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THEORETICAL REVIEW

Neural correlates of insight in dreaming and psychosis

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SUMMARY

The idea that dreaming can serve as a model for psychosis has a long and honourable tradition, however it is notoriously speculative. Here we demonstrate that recent research on the phenomenon of lucid dreaming sheds new light on the debate. Lucid dreaming is a rare state of sleep in which the dreamer gains insight into his state of mind during dreaming. Recent electroencephalogram (EEG) and functional magnetic resonance imaging (fMRI) data for the first time allow very specific hypotheses about the dream–psychosis relationship: if dreaming is a reasonable model for psychosis, then insight into the dreaming state and insight into the psychotic state should share similar neural correlates. This indeed seems to be the case: cortical areas activated during lucid dreaming show striking overlap with brain regions that are impaired in psychotic patients who lack insight into their pathological state. This parallel allows for new therapeutic approaches and ways to test antipsychotic medication.

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Introduction

Rapid eye movement (REM) sleep is the sleep stage associated with the most vivid and intense dreams. These internally generated perceptions and emotions typically show many cognitive peculiarities, with a bizarre plot, delusional thought, and a complete lack of insight into the true state of the subject. In this regard, dreaming resembles the psychosis of mental illness such as schizophrenia, characterized by hallucinations, loosening of associations, incongruity of personal experience, and a loss of self-reflective capacity [1,2]: both the psychotic patient and the dreamer fail to discern self-generated from non-self-generated percepts, and uncritically accept bizarre experiences as real [3].

The idea that dreaming can indeed serve as a model for psychosis has a long and honourable tradition: Kant [4] likened the madman to a waking dreamer, Schopenhauer [5] considered the dream a brief madness and madness a long dream, and also modern psychiatrists such as Bleuler, Kraepelin, Freud or Jung stressed the

similarities between dreaming and psychosis [6]. While these historical proposals to consider dreaming as a model for psychosis are notoriously speculative, they are supported by recent studies of dream phenomenology: dream reports of healthy subjects include more quasipsychotic experiences than their reports of experiences during wakefulness [7], and striking similarities in cognitive bizarreness measures were found between the waking thought of psychotic patients and dream reports of either patients or healthy controls [6,8–12]. In other words, whereas healthy subjects experience strong fluctuations of bizarre and hallucinated cognitive elements across the sleep–wake cycle, psychotic patients continuously experience such dream-like mentations during both waking and dreaming [13]. Interestingly, also during wakefulness, psychotic patients consider their dream reports as being less bizarre than healthy controls do, despite a similar density of bizarre elements as scored by external judges [14]. In addition, similarities between REM sleep and schizophrenia can also be observed at the neurobiological level [15], in particular noradrenergic demodulation was proposed to contribute to the cognitive disturbances that occur during dreaming and psychosis [16].

Insight in dreaming and psychosis

One of the most interesting aspects of the dreaming–psychosis model is the issue of insight: between 50 and 80% of the patients diagnosed with schizophrenia have poor insight into the presence

Abbreviations: EEG, electroencephalogram; fMRI, functional magnetic resonance imaging; MRI, magnetic resonance imaging; NREM sleep, non-REM sleep; REM sleep, rapid eye movement sleep; VBM, voxel-based morphometry.

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of their disorder [17], probably due to ineffective self-reflection processes [18]. Since such deficits are thought to lead to more relapses and rehospitalisations and poorer therapy success in general [19], the concept of insight is becoming an increasingly important area of investigation in schizophrenia research [20].

On the dreaming side of the model, lack of insight into the current state can be seen as a hallmark of dream cognition, characterizing almost any dream experience. From a theoretical point of view, this metacognitive deficit was proposed to be the most interesting feature of the dream state [21]. However in contrast to normal dreaming, a special kind of sleep mentation is characterized by a reinstatement of reflective capacity: during lucid dreaming, the sleeping subject becomes fully aware of his or her true state [22]. A lucid dreamer recognizes dream hallucinations as such. Despite this wake-like reflection, lucid REM sleep comprises all defining markers of REM sleep proper [22] and all basal dream features such as visuomotor hallucinations [23] – in fact, prototypical aspects of dream phenomenology such as bizarreness might even be more pronounced in lucid dreams [24]. This suggests that lucidity may be a good model for insight in the dreaming–psychosis model. Interestingly, historical approaches to psychosis used the term ‘lucidity’ to denote the awareness of the patient into his illness [25]. While the specific composition of the multiple facets of insight in psychosis is still under discussion [26–28], two crucial dimensions are classically considered to be the recognition that one has a mental illness and the ability to recognize unusual mental events (delusions and hallucinations) as pathological [29]. Hence, in the dreaming–psychosis model, lucidity during dreaming represents what patients during psychosis lack: full insight into the delusional nature of the current state of consciousness during that state.

This parallel between insight deficits in dreaming and psychosis allows for a new empirical test of the dreaming–psychosis model: If the model holds, insight into the current state of mind should share similar neural correlates during both dreaming and psychosis. Lucid dreaming can be trained [30,31], which makes this phenomenon a promising research topic despite the rarity of its occurrence in untrained subjects [32,33]. Two recent neurobiological studies on lucid dreaming show that significant results can be obtained even in limited subject samples [34,35]. These results can be compared with neurobiological studies of psychotic patients with insight deficits to critically evaluate the dreaming–psychosis model on a neural level. Thus, the specific hypotheses derived from the dreaming–psychosis model can be stated as follows: 1) neural correlates of dream insight (i.e., lucid dreaming) largely overlap with neural correlates of insight into the psychotic state. 2) means to achieve lucidity during normal dreaming will increase insight into the pathological state in psychotic patients. While the latter hypothesis has to be tested empirically with new studies, the former can be evaluated by reviewing the neuroscientific literature on dreaming and psychosis.

