The role of sleep problems in psychosis: causal relevance and clinical implications

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27th January 2021

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Plan

1. **Sleep basics**
2. Sleep and mental health
3. Sleep and psychosis – my research
4. Sleep and psychosis – clinical trials

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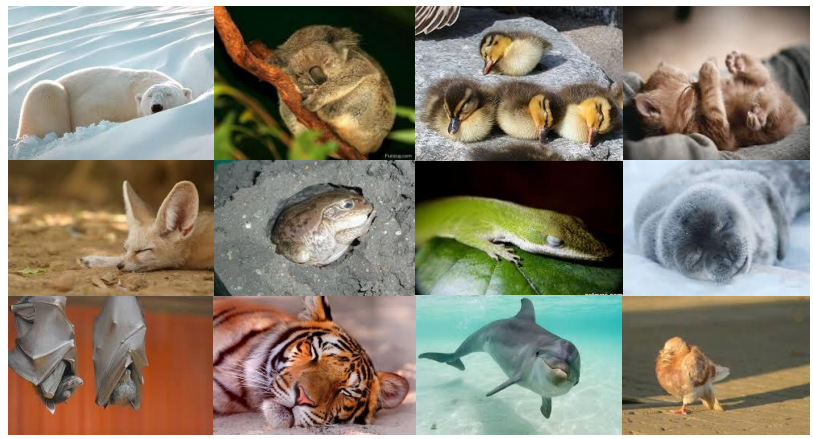
Sleep is fundamental



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Sleep system 1: Sleep pressure

How long have you been awake for?

The longer it is, the more sleep pressure you're under

When sleep pressure gets high enough you **will** fall asleep

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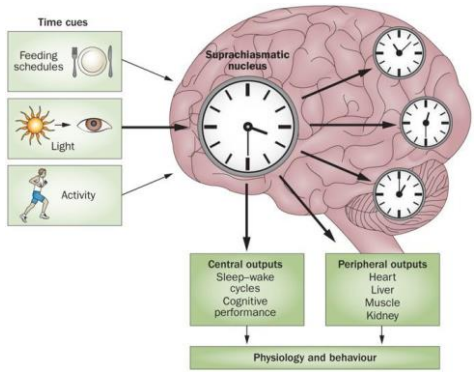
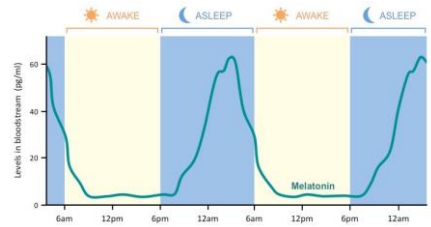
Sleep system 2: Circadian

https://www.youtube.com/watch?v=2BoLqqNuqwA





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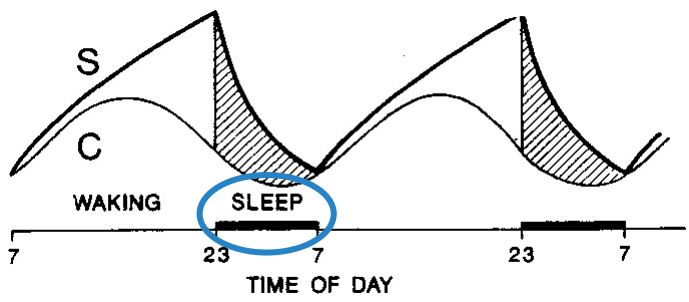
These two systems interact



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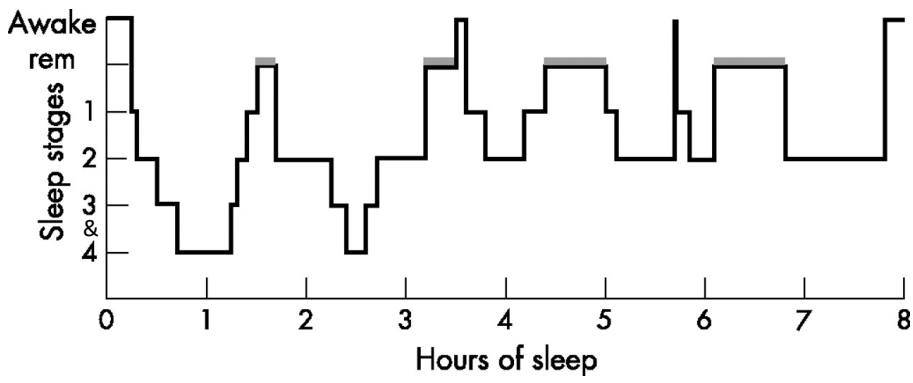
Structure of sleep



