What links schizophrenia and dreaming? Common phenomenological and neurobiological features of schizophrenia and REM sleep

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Summary

Aim. The aim of this theoretical study is to present common phenomenological and neurobiological features of schizophrenia and REM sleep.

Results. A review of professional literature was conducted in order to synthesize current findings about associations between schizophrenia and REM sleep. Many researches reveal that both states share some common phenomenological and neurobiological features. Autism, lack of insight and a loss of autonomy in relation to mental content are just some of the characteristics that occur on a phenomenological level in both dreams during REM sleep (lucid dreaming excluded) and schizophrenia. Data from experimental conditions revealed that the waking mentation of patients suffering from schizophrenia has a similar degree of formal cognitive bizarreness as dream narratives obtained from both non-clinical and clinical populations. On the other hand, some common neurobiological features of the REM sleep stage and schizophrenia are: lack of central inhibitory processes, intracerebral disconnections, dysfunction of the dorso-lateral prefrontal cortex or nucleus accumbens and disturbed responsiveness. Moreover, there is similar activation of dopamine, acetylcholine, noradrenaline, serotonin and glutamate in both states. **Conclusions**. Common phenomenological and neurobiological characteristics of these two states suggest

that data about REM sleep could help introduce a useful experimental model of schizophrenia.

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schizophrenia / REM sleep / dreaming

INTRODUCTION

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Schizophrenia is one of the most severe mental illnesses. Delusions, hallucinations, though disturbances, as well as emotional and behavioral changes are some of the most common symptoms of this disease. Dreams that occur during the REM (Rapid Eye Movement) sleep stage have several formal characteristics, such as sensory hallucinations, delusional beliefs, bizarre imagery, orientational instability, emotional disturbances or instinctual behaviors [1], which resemble some features of schizophrenia.

Similarities between these two states – dreaming and schizophrenia (or according to previous nomenclature and knowledge – psychosis, or even insanity) have been deliberated about by philosophers, neurophysiopathologist and psychiatrists at least since the 17th century. Immanuel Kant claimed that "the madman is a waking dreamer" [2], whereas Arthur Schopenhauer stated that "dreams are a short madness and madness a long dream" [3]. Wilhelm Wundt in "Grundzüge der physiologischen Psychologie" wrote: "we ourselves, in fact, can experience in dreams almost all the phenomena to be met with in [an] insane asylums" [4]. Eugen Bleuler considered the secondary symptoms of

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This study has not been aided by any grant. The authors had no conflict of interests.

schizophrenia to be similar with dreaming [4]. His assistant, Carl Gustav Jung in his work "The psychology of dementia praecox" noticed that we should "let the dreamer walk about and act like one awakened and we [will] have the clinical picture of dementia praecox" (schizophrenia) [5]. More recently, Hughlings Jackson advised us: "find out about dreams and you will find out about insanity"; or Henri Ey – "it is obvious, it cannot be but obvious that the dream and madness spurt from the same source" [6].

Although historical considerations about similarities between dreaming and insanity are quite common, only a handful of contemporary researchers have attempted to conduct a systematic study in this field. The main aim of this article is to review the current state of knowledge about common phenomenological and neurobiological features of schizophrenia and REM sleep stage. The evidence presented should serve to support the hypothesis that the dreaming brain resembles one suffering from schizophrenia, and that a dreaming brain may be considered an experimental model for this mental illness.

Common phenomenological features of schizophrenia and dreaming

The above presented quotes and definitions indicate the existence of phenomenological similarities between these two states. One of the most fundamental common features of dreaming and schizophrenia is autism, defined by Eugen Bleuler as having no contact with the outside world and living in an inner world [7]. Both the dreamer and a person suffering from schizophrenia are involved in internal, rather than external events. Dreaming is a cognitive (thus internal) process [8]. Similarly, it is common in schizophrenia to perceive internal events as being externally imposed (e.g. delusions of being controlled) [9]. A redirection of the locus of control suggests the existence of underlying abnormalities in monitoring the source of stimulation and in an ability to differentiate other people in both schizophrenia and dreaming [10].