The dreaming brain

Dream-like mental activity can be observed during all sleep stages, however REM sleep dreams are particularly vivid and intense. The specific phenomenal characteristics of dreaming have frequently been associated with neural activation patterns observed during REM sleep. For example, during normal REM sleep, higher visual and motor areas show strong metabolic activity [36,37], which is in line with visuomotor hallucinations as the hallmark of typical dreaming [38]. Also the amygdala, medial prefrontal cortex and anterior cingulate cortex show increased activity during REM sleep [36,37]. All these brain areas have been implicated in emotional processing, nicely mirroring the intense

emotions experienced in many dreams [38]. In contrast, the dorsolateral prefrontal cortex, parietal areas including the supra-marginal cortex and precuneus, and the cingulate cortex show low metabolic rates during REM sleep [36,37]. In particular prefrontal deactivations have been postulated to underlie cognitive deficiencies typical of ordinary dreaming such as impaired critical thinking and restricted volitional capacities [38,39]. Growing evidence suggests that many behaviors share similar neural substrates during wakefulness and dreaming [40]. For example, dreamed hand movements activate the contralateral motor cortex consistent to their respective neural activations related to actually executed hand movements during wakefulness [33]. In recent years, network analyses of neuroimaging data have prompted new insights into the principles of brain organization during wakefulness and sleep. A recent meta-analysis has pointed out a striking overlap between brain regions that show increased metabolism during REM sleep and regions of the default mode network [41].

The lucid brain

While lucid dreaming is characterized by all coarse electroencephalogram (EEG) features of REM sleep according to classical sleep stage scoring [42], brain activity during lucid REM sleep shows distinctive changes compared to non-lucid REM sleep. Fig. 1 shows the increased EEG activation that was observed over the right dorsolateral prefrontal cortex during lucid dreaming [34]. In this study, three subjects out of 20 undergraduate students participating in three months of lucidity training were able to become lucid in the laboratory setting. Results showed lucid dreaming to have higher-than-REM activity in the gamma band, the between-states-difference peaking around 40 Hz. Overall EEG coherence levels during lucid dreaming were significantly higher than in non-lucid REM sleep. Both power in the 40 Hz band and coherence levels were strongest over the dorsolateral prefrontal region.

Fig. 2 illustrates activation increases during lucid as compared to non-lucid REM sleep in a combined functional magnetic resonance imaging (fMRI)/EEG approach [35]. In this study, four experienced lucid dreamers slept several nights in a magnetic resonance imaging (MRI) scanner under concurrent polysomnography. One subject had two episodes of verified lucid REM sleep of sufficient length to be analyzed by fMRI. Insight into the dreaming state was associated with activation in a network of purely neo-cortical regions including the dorsolateral and frontopolar prefrontal cortex, thus confirming the Voss et al. data. Strong activation increases during lucid dreaming were also observed in parietal regions including the precuneus, inferior parietal lobules and supra-marginal gyrus and in occipito-temporal regions including the inferior/middle temporal gyri and lingual gyri. Prefrontal and parietal regions are involved in most higher cognitive processes like intelligence or working memory [43], in particular the dorsolateral prefrontal cortex has been associated with metacognitive evaluation [44,45]. The precuneus has been proposed to be the pivotal region involved in self-referential processing [46]. The frontoparietal activation pattern observed during lucid REM sleep therefore nicely mirrors the reinstatement of reflective capabilities experienced during lucid dreaming. In contrast to the default mode network-like activation patterns of normal REM sleep [41], brain regions activated during lucid dreaming comprise substantial parts of the frontoparietal control network [35]. This network has been postulated to integrate information coming from both the default mode and attention networks by switching between competing internally and externally directed processes [47]. Due to this role as a kind of meta-network, the frontoparietal control network might

Fig. 1. Quantitative EEG data of lucid dreaming. Shown is Gamma 40 Hz standardized current source density power during wakefulness, lucid rapid eye movement (REM) sleep, and non-lucid rapid eye movement (REM) sleep. The dorsolateral prefrontal cortex during lucid dreaming shows similar 40 Hz power as during wakefulness. Republished with permission of the American Academy of Sleep Medicine from Voss et al., 2008 [34], permission conveyed through Copyright Clearance Center, Inc.

be seen as an ideal candidate subserving processes of metacognition like dream lucidity [48].

The psychotic brain

During recent years, an increasing number of approaches has shed light on the neural mechanisms underlying impaired insight in psychotic patients. Numerous neuropsychological studies on schizophrenia observed a relationship between insight deficits and impaired performance in cognitive tasks primarily mediated by the prefrontal cortex [49,50].

Several neuroimaging studies confirmed an association of prefrontal brain areas with impaired insight in psychotic patients, however revealed also parietal areas and other brain regions to be relevant in this regard. A study assessing 11 schizophrenia patients with fMRI during a self-evaluation task found neural activation in the left superior frontal gyrus, right middle frontal gyrus, and the bilateral precuneus to be associated with insight [51]. Another fMRI study assessing 47 schizophrenia patients during a self-reflection task demonstrated that neural activation in the left inferior frontal gyrus, left insula, left inferior parietal lobule and left angular gyrus is correlated with insight [52]. During a clinical insight task, fMRI-measured neural activation in the medial prefrontal cortex, the posterior cingulate cortex and the frontopolar cortex correlated with insight in 21 schizophrenia patients [53]. In an fMRI study that aimed to examine insight as response to a simulation of hallucinatory experiences, 16 schizophrenic patients differed from 17 healthy controls in their brain activation patterns in the anterior cingulate, left frontopolar cortex, left occipito-temporal junction, and right amygdala [54]. In a longitudinal study, 14 schizophrenic patients underwent an fMRI scan during an acute episode of psychosis and again after clinical improvement. Increased activation of the left medial prefrontal cortex and right lingual gyrus in the follow-up session was significantly correlated with improvement in insight scores [55].

Functional differences in brain activity associated with impaired insight in psychosis have not only been reported for task-related study designs, but also for task-free scans: during resting state fMRI, 19 schizophrenia patients with low insight when compared to 25 patients with good insight showed impaired connectivity of the anterior cingulate cortex within the anterior component and of the precuneus within the posterior component of the default mode network [56]. Such precuneus-centered connectivity changes associated with impaired insight are in line with a diffusion-based investigation of 36 patients with schizophrenia spectrum disorders demonstrating white matter deficits adjacent to the right precuneus to be related to lack of insight [57].