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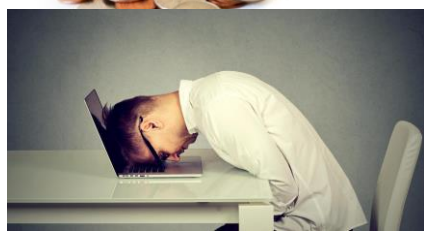
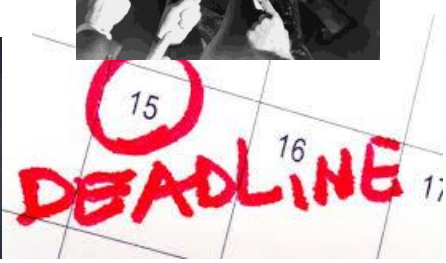
Disrupting system: arousal





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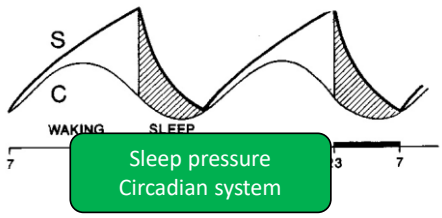
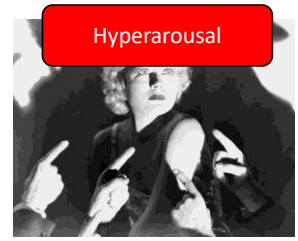
Most sleep work…



Sleep pressure
Circadian system

AND/OR

Hyperarousal



Increasing influence of sleep systems and
Decreasing the influence of disrupting systems
to **ALLOW sleep to happen**

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Sleep disorders

Insomnia	Subjective complaint of difficulty getting to or staying asleep, or waking up too early, despite adequate opportunity for sleep	**6-10%**
Nightmare disorder	Recurrent episodes of waking from sleep with recall of intensely disturbing dream content involving dysphoric emotions (fear, anxiety, anger, sadness)	**5%**
Circadian disorder	Advance /delay/movement of the sleep period in relation to desired sleep and wake time, resulting in inability to stay awake until desired time or wake up at desired time	**<1%** **7-16% YP**
Sleep paralysis	Recurrent inability to move limbs and trunk at onset or on waking from sleep, often accompanied by disturbing imagery or sensations	**7.6% lifetime**
Sleep apnea	Characterised by pauses in breathing or shallow breathing through the night, commonly associated with snoring and resulting in daytime sleepiness and non-restorative sleep.	**~17-22%**
Restless leg syndrome (RLS)	An urge to move the legs (often accompanied by unpleasant sensations) that gets worse in the evening, is relieved by movement, and disrupts sleep	**~1-29%**
Bruxism	Tooth grinding or clenching during sleep, can result in jaw pain or headaches on wakening	**~8-31%**
Night terrors	Sudden episodes of terror during sleep, distinguished from nightmares by amnesia for the episode and a lack of content recall (occurs in NREM sleep).	**30% children** **~1-6% adults**
Sleep walking	Ambulation occurring during sleep—while sleep walking individuals may carry out inappropriate, nonsensical, or dangerous behaviours	**~1-15%**

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Sleep disorder treatments

Insomnia	CBT for insomnia Hypnotic medication only for acute usage (2-4weeks max)	**6-10%**
Nightmare disorder	CBT/imagery rehearsal therapy Some medication (e.g. prazosin)	**5%**
Circadian disorder	Sleep scheduling Medication (e.g. melatonin)	**<1%** **7-16% YP**
Sleep paralysis	CBT/psychoeducation Sleep hygiene	**7.6%** **lifetime**
Sleep apnea	Continuous positive airway pressure (CPAP) Lifestyle changes (reduce weight etc.)	**~17-22%**
Restless leg syndrome (RLS)	Sleep hygiene/relaxation Medications (sort of – iron supplements sometimes work, some others can be tried)	**~1-29%**
Bruxism	Mouthguards Reduce stress/anxiety	**~8-31%**
Night terrors	Sleep hygiene	**30% children** **~1-6% adults**
Sleep walking	Sleep hygiene	**~1-15%**

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Some issues….

