP; Sleep-50; subjective recorded sleep diary data; actigraphically recorded sleep/wake variables.<br>QOL: EQ-5D-5L |

## 5.2.2 Analysis Plan

### 5.2.2.1 Sample size

Up to 55 participants will be recruited for Part 1, with the aim that at least 40 will remain at 3 month follow up. Within-subject correlation in repeated measure regression profiles are rarely higher than 0.2 - 0.25 so a pessimal value of 0.3 was used for the sample size calculations. Cohen's method (Cohen, 2003), combined with Rao's variance inflation factor technique to allow for within-subject correlation, was used to produce the graph of Power versus Sample size (assuming 3 repeated measures per subject). The proposed sample size of 55 relating to the primary objective is marked by the red dotted line.




### 5.2.2.2 Analysis

Descriptive statistics for all variables, then objectives addressed as below.

**Objective 1:** We will be fitting a series of 2-level multi-level models (to account for repeated measures on the same patient) for the prediction of each dimension of psychotic experience (one for each of the SPEQ subscales paranoia, grandiosity, hallucinations, anhedonia and cognitive disorganisation) by insomnia severity (Sleep-50 and DISP insomnia subscale scores). Age, gender, depression and anxiety will also be included in each model to control for their effects. Since the responses are on integer scales of fixed length, modelling with linear mixed effects models with folded transformations of the response variables will be tried and multilevel Generalised Linear Models (GLMs) from the binomial family will also be fitted. Careful diagnostic tests will be carried out on both kinds of model in order to

assess their relative quality. All 3 time points will then be entered in this same model with an indicator variable to identify the time point and include interaction terms for that variable with all of the others. This will allow us to test for predictive effects across time.

**Objective 2:** The method will mirror that taken for Objective 1 above, except sleep efficiency (as measured by actigraphy and sleep diary) and/or total sleep time (as measured by actigraphy and sleep diary) will replace insomnia severity from Sleep-50/DISP as predictor variable. We will also carry out exploratory analysis to test the relative predictive strength of sleep efficiency versus total sleep time, and whether these variables as recorded in sleep diary or by actigraphic monitoring hold differing predictive value for psychotic experiences (at the same time or at a later time point). To establish a hierarchy in these predictors we will firstly develop the best fitting linear model, and then use a stepwise method to examine which order of predictors yields the most explanatory value.

**Objectives 3 and 4:** Our approach will again mirror that taken for objective 1 and 2, involving fitting a series of 2-level multi-level models but with mood/cognitive/perceptual factors as dependents rather than SPEQ subscales. We will also explore the possibility of these factors acting as mediators or moderators on the models developed in 1) and 2).

**Objective 5:** Another 2-level multi-level model will be fitted, but with QOL as the dependent variable instead of the SPEQ subscales.

## 6.1 Epworth Sleepiness Scale (ESS)

The appendix originally presented here cannot be made freely available via ORA because of copyright.