The majority of neuroimaging studies of insight deficits in psychosis focused on structural measures. An early computed tomography study found significant correlations between frontal lobe atrophy and insight measures in 20 schizophrenia patients [58]. A volumetric MRI study manually tracing frontal regions in 28 schizophrenia patients revealed significant correlations of grey matter volumes with insight scores, in particular for the right superior frontal gyrus [59].

A morphometric MRI study comparing 18 schizophrenia patients with poor insight to 17 patients with good insight into their condition revealed manually assessed decreases in right dorsolateral prefrontal cortex grey matter volumes to be associated with insight deficits [60]. When frontal lobe subregions were manually traced in 15 schizophrenia patients, unawareness of illness was found to be specifically associated with decreased volumes of bilateral middle frontal gyri, right gyrus rectus and left anterior cingulate gyrus, while symptom misattribution was tied to smaller bilateral superior frontal gyrus volumes [61].

A voxel-based morphometry (VBM) study with 35 paranoid schizophrenia patients found grey matter reductions in the left posterior and right anterior cingulate cortex and bilateral inferior temporal gyri to be associated with poor insight [62]. Another VBM

Fig. 2. functional magnetic resonance (fMRI) imaging data of lucid dreaming. During lucid rapid eye movement (REM) sleep, dorsolateral prefrontal and frontopolar regions including the inferior, middle and superior frontal gyri, parietal regions including the precuneus, inferior parietal lobule and supramarginal gyrus, and temporal regions including the inferior and middle temporal gyri activated strongly as compared with non-lucid rapid eye movement (REM) sleep. Republished with permission of the American Academy of Sleep Medicine from Dresler et al., 2012 [35], permission conveyed through Copyright Clearance Center, Inc.

study with 21 first-episode psychosis patients demonstrated an association between unawareness of the disorder and grey matter volume reductions in bilateral superior frontal gyri, right inferior frontal gyrus, right inferior temporal gyrus and left cerebellum [63]. When several self-reported and observer-rated aspects of insight were compared to VBM-measured grey matter volumes in 52 schizophrenia spectrum disorder patients, the ability to recognize experiences as abnormal was found to be related to right superior temporal gyrus volumes, awareness of problems was found to be related to the left precuneus volume, while awareness of symptoms and attributing them to illness was found to be related to grey matter volumes in the left superior-middle temporal gyrus, the right inferior temporal gyrus, the right inferior parietal lobule, and the right supramarginal gyrus [64]. A VBM study assessing 82 psychotic patients did not find significant correlations between grey matter volume in any brain subregions and insight measures, however when comparing 20 psychotic patients with a complete lack in symptom relabeling ability with 62 psychotic patients with at least some such ability, differences were found in the left insula, bilateral superior temporal gyrus, bilateral posterior cingulate gyrus, bilateral superior parietal lobule, bilateral precuneus, right cuneus and medial occipital gyrus [65].

A recent cortical thickness study with 52 first-episode psychosis patients demonstrated various symptom misattributions to be related with reduced thickness of the left middle frontal gyrus, left inferior temporal gyrus, and bilateral precuneus [66]. With the same method, the authors found in 79 first-episode psychosis patients that poorer awareness of illness was associated with regional thinning in left middle and inferior frontal gyri, bilateral precentral gyri, left inferior temporal gyrus and right inferior occipital gyrus, while poorer awareness of treatment need was associated with cortical thinning in left middle frontal gyrus, right inferior frontal gyrus, bilateral paracentral lobules, bilateral precuneus, bilateral supramarginal gyri, bilateral superior temporal gyri, left inferior and middle temporal gyri, bilateral parahippocampal gyri, right lingual gyrus, right fusiform gyrus, and left middle occipital gyrus [67].

Two studies focused their analysis on very specific regions: manually segmented bilateral hippocampal volumes correlated with self-certainty subscale of the Beck cognitive insight scale in 61 first-episode psychosis patients [68], while right posterior insular volumes were related to the degree of insight in 57 schizophrenia patients [69]. Of note, while all structural data reviewed so far demonstrated positive associations between insight and grey matter volumes – the less grey matter, the less insight –, three studies reported negative correlations between insight and grey matter volumes in a variety of brain regions including the orbitofrontal cortex [65], bilateral caudate, right thalamus, left insula or putamen [70]. Furthermore, several studies restricted their analysis to whole brain grey matter volume or ventricles only [71–75] or failed to find any association with insight measures [76].

Insight in dreaming and psychosis: neural similarities

On first sight, this short literature review presents a rather scattered picture, with a great variety of brain regions found to be involved in insight deficits in psychosis. However, the most robust findings seem to be prefrontal, medial parietal and cingulate cortex contributions underlying insight deficits in psychosis. Interestingly, grey matter volume reductions in frontal and parietal regions are not only state markers of insight deficits, but also have predictive value: In a longitudinal study of 53 adolescent schizophrenia spectrum disorders patients, frontal and parietal grey matter volumes at baseline predicted insight deficits after two years [77]. Of note, also in neurological disorders disturbed insight has been

associated with frontal and parietal regions, particularly of the right hemisphere [78].

While for all brain regions associated with lucid dreaming at least one study demonstrated involvement of the respective region also in psychotic insight deficits, a more specific picture emerges if only brain regions are considered whose association with psychotic insight deficits has been replicated at least once with the same or a different modality: the dorsolateral and frontopolar prefrontal cortices in general and specifically the bilateral superior, bilateral middle and right inferior frontal gyri, and the bilateral medial prefrontal cortex, the bilateral anterior and posterior cingulate cortices, the bilateral precuneus, the bilateral superior, left middle and bilateral inferior temporal cortices, and the right lingual gyrus. Of these regions, the medial prefrontal and anterior cingulate cortices show strong activity already in non-lucid REM sleep. In contrast the superior, middle and inferior frontal gyri and the precuneus are downregulated in non-lucid REM sleep, however become strongly activated during lucid dreaming. Lateral temporal regions do not undergo major activation changes during non-lucid REM sleep compared to wakefulness or non-REM sleep (NREM sleep), however the inferior and middle temporal gyri show activation increases during lucid dreaming.