Lack of sleep training:

Medicine: median 2hr, ~15% receive none Urquhart et al., 2012

ClinPsy: median 1.5hr, ~10% receive none Meltzer et al., 2009

CBT Therapists: 3hr workshop

Nurses: 20 minutes (n=3 informal sample!)

Lack of sleep awareness:

General population mostly unaware that e.g. insomnia or nightmares can be treated, or assume/demand treatment by medication (Morin et al., 2006, Nadorff et al., 2015)

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Plan

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4. Sleep and psychosis – clinical upshot

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Sleep and mental health

*"Sleep is just **so non-specific**"* – anon. conference attendee

Sleep alongside MH problems historically dismissed

- seen as 'epiphenomenal' i.e. a symptom or result of MH problem only
- seen as 'less severe' than the presenting issue
- extent of sleep issues in MH masked by 'trumping' diagnoses (e.g. schizophrenia) or sleep being included in diagnostic criteria (e.g. depression)
- presumption that MH medication/treatment will fix sleep issues
- or that sleep issues an unchangeable trait (no point trying)

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Sleep and mental health

Which way does the causal relationship go?

1) Do people with sleep problems have more mental health problems?

YES

2) Do sleep problems precede later mental health problems?

YES

3) If we worsen or improve sleep problems in randomised conditions, do we get a corresponding change in mental health?

YES!

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Improving sleep, better MH

DIALS trial (Espie et al., 2019)

1711 participants with insomnia

Randomised to CBT for insomnia (via Sleepio) vs Sleep Hygiene Education (SHE)

Compared to SHE, CBT for insomnia resulted in significant improvements in:

1. Insomnia (d=-1.5)
2. Depression (PHQ9 d=-0.4)
3. Anxiety (GAD7 d=-0.3)
4. + many more outcomes

Espie et al. (2019). Effect of Digital Cognitive Behavioural Therapy for Insomnia on Health, Psychological Well-being, and Sleep-Related Quality of Life: A Randomized Clinical Trial. JAMA Psychiatry.

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Sleep as new MH target

Preventative (e.g. Freeman et al., 2017)
- Sleep problems occur early in course of a range of MH problems
- Non-stigmatising to access treatment for
- Knock on benefits for physical health etc.

Chronic/concurrent (e.g. Christensen et al., 2016)
- Sleep problems exacerbate other MH issues
- Sleep problems can interfere with other MH treatment
- Sleep problems don't always improve with other MH treatment
- Sometimes, people want help with sleep above their 'more serious' MH

Acute (e.g. Sheaves et al., 2018)
- Sleep can be improved in this setting
- Can reduce need for polypharmacy
- Sleep loss can be a trigger for acute exacerbation of symptoms – relapse prevention
- Engagement easier than with some other treatments

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Plan

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4. Sleep and psychosis – clinical trials

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Setting

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OXFORD COGNITIVE APPROACHES TO PSYCHOSIS

Freeman (2016) Persecutory delusions: a cognitive perspective on understanding and treatment. Lancet Psychiatry.

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Background as of 2014

We knew that

- Sleep problems and psychotic experiences co-occur
- Sleep problems predict subsequent psychotic experiences

But only limited evidence for causal contribution:

- Total sleep deprivation does lead to psychotic experiences
  - But that's pretty extreme (and uncommon)

So, first study was to test causal role of insomnia in psychosis…

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.

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Do sleep problems cause psychosis?

68 non-clinical (MH screened) participants going through below conditions:

- Restricted sleep (4hrs/night for 3 nights)
- Normal sleep (whatever they normally got)

Compared to normal sleep condition, when sleep restricted ….

- Paranoia was significantly increased (d=0.4)
- Hallucinations were significantly increased (d=0.8)
- Depression and anxiety increases mediated psychotic experience increases

Reeve et al. (2018). Disrupting Sleep: The Effects of Sleep Loss on Psychotic Experiences Tested in an Experimental Study With Mediation Analysis. Schizophrenia Bulletin.

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Sleep disorders in psychosis

We know there is a high prevalence of sleep disorders in psychosis

- e.g. Insomnia 30% (versus 6-10% general population)

BUT

Studies tend to only look at one (usually insomnia) and our clinical experience was of multiple sleep problems as norm

AND

We don't know if/to what extent sleep problems being addressed in routine care for people with psychosis?