Among the misidentification syndromes that may appear in the course of schizophrenia are: Capgras syndrome (a belief that a known person has been replaced by a doppelganger or an "impostor" [11]) which occurs in 15% of patients [12] and Frègoli syndrome (conviction or belief that a familiar person or persons changed their physical appearance while retaining their psychological identity [13]) that is less common, but its prevalence is underdetermined in this population [14]. A change of characters by way of hyper- or hyporecognition occurs in approximately 1% of dreams [15].

The similarities with dream phenomenology are most often exhibited by positive symptoms of schizophrenia, such as abnormal senso-perceptual experiences or delusions, rather than the negative ones (i.e. withdrawal from the external world) [16]. Although the dreamer experiences a dream as any perceptual phenomenon, it is in fact a hallucination [8]. Hallucinations are also one of the very common symptoms of schizophrenia. However, in contrast with dreams where there is a predominance of visual over auditory imagery [17], in schizophrenia (especially in a paranoid type of the disease) auditory hallucinations are more frequent [18]. This difference has not yet been explained.

Once we exclude misidentifications delusions, there are at least two other common kinds of false beliefs that can be found in both dreams and in schizophrenia. Firstly, persecution delusions occur in approximately 58.3% of patients suffering from paranoid schizophrenia [19], while topics related to harassment and being chased are among the most frequent and typical dream contents [20]. Secondly, a belief that one is younger than one actually is also appears in these two states [21]. A confusion regarding ones' age affects about 35% of patients currently hospitalized or suffering from chronic schizophrenia. Approximately 25% of them express a belief that they are five or more years younger, and about 9-12% that they are younger by less than five years [22]. Since dreaming of the past is relatively common, it is possible that the confusion as to ones age may be associated with the memory of events occurring in dreams [15]. Analysis of a long series of dream narratives revealed that events from the past that took place 8-21 years ago appeared in 15-40% of descriptions [23].

Once lucid dreaming is left out of the analysis we can see that what characterizes both states is not only a loss of autonomy in relation to mental

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content, but also a lack of insight [7]. These are some of the defining conditions of dreams [7]. Similarly a lack of awareness of one's own illness is typical for 97% of persons suffering from schizophrenia in the first episode, and for 30% of patients with chronic course of the disease [24]. What is more, Charles McCreery [7] also distinguishes flattened or inappropriate affect, as well as disorders of language and thought as common phenomenological features of psychosis (schizophrenia) and dreams.

Persons suffering from schizophrenia exhibit deficits in the theory of mind – a condition which in their case may be associated with other aspects of cognitive impairment [25]. Approximately 75% of patients experience significant cognitive impairment of, among others, memory, attention and executive functions [26]. Furthermore, persons with schizophrenia are characterized by deficits in cognitive (emotion recognition) and affective (emotional reaction to an emotional state of other) aspects of empathy [27]. Similarly, a dreamer usually exhibits little empathy for other dream characters. The ability to empathically relate to others' mental states, understanding their wishes and beliefs, and the ability to think about thinking, abstraction, execution control and reflectivity are also absent during dreaming [28].

In addition to the above described common features of schizophrenia and dreaming, research on cognitive bizarreness conducted by Scarone and colleagues [29] supports the hypothesis that due to similarities between these two states, a dreaming brain may be a useful model for this disease. The level of cognitive bizarreness, defined as discontinuity and incongruity of dream perception and cognition is comparable in both non-clinical subjects, and ones suffering from schizophrenia. A comparison of stories from the Thematic Apperception Test obtained from both patients and non-clinical subjects revealed that although the level of cognitive bizarreness is significantly higher in the former than in the latter, it still oscillates at a level similar to that which occurs in dreams [29]. Therefore, it seems that while bizarreness constitutes a kind of cognitive model for dreaming mental state (for both clinical and non-clinical populations), it is still present as a characteristic feature of waking cognitive organization in schizophrenia. On the other hand, in a study by Noreika, Valli, Markkula, Seppäla and Revonsuo [30] the authors managed to only partially confirm this relationship. It was found that the dream content of persons suffering from schizophrenia is more bizarre than of a non-clinical population. In addition, contrary to data obtained from the control group, judges had a greater difficulty in discerning between dream narratives and waking thoughts when data was obtained from patients with schizophrenia.