To summarize, the empirical findings reviewed here constitute neurobiological evidence of the theoretical idea that dreaming indeed might serve as a model of psychosis: cortical, in particular prefrontal, medial parietal and inferior temporal regions that are linked to insight problems in psychosis show striking overlap with brain regions in which activation increases during dreaming are associated with the gain of insight into the current state of mind (see Fig. 3). From a network point of view, schizophrenia patients show disconnectivity within the frontoparietal network and stronger connectivity within the default mode network [79,80], with the exception of default mode network regions implicated in self-referential processing, within which patients with poor insight show decreased connectivity [56].

Only two brain regions have repeatedly been associated with insight deficits in psychosis, but do not seem to be strongly activated during lucid REM sleep: the superior temporal gyrus and the posterior cingulate cortex. Abnormalities in the superior temporal gyrus are the most common finding in schizophrenia in general [81], which might lead to confounds through general illness severity in insight studies. Furthermore, schizophrenia has recently been demonstrated to be associated with an anterior-to-posterior shift in introspection-related activation, leading to a more pronounced involvement of the posterior cingulate in schizophrenia patients compared to healthy controls [82]. However, both explanations for the mismatch of these two regions in the dreaming—psychosis model remain speculative. Laboratory studies with lucid dreamers mostly remain on the level of case studies so far, rendering all conclusions about the neural correlates of dream lucidity preliminary. More research on the brain basis of lucid dreaming with larger sample sizes is needed, which would also allow for a more specific approach to dream insight: if different aspects of dream lucidity could be differentially associated with their neural correlates [83], these could in turn be compared with neural correlates of specific insight subscales in psychotic patients.

Clinical implications

Since the majority of studies support the assumption that insight in schizophrenia is associated with compliance during treatment [19], interventions to promote insight are thought to be crucial for therapy success [20]. Insight deficits in psychosis have been targeted with a great variety of interventions, however there is still a paucity of reliable data on successful treatment options

Fig. 3. Dreaming as a model for psychosis, lucid dreaming as a model for insight into the psychotic state. Regions in which neural correlates of insight into the dreaming state (i.e., lucid dreaming) and insight into the psychotic state show reliable overlap. For brain regions that have been involved in one state, but not the other, see discussion.

[84]. Interventions with at least some empirical support include pharmaceuticals [75], psychoeducation [85], cognitive-behavioral therapy [86,87], videotaped self-observation [88,89] and meta-cognitive training [90,91]. It has been demonstrated that prefrontal cortex function in schizophrenia patients can indeed be improved through cognitive training [92]. Metacognitive training approaches are of particular interest, since also skilled lucid dreamers typically gained their frequent insight into the dreaming state by meta-cognitive training, in particular by developing autosuggestions and the habit of frequently contemplating about their state of consciousness [30,31]. In untrained subjects, lucid dreaming is a rare state of consciousness: less than 5% of the general population dreams lucidly on a weekly basis, only about 30% has a lucid dream more than once a year, and about 50% has never experienced a lucid dream at all [33]. Metacognitive lucidity training has already been utilized successfully in clinical settings, e.g., in nightmare therapy [93]. By teaching schizophrenia patients such training regimens, enhancing insight-related prefrontal and medial parietal functions might well lead to enhanced insight capabilities during acute psychosis.

Besides metacognitive training, also several other cognitive approaches like prospective memory training or focused intentions have been shown to increase the probability to acquire lucidity during dreams and hence might be of value as therapeutic tools for psychotic patients [31]. Furthermore, brain stimulation methods have been suggested as promising techniques to induce lucidity during REM sleep [94,95]. If such approaches turn out to be successful, they might either serve as direct tools to improve insight in psychosis, or they might be used indirectly by inducing lucidity during REM sleep, which in turn might lead to a generalization of increased insight across altered states of consciousness. Of note, a recent case study provides evidence that brain stimulation might indeed transiently attenuate insight problems in psychosis [96].

Lucid dreaming as a model for the successful treatment of psychotic symptoms might also help to develop and test new antipsychotic medication: if a given pharmacological agent

increases the frequency of lucid dreams in healthy individuals, it can be considered as a promising candidate to enhance insight also in psychotic patients [97].

While there are currently no contra-indications known for lucid dreaming induction techniques, a number of potential concerns have to be mentioned. Dream memories have been suggested to play an important role in the generation of delusions [98], and it is uncertain if a manipulation of dream mentation towards better insight would have only positive effects. Since lucid dreaming can be considered as a dissociative state [83], it can be argued that lucid dreaming training might increase the probability of state dissociations in general, including psychotic dissociations. However, individual differences in lucid dreaming capability do not appear to be related with measures of dissociation during wakefulness [99]. Furthermore, we do not know if dream lucidity interferes with the emotion regulation functions of REM sleep, and reliable data on long-term consequences of dream lucidity induction attempts do not exist. Of note, a recent study observed lucid dreaming frequency to be correlated with measures of depressed mood in normal subjects [100]. On the background of the model discussed here, this finding is in line with reports about high insight in psychotic patients being a risk factor for depression [101]. A recent meta-analysis raised doubts about the insight-depression association in psychosis [84], however this issue deserves further attention in attempts to utilize lucid dreaming induction techniques in the therapy of psychosis.

Limitations

While the large overlap between neural correlate of insight in dreaming and psychosis provides evidence for the dreaming–psychosis model, this confirmation cannot be generalized to all aspects of the model: the neural basis of self-reflection might be similar during dreaming and psychosis, however this similarity might theoretically be an exception, independent from the general validity of the model. Hence, other aspects of the model will have to be tested in further studies.

Furthermore, it might be argued that lucid dreaming is not special with regard to insight, since also during wakefulness metacognitive activity shows great variability. However, absence of metacognition e.g., during daydreaming is only a transient feature of wakefulness: it is hardly imaginable, at least for non-pathological cases, that the day-dreaming subject misinterprets the daydream for reality once paying attention to his current state. For the dreaming state, in contrast, this is completely normal – unless the dreamer eventually achieves lucidity through these “prelucid” reflections. After such a qualitative state shift, lucidity appears to be achieved (at least for a while) without continuous active self-reflection. Also in the two studies described above [34,35], neural correlates are reported for the whole state of lucid dreaming, which was not (necessarily) filled with continuous self-reflection. Hence, brain areas demonstrated to be associated with lucidity probably subserve a global state of self-reflective capability rather than specific reflective mentation [39].