So: diagnostic sleep disorder interview with 60 individuals with non-affective psychosis (recruited via local MH services)

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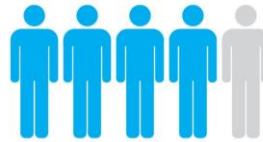
Sleep disorders in psychosis are common, and comorbid

Eight out of ten screened positive for a sleep disorder diagnosis



Of those, four in five have more than one sleep disorder (i.e. 64% of whole sample)

Reeve S, Sheaves B, Freeman D (2019). Sleep disorders in early psychosis: incidence, severity, and association with clinical symptoms. Schizophrenia Bulletin.

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…varied, severe….

Sleep problem	Diagnosis %	Diagnosis n	N (%) of which severe
Insomnia	50.0	30	17 (60.0)
Nightmare Disorder	48.3	29	16 (55.2)
Sleep-related hallucinations	41.7	25	16 (64.0)
Excessive sleepiness	23.3	14	9 (64.3)
RLS	23.3	14	7 (50.0)
PLMS	20.0	12	n/a
Bruxism	18.3	11	3 (27.3)
Sleep paralysis	15.0	9	3 (33.3)
Night terror	8.3	5	4 (80.0)
Circadian	8.3	5	1 (20.0)
Sleep walking	5.0	3	n/a
REMSBD	3.3	2	0 (0.0)
Enuresis	1.7	1	1 (100.0)
Any sleep disorder	**80**	**48**	-
Total	**-**	**160**	**77 (52.0)**

Reeve S, Sheaves B, Freeman D (2019). Sleep disorders in early psychosis: incidence, severity, and association with clinical symptoms. Schizophrenia Bulletin.

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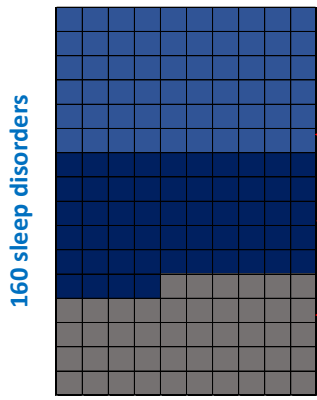
Have you discussed this problem with a healthcare professional?



Discussed with clinician (n=60, 38%)

Not discussed with clinician (n=54, 34%)

Not sure (n=46, 29%)

Reeve S, Sheaves B, Freeman D (2019). Sleep disorders in early psychosis: incidence, severity, and association with clinical symptoms. Schizophrenia Bulletin.

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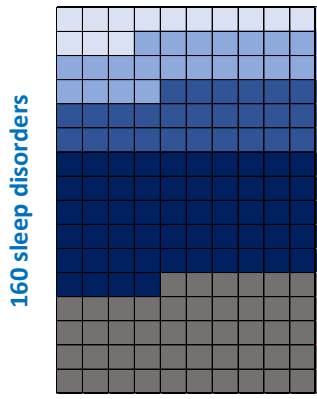
…rarely treated…

Have you discussed this problem with a healthcare professional?



Received **recommended treatment** (n=13, 8%)

Received **any treatment** (n=34, 21%)

Discussed with clinician (n=60, 38%)

Not discussed with clinician (n=54, 34%)

Not sure (n=46, 29%)

Reeve S, Sheaves B, Freeman D (2019). Sleep disorders in early psychosis: incidence, severity, and association with clinical symptoms. Schizophrenia Bulletin.

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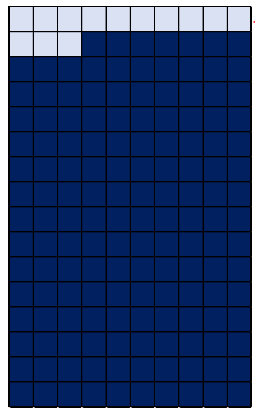
…and poorly treated



Received **recommended treatment** (n=13, 8%)

- N=5 insomnia: hypnotic medication
- N=4 bruxism: dentist providing mouthguard
- N=1 enuresis: about to have surgery
- N=2 nightmares: CBT/IRT in our trial
- N= 1 insomnia: CBT in our trial

Only treatment offered by MH team was hypnotic medication
(contrary to NICE guidelines)

Reeve S, Sheaves B, Freeman D (2019). Sleep disorders in early psychosis: incidence, severity, and association with clinical symptoms. Schizophrenia Bulletin.