The convergence of phenomenological aspects of mental organization of both schizophrenia and dreaming is not sufficient to hypothesize that a dreaming brain may be a model for this disease. However, there are also neurobiological similarities between these two states which are being investigated more rigorously.

Neurobiological similarities between schizophrenia and the REM sleep stage

In 1953 Eugene Aserinsky and Nathaniel Kleitman discovered the REM sleep stage and revealed that in this phase dreams are longer, more vivid and bizarre, as well as containing more elements connected with movement than in nREM sleep stage [1]. Several studies showed that the neurobiological support of REM sleep is necessary for the process of dreaming, even if not all of its criteria are "identified" [6]. For this reason, most researchers restrict their investigations to the REM sleep stage.

Evidence of common neurobiological characteristics of schizophrenia and REM sleep come from electrophysiological studies, topographic approach, neurochemistry and pharmacology. These kinds of analyses compare the activity of the cerebral cortex, the blood flow and the secretion of neuromodulators and neurotransmitters in non-clinical sleeping subjects (during the REM sleep stage) and awake patients suffering from schizophrenia.

The results of electrophysiological studies on the relationship between schizophrenia and REM sleep stage dreaming have been extensively presented by Claude Gottesmanna [6, 31]. Main results indicate a lack of central inhibitory processes in both schizophrenia and REM sleep stage. The negative component (N100) of

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the evoked potential achieves the same increase in the amplitude of the REM sleep in both nonclinical and clinical subjects, which indicates a disinhibition process present in this state [6]. Central inhibition is not observed in non-clinical subjects during dreaming, it is however present in waking states. In persons with schizophrenia it appears neither in REM sleep stage nor in active waking [31]. As a consequence, it seems that due to the distortion of cortical function, mentation present in REM sleep stage is similar to psychotic thinking.

Additionally, electrophysiological data revealed that the gamma rhythm is synchronized in the cortical regions during wakefulness, whereas it is suppressed between visual areas, the frontal cortex and the prefrontal cortex [32] as well as between the hippocampus and the cerebral cortex during REM sleep [33]. The disconnection of the gamma rhythm between central structures of the brain in REM sleep in non-clinical individuals corresponds to the disturbances in cortical connectivity typical for schizophrenia [6].

Similarities between REM sleep and schizophrenia are also indicated by data from the tomographic study of the cerebral blood flow. Some structures involved in mentation are active not only during waking, but also during REM sleep, whereas in the latter state some structures are deactivated [34]. For example, the dorsolateral prefrontal cortex is not active during REM sleep [35]. Dysfunctions of the same area are also observed in schizophrenia [36]. Deactivation of this area may explain the disturbances in mentation, especially a reduction in control associated with self-reflectiveness. Furthermore, the results obtained from the CT scans allowed formulating a hypothesis about the formation of hallucinations in schizophrenia. It is assumed that hallucinations could be under-constrained perceptions which occur when the impact of sensory input on activation of thalamacortical circuits and synchronization of thalamacortical gamma rhythm are reduced [37]. A similar phenomenon is observed during REM sleep [31], therefore it could at least partially explain the hallucinatory characteristic of dreaming.

A very important group of evidence of similarities between schizophrenia and REM sleep stage dreaming relates to the activation of neuromodulators (dopamine and noradrenaline) and neurotransmitters (glutamate and acetylcholine). While playing an essential role in the differentiation between states of dreaming and waking, they also play a fundamental part in schizophrenia. The importance of their role is shown by several hypotheses regarding the relationships between the activity of various neuromodulators and neurotransmitters and the etiology of the disease. The most general assumption concerning the comparison of REM sleep stage and schizophrenia in terms of secretion and activity of neuromodulators and neurotransmitters suggests that their level during REM sleep in nonclinical subjects is similar to their levels in patients being awake.