Finally, both non-lucid and lucid dreaming are not restricted to REM sleep, but are assumed to occur during all sleep stages [102,103]. Since the classical method to investigate lucid dreaming, i.e., eye signaling [22], is not applicable to NREM sleep, the neural correlates of NREM sleep lucid dreaming are unknown. It might turn out that REM and NREM sleep lucidity do not share similar neural substrates, which would hinder generalization of the observations presented here. However, since REM and NREM sleep dreams differ particularly in those aspects that are commonly seen as psychosis-like – e.g., dream bizarreness and hallucinations are more common in REM dreams compared to NREM dreams – REM sleep lucidity appears to be the most straightforward candidate to test aspects of insight in the dream-psychosis model.

Conclusions

In conclusion, recent EEG and neuroimaging research shows that regions that have been related to psychotic insight deficits are highly activated in lucid compared to non-lucid dreaming. This fact empirically substantiates the analogy between the metacognitive impairments in psychosis and non-lucid dreaming. While research into lucid dreaming is currently limited by the rarity of the phenomenon, metacognitive training or other lucid dreaming induction methods might lead to new therapeutic approaches by improving insight in psychosis. Lucid dreaming therefore transforms the dreaming–psychosis model from an interesting idea

Practice points

- 1) Lucid dreaming is a trainable skill that allows the dreamer to become aware of his dreaming state during dreaming.
- 2) The idea that dreaming can serve as a model for psychosis has a long and honourable tradition, however is notoriously speculative. Parallels between insight into the dreaming state, i.e., lucid dreaming, and insight into the psychotic state allow for an empirical test of the model.
- 3) Neural correlates of lucid dreaming and of insight deficits in psychosis show striking overlap, in particular fronto-parietal regions are involved in both phenomena.
- 4) Techniques aimed at increasing lucid dreaming frequency might also be utilized in psychosis patients to increase insight.

Research agenda

- 1) Neurobiological data on lucid dreaming so far stems from studies with limited sample sizes. Studies into the neural correlates of lucid dreaming with larger sample sizes are needed.
- 2) Lucid dreaming is a rare phenomenon. More research is needed to identify the optimal combination of lucidity induction techniques, including different cognitive training regimes, pharmaceuticals and brain stimulation methods.
- 3) Both dream insight (i.e., lucid dreaming) and psychosis insight are multifaceted. Neural correlates of specific aspects of both phenomena have to be identified and compared in future studies.
- 4) The hypothesis that dream insight (i.e., lucid dreaming) and psychosis insight rely on similar neural mechanisms needs more direct tests. Studies are needed that investigate if lucid dreaming induction methods indeed help to improve insight in psychotic patients.

with a long history into a testable scientific hypothesis and a promising new therapeutic approach.

Disclosure

The authors declare no conflict of interest.

References

- [1] Hobson JA. A model for madness? *Nature* 2004;430:21.
- [2] Palagini L, Rosenlicht N. Sleep, dreaming, and mental health: a review of historical and neurobiological perspectives. *Sleep Med Rev* 2011;15:179–86.
- [3] D'Agostino A, Castelnuovo A, Scarone S. Dreaming and the neurobiology of self: recent advances and implications for psychiatry. *Front Psychol* 2013;4:680.
- [4] Kant I. *Träume eines Geistersehers, erläutert durch Träume der Metaphysik*. Königsberg: Kanter; 1766.
- [5] Schopenhauer A. *Die welt als wille und vorstellung*. Leipzig: F.A. Brockhaus; 1819.
- [6] Limosani I, D'Agostino A, Manzone ML, Scarone S. The dreaming brain/mind, consciousness and psychosis. *Conscious Cogn* 2011;20:987–92.
- [7] Mason O, Wakerley D. The psychomimetic nature of dreams: an experimental study. *Schizophr Res Treat* 2012;872307.
- [8] Limosani I, D'Agostino A, Manzone ML, Scarone S. Bizarreness in dream reports and waking fantasies of psychotic schizophrenic and manic patients: empirical evidences and theoretical consequences. *Psychiatry Res* 2011;189:195–9.
- *[9] Scarone S, Manzone ML, Gambini O, Kantzas I, Limosani I, D'Agostino A, et al. The dream as a model for psychosis: an experimental approach using bizarreness as a cognitive marker. *Schizophr Bull* 2008;34:515–22.
- [10] Noreika V, Valli K, Markkula J, Seppälä K, Revonsuo A. Dream bizarreness and waking thought in schizophrenia. *Psychiatry Res* 2010;178:562–4.
- [11] D'Agostino A, Aletti G, Carboni M, et al. Are delusional contents replayed during dreams? *Conscious Cogn* 2013;22:708–15.
- [12] Cavallotti S, Castelnuovo A, Ranieri R, D'agostino A. Stability of cognition across wakefulness and dreams in psychotic major depression. *Psychiatry Res* 2014;216:31–6.
- [13] D'Agostino A, Scarone S. Such stuff as psychoses are made on? *Behav Brain Sci* 2013;36:612–3.
- [14] Lusignan FA, Zadra A, Dubuc MJ, Daoust AM, Mottard JP, Godbout R. Dream content in chronically-treated persons with schizophrenia. *Schizophr Res* 2009;112:164–73.
- [15] Gottesmann C. The dreaming sleep stage: a new neurobiological model of schizophrenia? *Neurosci* 2006;140:1105–15.

* The most important references are denoted by an asterisk.