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The main questions

We have (psychological) treatments for the most common problems

- Insomnia (CBTi)
- Nightmares (CBT plus imagery rehearsal therapy)

So

1. Do these treatments have acceptability/feasibility/efficacy at treating sleep problems in psychosis populations?
2. Do these treatments lead to improvements in psychotic symptoms or other clinical issues?

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1: Better Sleep Trial (BeST RCT)

50 outpatients with

- Schizophrenia spectrum diagnosis
- Persistent and distressing delusions and hallucinations
- Insomnia

Aim: assess acceptability/feasibility of sleep intervention, initial estimates of efficacy

Randomly allocated to CBTi + TAU vs TAU

96% of patients offered CBT completed therapy

CBT led to

- **Large** reductions in insomnia symptoms (d=-1.9)
- **Unclear** impact on psychotic symptoms (effect size d=+0.3, CI -2 to +2.6 for delusions, d=-2.9, CI -6.5 to +2.7 for hallucinations)

Freeman et al., (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. Lancet Psychiatry.

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Treatment adaptations (BEST)

Practical assistance with sleep environment

Increasing daytime activity

Reducing use of bed as escape

Use of light and other circadian cues to schedule the day

Waite et al., (2016). Treating Sleep Problems in Patients with Schizophrenia. Behavioural and Cognitive Psychotherapy.

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2: OWLS RCT

40 inpatients on acute ward with
- Insomnia
- Any diagnosis

Aim: assess acceptability/feasibility of sleep intervention, initial estimates of efficacy

Randomly allocated to STAC (sleep treatment at acute crisis, 2 week long intervention) + TAU vs TAU alone

100% of participants offered STAC completed treatment

STAC led to:
- **Large** reductions in insomnia symptoms (d=-0.9)
- **Small** improvements in wellbeing (d=+0.3)
- **Earlier discharge** (-8.5 days average vs control group)

Sheaves et al., (2018) Stabilising sleep for patients admitted at acute crisis to a psychiatric hospital (OWLS): an assessor-blind pilot randomised controlled trial. Psychological Medicine.

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Treatment adaptations (OWLS)

Working with ward on checks, medication, activity prompts

Increasing daytime activity

Sleep monitoring via devices – immediate feedback and assessment

Managing discharge (planning for sleep challenges at home)

Sheaves et al., (2018) Adapted CBT to Stabilize Sleep on Psychiatric Wards: a Transdiagnostic Treatment Approach. Behavioural and Cognitive Psychotherapy.

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3: NiteS (Nightmares) RCT

24 outpatients with
- Nightmares
- Persecutory delusions

Aim: assess acceptability/feasibility of sleep intervention, initial estimates of efficacy

Randomly allocated to immediate CBT for nightmares + TAU vs waitlist + TAU

100% of participants offered CBT completed therapy

CBT for nightmares resulted in
- **Large** improvements in nightmares (d=-1.1)
- **Large** reductions in insomnia (d=-1.4)
- **Small (n.s.)** reductions in paranoia (d=-0.5)

Sheaves et al., (2019) Cognitive Behavioural Therapy for Nightmares for Patients with Persecutory Delusions (Nites): An Assessor-Blind, Pilot Randomized Controlled Trial. Psychological Medicine.

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Treatment adaptations (Nites)

Psychoeducation about nightmares

Reducing nightmare preoccupation/rumination

Grounding from nightmares

Rescripting of nightmare content

Sheaves et al., (2019) Cognitive Behavioural Therapy for Nightmares for Patients with Persecutory Delusions (Nites): An Assessor-Blind, Pilot Randomized Controlled Trial. Psychological Medicine.

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4: SleepWell pilot case series

12 young people (age 14-24)

- Ultra high risk of psychosis (CAARMS assessment)
- Current sleep problems

Aim: assess acceptability/feasibility of treatment for sleep problems

11/12 (91.6%) completed the intervention

Treatment resulted in

- **Large and sustained** improvements in sleep (pre-post, d=6.8 on ISI)
- **Indicated improvements** in depression (d=-0.5), anxiety (d=-0.2), wellbeing (d=+0.7), paranoia (d=-0.6) and hallucinations (d=-0.3) – but all CIs include 0 so caution in interpretation.

Bradley et al., (2017) Treating Sleep Problems in Young People at Ultra-High Risk of Psychosis: A Feasibility Case Series. Behavioural and Cognitive Psychotherapy.