The dopamine hypotheses have a significant impact on explaining the neurobiological causes of schizophrenia [38]. On the most basic level, they assume diverse activity of different dopamine receptors in various brain regions. Negative symptoms of schizophrenia are associated with decreased dopaminergic activity particularly in the prefrontal cortex, while the positive ones - with increased activity in the midbrain region (mainly the nucleus accumbens) [19]. Dopamine is active during waking, slow wave sleep and REM sleep. What is important is that dopaminergic neurons are the only release monoamines during REM sleep [31]. The release of dopamine in the nucleus accumbens during REM sleep state is slightly greater than in the waking state. On the other hand, dopamine release in the prefrontal cortex is significantly smaller during REM sleep stage than when awake. These trends in dopamine release observed during REM sleep stage show the same tendency as the one postulated for schizophrenia [6]. Thus, the maximal release of dopamine in nucleus accumbens during REM sleep stage could be associated with hallucinatory activity of dreaming, whereas in schizophrenia - with delusions and bizarre thought content. What is more, in schizophrenia the reduced level of dopamine in prefrontal cortex is partially connected with cognitive impairment, while in REM stage with decrease of the critical faculty. A reduction of dopamine in prefrontal cortex beyond optimal level can also explain the decrease or loss of reflectiveness, characteristic for both schizophrenia and REM sleep stage dreaming [6, 31].

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Glutamate hypothesis assumes that hypofunction of the NMDA receptor may contribute to the patophysiology of schizophrenia [38]. There is also a dysfunction in glutamate level in REM sleep stage. When compared with wakefulness and slow wave sleep stage, nucleus accumbens shows the lowest concentration of glutamate during REM sleep. This is connected with the release of glutamate in the hippocampus, amygdala and prefrontal cortex. In schizophrenia, as in the REM sleep state, decreased release of glutamate from the ventral part of the hippocampus prevents the activity of glutamate released in the prefrontal cortex. As a consequence, the amygdala becomes particularly active [6]. An increased activity of this structure results in problems with perceiving and experiencing emotions in both schizophrenia and REM sleep.

Another neuromodulator affecting the nucleus accumbens and prefrontal cortex is noradrenaline. Noradrenergic neurons are the most active in both structures during waking, whereas during REM sleep stage their activity decreases significantly. More importantly, in this state a lack of serotonergic neuron activity can also be observed. Similarly, both noradrenaline and serotonin deficits occur in schizophrenia [6]. Acetylcholine, being of great importance to the process of thinking, maintains high levels in the cerebral cortex both in waking and REM sleep, but at REM stage its concentration is lower [6]. In schizophrenia, there is also a decreased acetylcholine activity, which may be associated with the development of hallucinations [40].

Data indicates that some characteristic features of REM sleep stage dreaming, resulting to some extend from the neurobiological processes in the brain, resemble some of the symptoms of schizophrenia. However, despite significant similarities, there are still differences between these two states (for instance, dreams are mostly images, while in schizophrenia auditory hallucinations are dominant).

CONCLUSIONS

Schizophrenia and REM sleep stage dreaming are characterized by common phenomenological and neurobiological features. Similarities between these two states indicate that a dreaming

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brain during REM sleep could be a useful experimental model for schizophrenia [6, 16, 29, 31]. While dreaming may be a condition advantageous to a better understanding of schizophrenia, it is important to remember that these states are not identical.

The evidence presented in this article does not exhaust all the concepts regarding links between schizophrenia and dreaming or REM sleep. There are some theories that need to be mentioned. Sue Llewellyn [40] formulated a hypothesis about a possible etiology of schizophrenia. According to the evidence based on the activity of neurotransmitters and neuromodulators, the chaos theory, creativity, as well as the membrane theory of schizophrenia, the disease is a state of mind/ brain "trapped" between waking and dreaming. Professional literature provides reports on convergence between dreaming, schizophrenia and a drug induced hallucinogenic state. In this case, the hallucinogenic mental state induced by drugs has been considered a model of psychosis [41]. A broader view concerning psychosis as not confined to schizophrenia has been considered by Charles McCreery [7]. He proposes that this state is based on a link between sleep and hyperarousal. On the other hand, due to the nature of hallucination, intensity of emotions and cognitive deficits such as confusion, memory impairment or tendency to confabulate, Allan Hobson [42] compares dreaming to psychosis similar not with schizophrenia but with delirium tremens. Regardless of the type of psychosis, prospecting similarities of this state and REM sleep stage dreaming is a very promising direction for further research allowing for a better understanding of not only the mental illness, but also of the process of dreaming.

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