- [16] Gottesmann C. The involvement of noradrenaline in rapid eye movement sleep mentation. *Front Neurol* 2011;2:81.
- *[17] Lincoln TM, Lüllmann E, Rief W. Correlates and long-term consequences of poor insight in patients with schizophrenia. A systematic review. *Schizophr Bull* 2007;33:1324–42.
- [18] Henriksen MG, Parnas J. Self-disorders and schizophrenia: a phenomenological reappraisal of poor insight and noncompliance. *Schizophr Bull* 2014 May;40(3):542–7.
- [19] Mintz AR, Dobson KS, Romney DM. Insight in schizophrenia: a meta-analysis. *Schizophr Res* 2003;61:75–88.
- [20] Baier M. Insight in schizophrenia: a review. *Curr Psychiatry Rep* 2010;12:356–61.
- [21] Metzinger T. Being no one: the self-model theory of subjectivity. Cambridge: MIT Press; 2003.
- *[22] LaBerge SP, Nagel LE, Dement WC, Zarcone VP. Lucid dreaming verified by volitional communication during REM sleep. *Percept Mot Ski* 1981;52:727–32.
- [23] Windt JM. The immersive spatiotemporal hallucination model of dreaming. *Phenom Cogn Sci* 2010;9:295–316.
- [24] McCarley RW, Hoffmann E. REM sleep dreams and the activation-synthesis hypothesis. *Am J Psychiatry* 1981;138:904–12.
- [25] Berrios GE, Markova IS. Insight in the psychoses – a conceptual history. In: Amador XF, David AS, editors. *Insight and psychosis*. Oxford University Press; 1998.
- [26] Quee PJ, van der Meer L, Bruggeman R, et al. Insight in psychosis: relationship with neurocognition, social cognition and clinical symptoms depends on phase of illness. *Schizophr Bull* 2011;37:29–37.
- [27] David AS, Bedford N, Wiffen B, Gillean J. Failures of metacognition and lack of insight in neuropsychiatric disorders. *Phil Trans R Soc B* 2012;367:1379–90.
- [28] McCormack M, Tierney K, Brennan D, Lawlor E, Clarke M. Lack of insight in psychosis: theoretical concepts and clinical aspects. *Behav Cog Psychother* 2013 [in press].
- [29] David AS. Insight and psychosis. *Br J Psychiatry* 1990;156:798–808.
- *[30] Purcell S, Mullington J, Moffitt A, Hoffmann R, Pigeau R. Dream self-reflectiveness as a learned cognitive skill. *Sleep* 1986;9:423–37.
- *[31] Stumbrys T, Erlacher D, Schädlich M, Schredl M. Induction of lucid dreams: a systematic review of evidence. *Conscious Cogn* 2012;21:1456–75.
- [32] Schredl M, Erlacher D. Frequency of lucid dreaming in a representative German sample. *Percept Mot Ski* 2011;112:104–8.
- [33] Dresler M, Koch SP, Wehrle R, Spoormaker VI, Holsboer F, Steiger A, et al. Dreamed movement elicits activation in the sensorimotor cortex. *Curren Biol* 2011;21:1833–7.
- *[34] Voss U, Holzmann R, Tuin I, Hobson JA. Lucid dreaming: a state of consciousness with features of both waking and non-lucid dreaming. *Sleep* 2008;32:1191–200.
- *[35] Dresler M, Wehrle R, Spoormaker VI, Koch SP, Holsboer F, Steiger A, et al. Neural correlates of dream lucidity obtained from contrasting lucid versus non-lucid REM sleep: a combined EEG/fMRI case study. *Sleep* 2012;35:1017–20.
- [36] Maquet P, Péters J, Aerts J, Delfiore G, Degueldre C, Luxen A, et al. Functional neuroanatomy of human rapid-eye-movement sleep and dreaming. *Nature* 1996;383:163–6.
- [37] Braun AR, Balkin TJ, Wesensten NJ, Gwadrly F, Carson RE, Varga M, et al. Dissociated pattern of activity in visual cortices and their projections during human rapid eye movement sleep. *Science* 1998;279:91–5.
- *[38] Hobson JA, Pace-Schott EF, Stickgold R. Dreaming and the brain: toward a cognitive neuroscience of conscious states. *Behav Brain Sci* 2000;23:793–842.
- [39] Dresler M, Eibl L, Fischer CF, Wehrle R, Spoormaker VI, Steiger A, et al. Volitional components of consciousness vary across wakefulness, dreaming and lucid dreaming. *Front Psychol* 2013;4:987.
- [40] Erlacher D, Schredl M. Do REM (lucid) dreamed and executed actions share the same neural substrate? *Int J Dream Res* 2008;1:8–14.
- [41] Fox KC, Nijboer S, Solomonova E, Domhoff GW, Christoff K. Dreaming as mind wandering: evidence from functional neuroimaging and first-person content reports. *Front Hum Neurosci* 2013;7:412.
- [42] Rechtschaffen A, Kales A. A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects. National Institutes of Health, Neurological Information Network; 1968.
- [43] Duncan J. The multiple-demand (MD) system of the primate brain: mental programs for intelligent behaviour. *Trends Cogn Sci* 2010;14:172–9.
- [44] Schmitz TW, Kawahara-Baccus TN, Johnson SC. Metacognitive evaluation, self-relevance, and the right prefrontal cortex. *Neuroimage* 2004;22:941–7.
- [45] Fleming SM, Weil RS, Nagy Z, Dolan RJ, Rees G. Relating introspective accuracy to individual differences in brain structure. *Science* 2010;329:1541–3.
- [46] Cavanna AE, Trimble MR. The precuneus: a review of its functional anatomy and behavioural correlates. *Brain* 2006;129:564–83.
- [47] Vincent JL, Kahn I, Snyder AZ, Raichle ME, Buckner RL. Evidence for a frontoparietal control system revealed by intrinsic functional connectivity. *J Neurophysiol* 2008;100:3328–42.
- [48] Spoormaker VI, Cizich M, Dresler M. Lucid and non-lucid dreaming: thinking in networks. *Int J Dream Res* 2010;3:49–51.
- [49] Shad MU, Tamminga CA, Cullum M, Haas GL, Keshavan MS. Insight and frontal cortical function in schizophrenia: a review. *Schizophr Res* 2006;86:54–70.