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Treatment adaptations (at-risk)

Circadian focus

Check-ins between sessions (texting/phone calls) to maintain goals

Device usage in bed

Working with family – 'sleep team'

Bradley et al., (2017) Treating Sleep Problems in Young People at Ultra-High Risk of Psychosis: A Feasibility Case Series. Behavioural and Cognitive Psychotherapy.

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Clinical reflections

(Relatively) easy to recruit, common-sense rationale: 'when we sleep better we feel better' shared by all parties.

(Relatively) straightforward, targeted, practical treatment - appealing for patients and clinicians.

Side-benefits include

- Building trust
- Building engagement/understanding of ways of working (on both sides)
- Plus reduces other appointments missed due to sleep issues

Springboard for thinking about physical health in general (activity, drinking/drugs/smoking/diet – all can be explored via sleep work)

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Concerns (and rebuttals)

Tried sleep hygiene, didn't work

- Sleep hygiene on its own is **not effective** (especially in worksheet form!) – need to take sleep seriously as a proper intervention, build it around the individual and their problems

We're not supposed to be treating sleep

- Treating sleep will lead to a lot of benefits; good way to engage; as brief starter to other treatment?

Patients won't be able to (psychotic symptoms/chaotic lifestyle will get in the way)

- Our trials say otherwise! Key is remembering standard therapy skills – one step at a time, encouragement, generating willingness to try out something different
- Sleep can give motivation/opportunity to address these same factors via shared goal

Medication should be helping with sleep anyway

- Antipsychotic medication does improve sleep duration and sleep quality, but not enough – majority of patients in all this research were taking antipsychotic medication, still may had severe sleep issues.
- (also NB sedation ≠ better sleep)

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5. OASIS study (non-psychosis population)

3755 university students with insomnia

Aim: determine if treating insomnia leads to a reduction in paranoia and hallucinations

Randomised to online CBTi (Sleepio) or usual care

Treatment led to

- **Large** reductions in insomnia (d=-1.1)
- **Small** reductions in paranoia (d=-0.2) and hallucinations (d=-0.2)
- **Moderate** reductions in depression (d=-0.5) and anxiety (d=-0.3)
- **Moderate** improvements in functioning (d=+0.5) and wellbeing (d=+0.3)

Freeman et al., (2017) The effects of improving sleep on mental health (OASIS): a randomised controlled trial with mediation analysis. Lancet Psychiatry.

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Upshot as of January 2021

Sleep problems are common and severe among people with psychosis

Sleep problems **are** treatable in this group, with sensible adaptation of existing CBT protocols

- The treatment is both effective and popular (>90% uptake of treatment in our studies so far, self-rated priority in Freeman et al., 2019 patient survey, n=1809)
- Sleep problems should be treated in their own right (DSM-5 guidance)

Treating sleep **may also** improve psychotic symptoms

- Causal relationship demonstrated in non-clin population (i.e. worsening sleep worsens psychotic experiences, improving sleep improves psychotic experiences)
- No study **yet** adequately powered to show improving sleep improves psychotic symptoms in clinical population but strong indications that it also helps here

Clinical services should be routinely assessing and treating sleep problems in psychosis

Waite F, Sheaves B, Isham L, Reeve S, Freeman D (2019) Sleep and schizophrenia: From epiphenomenon to treatable causal target. Schizophrenia Research

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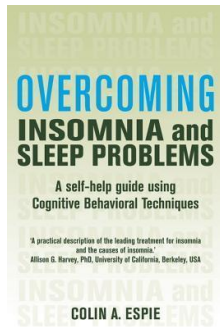
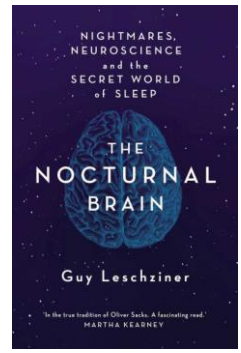
Reading





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Acknowledgements

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especially supervisors Prof Daniel Freeman and Dr Bryony Sheaves

Funding:

MRC Medical Research Council

DEPARTMENT OF PSYCHIATRY
Medical Sciences Division
UNIVERSITY OF OXFORD

BALLIOL COLLEGE
UNIVERSITY OF OXFORD

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Thank you!

Please go to menti.com and use the code **69 46 51 7** to (anonymously) answer:

'What is your ONE takeaway from today? How will you put it into practice?'

Also, questions?

Email for contact: sarah.reeve.18@ucl.ac.uk

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