- [50] Kumar A, Sharma P, Das S, Nath K, Talukdar U, Bhagabati D. Insight in psychotic disorder: relation with psychopathology and frontal lobe function. *Psychopathology* 2014;47:32–8.
- [51] Bedford NJ, Surguladze S, Giampietro V, Brammer MJ, David AS. Self-evaluation in schizophrenia: an fMRI study with implications for the understanding of insight. *BMC Psychiatry* 2012;12:106.
- [52] Lee KH, van der Meer L, de Vos AE, Stiekema AP, Pijnenborg GH, van Tol MJ, Nolen WA, et al. Insight in Schizophrenia: involvement of self-reflection networks? *Schizophr Bull* 2013;39:1288–95.
- [53] Raji TT, Riekkki TJ, Hari R. Association of poor insight in schizophrenia with structure and function of cortical midline structures and frontopolar cortex. *Schizophr Res* 2012;139:27–32.
- [54] Kim JJ, Ku J, Lee H, Choi SH, Kim IY. Distinct neural responses used to gain insight into hallucinatory perception in patients with schizophrenia. *J Psychiatr Res* 2012;46:1318–25.
- [55] Lee KH, Brown WH, Eggleston PN, Green RD, Farrow TF, Hunter MD, et al. A functional magnetic resonance imaging study of social cognition in schizophrenia during an acute episode and after recovery. *Am J Psychiatry* 2006;163:1926–33.
- [56] Liemburg EJ, van der Meer L, Swart M, Curcic-Blake B, Bruggeman R, Kneegtinger H, et al. Reduced connectivity in the self-processing network of schizophrenia patients with poor insight. *PLoS One* 2012;7:e42707.
- [57] Antonius D, Prudent V, Rebani Y, D'Angelo D, Ardekani BA, Malaspina D, et al. White matter integrity and lack of insight in schizophrenia and schizoaffective disorder. *Schizophr Res* 2011;128:76–82.
- [58] Larøi F, Fannemel M, Rønneberg U, Flekkøy K, Opjordsmoen S, Dullerud R, et al. Unawareness of illness in chronic schizophrenia and its relationship to structural brain measures and neuropsychological tests. *Psychiatry Res* 2000;100:49–58.
- [59] Sapara A, Cooke M, Fannon D, Francis A, Buchanan RW, Anilkumar AP, et al. Prefrontal cortex and insight in schizophrenia: a volumetric MRI study. *Schizophr Res* 2007;89:22–34.
- [60] Shad MU, Muddasani S, Prasad K, Sweeney JA, Keshavan MS. Insight and prefrontal cortex in first-episode schizophrenia. *NeuroImage* 2004;22:1315–20.
- [61] Flashman LA, McAllister TW, Johnson SC, Rick JH, Green RL, Saykin AJ. Specific frontal lobe subregions correlated with unawareness of illness in schizophrenia: a preliminary study. *J Neuropsychiatry Clin Neurosci* 2001;13:255–7.
- [62] Ha TH, Youn T, Ha KS, Rho KS, Lee JM, Kim IY, et al. Gray matter abnormalities in paranoid schizophrenia and their clinical correlations. *Psychiatry Res* 2004;132:251–60.
- [63] Bergé D, Carmona S, Rovira M, Bulbena A, Salgado P, Vilarroya O. Gray matter volume deficits and correlation with insight and negative symptoms in first-psychotic-episode subjects. *Acta Psychiatr Scand* 2011;123:431–9.
- [64] Cooke MA, Fannon D, Kuipers E, Peters E, Williams SC, Kumari V. Neurological basis of poor insight in psychosis: a voxel-based MRI study. *Schizophr Res* 2008;103:40–51.
- [65] Morgan KD, Dazzan P, Morgan C, Lappin J, Hutchinson G, Suckling J, et al. Insight, grey matter and cognitive function in first-onset psychosis. *Br J Psychiatry* 2010;197:141–8.
- [66] Buchy L, Ad-Dab'bagh Y, Lepage C, Malla A, Joobar R, Evans A, et al. Symptom attribution in first episode psychosis: a cortical thickness study. *Psychiatry Res* 2012;203:6–13.
- [67] Buchy L, Ad-Dab'bagh Y, Malla A, Lepage C, Bodnar M, Joobar R, et al. Cortical thickness is associated with poor insight in first-episode psychosis. *J Psychiatry Res* 2011;45:781–7.
- [68] Buchy L, Czechowska Y, Chochol C, Malla A, Joobar R, Pruessner J, et al. Toward a model of cognitive insight in first-episode psychosis: verbal memory and hippocampal structure. *Schizophr Bull* 2010;36:1040–9.
- [69] Palaniyappan L, Mallikarjun P, Joseph V, Liddle PF. Appreciating symptoms and deficits in schizophrenia: right posterior insula and poor insight. *Prog Neuro-Psychopharmacol Biol Psychiatry* 2011;35:523–7.
- [70] McFarland J, Cannon DM, Schmidt H, Ahmed M, Hehir S, Emsell L, et al. Association of grey matter volume deviation with insight impairment in first-episode affective and non-affective psychosis. *Eur Arch Psychiatry Clin Neurosci* 2013;263:133–41.
- [71] Takai A, Uematsu M, Ueki H, Sone K, Kaiya H. Insight and its related factors in chronic-schizophrenic patients – a preliminary study. *Euro J Psychiatry* 1992;6:159–70.
- [72] David A, van Os J, Jones P, Harvey I, Foerster A, Fahy T. Insight and psychotic illness. Cross-sectional and longitudinal associations. *Br J Psychiatry* 1995;167:621–8.
- [73] Flashman LA, McAllister TW, Andreasen NC, Saykin AJ. Smaller brain size associated with unawareness of illness in patients with schizophrenia. *Am J Psychiatry* 2000;157:1167–9.
- [74] Rossell SL, Coakes J, Shapleske J, Woodruff PW, David AS. Insight: its relationship with cognitive function, brain volume and symptoms in schizophrenia. *Psychol Med* 2003;33:111–9.
- [75] McEvoy JP, Johnson J, Perkins D, Lieberman JA, Hamer RM, Keefe RS, et al. Insight in first-episode psychosis. *Psychol Med* 2006;36:1385–93.

- [76] Bassitt DP, Neto MR, de Castro CC, Busatto GF. Insight and regional brain volumes in schizophrenia. *Eur Arch Psychiatry Clin Neurosci* 2007;257: 58–62.
- [77] Parellada M, Boada L, Fraguas D, Reig S, Castro-Fornieles J, Moreno D, et al. Trait and state attributes of insight in first episodes of early-onset schizophrenia and other psychoses: a 2-year longitudinal study. *Schizophr Bull* 2011;37:38–51.
- [78] Barr WB. Neurobehavioral disorders of awareness and their relevance to schizophrenia. In: Amador XF, David AS, editors. *Insight and psychosis*. Oxford University Press; 1998.
- [79] Woodward ND, Rogers B, Heckers S. Functional resting-state networks are differentially affected in schizophrenia. *Schizophr Res* 2011;130:86–93.
- [80] Tu PC, Lee YC, Chen YS, Li CT, Su TP. Schizophrenia and the brain's control network: aberrant within- and between-network connectivity of the frontoparietal network in schizophrenia. *Schizophr Res* 2013;147:339–47.
- [81] Vita A, De Peri L, Deste G, Sacchetti E. Progressive loss of cortical gray matter in schizophrenia: a meta-analysis and meta-regression of longitudinal MRI studies. *Transl Psychiatry* 2012;2:e190.
- [82] Holt DJ, Cassidy BS, Andrews-Hanna JR, Lee SM, Coombs G, Goff DC, et al. An anterior-to-posterior shift in midline cortical activity in schizophrenia during self-reflection. *Biol Psychiatry* 2011;69:415–23.
- [83] Voss U, Schermelleh-Engel K, Windt J, Frenzel C, Hobson A. Measuring consciousness in dreams: the lucidity and consciousness in dreams scale. *Conscious Cogn* 2013;22:8–21.
- [84] Pijnenborg GH, van Donkersgoed RJ, David AS, Aleman A. Changes in insight during treatment for psychotic disorders: a meta-analysis. *Schizophr Res* 2013;144:109–17.
- [85] Cunningham-Owens DG, Carroll A, Fattah S, Clyde Z, Coffey E, Johnstone EC. A randomized, controlled trial of a brief interventional package for schizophrenic outpatients. *Acta Psychiatr Scand* 2001;103:362–9.
- [86] Turkington D, Kingdon D, Turner T. Effectiveness of a brief cognitive-behavioural therapy intervention in the treatment of schizophrenia. *Br J Psychiatry* 2002;180:523–7.
- [87] Penn DL, Meyer PS, Evans E, Wirth RJ, Cai K, Burchinal M. Randomized controlled trial of group cognitive-behavioral therapy vs. enhanced supportive therapy for auditory hallucinations. *Schizophr Res* 2009;109:52–7.
- [88] David AS, Ster IC, Zavarei H. Effect of video self versus other observation on insight in psychotic disorders. *J Nerv Ment Dis* 2012;200:358–61.
- [89] Davidoff SA, Forester BP, Ghaemi SN, Bodkin JA. The effect of video self observation on development of insight in psychotic disorders. *J Nerv Ment Dis* 1998;186:697–700.
- [90] Favrod J, Mire A, Bardy S, Pernier S, Bonsack C. Improving insight into delusions: a pilot study of metacognitive training for patients with schizophrenia. *J Adv Nurs* 2010;67:401–7.
- [91] Moritz S, Veckenstedt R, Randjbar S, Vitzthum F, Woodward TS. Anti-psychotic treatment beyond antipsychotics: metacognitive intervention for schizophrenia patients improves delusional symptoms. *Psychol Med* 2011;41:1823–32.
- [92] Edwards BG, Barch DM, Braver TS. Improving prefrontal cortex function in schizophrenia through focused training of cognitive control. *Front Hum Neurosci* 2010;4:32.
- [93] Spoormaker V, van den Bout J. Lucid dreaming treatment for nightmares: a pilot study. *Psychother Psychosom* 2006;75:389–94.
- *[94] Voss U, Holzmann R, Hobson A, Paulus W, Koppehele-Gossel J, Klimke A, et al. Induction of self awareness in dreams through frontal low current stimulation of gamma activity. *Nat Neurosci*. 2014 Jun;17(6):810–2.
- [95] Stumbrys T, Erlacher D, Schredl M. Testing the involvement of the prefrontal cortex in lucid dreaming: a tDCS study. *Conscious Cogn* 2013;22: 1214–22.
- [96] Gerretsen P, Diaz P, Mamo D, Kavanagh D, Menon M, Pollock BG, et al. Transient insight induction with electroconvulsive therapy in a patient with refractory schizophrenia: a case report and systematic literature review. *J ECT* 2011;27:247–50.
- [97] Dresler M, Spoormaker VI, Beiting P, Czigic M, Kimura M, Steiger A, et al. Neuroscience-driven discovery and development of sleep therapeutics. *Pharmacol Ther* 2014;141:300–34.
- [98] Kelly PH. Defective inhibition of dream event memory formation: a hypothesized mechanism in the onset and progression of symptoms of schizophrenia. *Brain Res Bull* 1998;46:189–97.
- [99] Watson D. Dissociations of the night: individual differences in sleep-related experiences and their relation to dissociation and schizotypy. *J Abnorm Psychol* 2001;110:526–35.
- [100] Taitz I. Learning lucid dreaming and its effect on depression in undergraduates. *Int J Dream Res* 2011;5:117–26.
- [101] Moore O, Cassidy E, Carr A, O'Callaghan E. Unawareness of illness and its relationship with depression and self-deception in schizophrenia. *Eur Psychiatry* 1999;14:264–9.
- [102] Nielsen TA. A review of mentation in REM and NREM sleep: “covert” REM sleep as a possible reconciliation of two opposing models. *Behav Brain Sci* 2000;23:851–66.
- [103] Stumbrys T, Erlacher D. Lucid dreaming during NREM sleep: two case reports. *Int J Dream Res* 2012;5:151–5.