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The effect of sleep deprivation on the induction of hallucinations & psychosis

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Foreword

This thesis focuses on how sleep deprivation may lead to the onset of hallucinations and psychosis. The basis for this thesis initially came from my personal environment. Whilst getting older, multiple close friends stated that they have experienced some sort of hallucination or delusion recently. I suspected this could be due to an overall decrease in sleep they were getting the past few years. This suspicion led to the focus of this thesis. My interest was awakened about what happens inside of the brain during psychosis and sleep deprivation, and whether there is a link between the two. Studying the effects of sleep deprivation is very relevant since it's more and more common nowadays. More knowledge about the possible effects of sleep deprivation is valuable for everyone to live a healthier and happier life.

Summary

Sleep deprivation is a world-wide problem we all suffer from. Today's society will easily give up a night of sleep to get some extra work done or to party. Missing and/or skipping sleep comes with its consequences. To learn about the effects that this reduction of sleep has on you, researchers investigate in the results of missing sleep. This is done by sleep deprivation studies. Sleep deprivation studies are extremely valuable in understanding why we sleep and, most importantly for this review, to learn about some of the consequences of sleep loss. We are aware that a reduction of sleep can have some bad short-term consequences to our body. However, we know less about the long-term consequences of sleep deprivation and how it can affect our mental wellbeing. Multiple psychiatric disorders are linked to sleep deprivation, which means that sleep loss does have a big impact on our mental wellbeing. This review focuses on the link between hallucinations and delusions, belonging to psychosis, and sleep deprivation. For this review, an extensive literature search was done in all the major databases for “psychosis” and “sleep deprivation”. The main conclusion of this review is that the onset of hallucinations and delusions, possibly leading into psychosis, can be linked to a decrease in sleep. This is because a loss of sleep results in prefrontal dysfunctions, and this phenomenon is closely linked to the onset of hallucinations and delusions.

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Introduction

Sleep deprivation (SD), also called sleep insufficiency or sleep loss, are general terms used to describe a state that is caused by insufficient quantity and/or quality of sleep (*Sleep Deprivation - Better Health Channel*, 2014). This insufficiency includes voluntary, and involuntary SD. For voluntary SD you can hold yourself accountable. Voluntary SD can be changed and fixed by yourself. It includes drinking coffee/energy drinks, looking at your phone before bed, staying up late to study or work, etc. All factors which contribute to staying awake longer. Involuntary SD includes SD from mental disorders and the environment (noise, extreme heat/cold), this is something you cannot control and change by yourself. SD can be divided into acute, meaning 1 night of total sleep loss, and extreme, missing sleep for a period longer than 48 hours (Nunez, 2020). When a person is missing sleep and so has an increased time in being awake, psychotic symptoms can develop. Being awake for a longer period of time, and so leading to SD, has multiple affects on the brain. Mental disorders have multiple effects on the brain as well. This said, psychotic symptoms take their origin in the brain. SD and psychosis can be linked together and form a causal relationship since some effects occurring in the brain after SD, are also seen in people experiencing psychosis. Extreme SD can even lead to hallucinations. The experience of hallucinations leads to a condition resembling acute psychosis (Waters et al., 2018). The average adult needs around 7-8 hours of sleep per night (Bixler, 2009). Since SD can already occur after 24 hours (acute SD), 1 night without sleep will already leave you sleep deprived. SD is a common problem in today's society. 35% of adults report suffering from insufficient amounts of sleep (MicroHealth, 2019). This means that around 1 out of 3 people is sleep deprived. In 1910, people slept around 9 hours per night, this is a huge difference compared to the less than 7 hours we get on average now (National Heart, Lung, & Blood Institute & National Heart, 2005). The world's SD nowadays can largely be attributed to the increase in voluntary SD. In todays' society, social and professional demands can make it compulsory to sacrifice your night of rest. This can be to increase your productivity. Leading to SD not being a 1 night occasional occurrence, but a major public health issue. Most people still participate in these acts of missing sleep, even in despite of the fact that it is well known that SD overall negatively affects the quality of life. SD has many bad effects on the body and brain. The effects SD has on the body include, among many more, increased risks for; diabetes, obesity, cardiovascular risks, depression, high blood pressure and immunity impairment. The effects on the brain include reduced cerebral metabolism within the thalamic, parietal, temporal and prefrontal regions. Reduced cerebral metabolism within the prefrontal cortex is a finding also observed in some psychiatric disorders (Kahn-Greene et al., 2007). Schizophrenia is such a psychiatric disorder where this reduced cerebral metabolism is seen in. Schizophrenia and psychosis go hand in hand. Psychosis is a symptom of multiple mental disorders but mainly seen in schizophrenic patients. With psychosis, thoughts and emotions are so much impaired that there is a lost connection with the external reality. Most common belongings to psychosis are delusions and hallucinations. Schizophrenia patients also show reduced brain activity and reduced gray matter volume within the prefrontal cortex and anterior cingulate gyrus. These reductions correlate with psychotic symptoms as well. (Kahn-Greene et al., 2007). This review will focus on the effects

SD has on the brain, specifically on the induction of hallucinations and psychosis. The neurobiology of psychosis and SD will be reviewed to form a link between the two.

What is psychosis

Back in the days, psychosis was considered as a loss of ego boundaries that interferes with the capacity to meet the ordinary demands of life (Arciniegas, 2015). Nowadays, psychosis is a word used to describe a condition in which there is some loss with reality. Psychosis affects the mind and takes its origin in the brain. It has an influence on the way that your brain processes information. Psychosis is not considered an illness itself, but a symptom caused by other factors such as mental or physical illness. Triggers such as substance abuse, extreme stress, lack of sleep or trauma can result in psychosis as well (*Psychosis and Psychotic Episodes*, 2015). Since each case of psychosis is different, it is hard to pin down the exact reason causing it. People that are suffering from psychosis experience psychotic episodes. During these episodes, a person's thoughts and perceptions are disturbed. The individual may have some problems in differentiating between what is real and what is not. The most common symptoms of psychosis are hallucinations and delusions. Hallucinations are sensory perceptions that occur in the absence of external stimuli (*Hallucination*, 2021). Delusions are fixed beliefs that are not amenable to change, even not with conflicting evidence (Bortolotti, Lisa (7 June 2013). "Delusions in the DSM 5". *Imperfect Cognitions*.). Some other symptoms include incoherent or nonsense speech, and inappropriate behaviour to a situation, but those symptoms are much less common than hallucinations and delusions. A person suffering from psychosis is mostly not suffering from psychosis alone. Experiencing psychosis goes hand in hand with the experience of depression, anxiety, social withdrawal, lack of motivation, difficulty functioning and sleep problems (*NIMH » What Is Psychosis?*, 2021).
To create a better understanding of psychosis, we need to take a look at where it occurs in the brain and the underlying mechanisms behind it.

Neurobiology of psychosis

This review mainly looks at schizophrenic patients to investigate the neurobiology of psychosis. This is because most scientific research on psychosis has been done with schizophrenic patients. These patients experience psychotic symptoms such as hallucinations and delusions and can therefore be used to study psychosis. Psychosis takes its origin in the brain. It is associated with changes in the structure and in the functioning of multiple brain systems, as well as in connections between different cortical regions, including the prefrontal and medial temporal lobe regions. Psychosis can be viewed as a disorder of disrupted neural connectivity (Karlsgodt et al., 2010). Schizophrenia patients show significantly decreased mean intracranial volume (ICV). ICV is driven by brain growth. The brain stops growing around 13 years of age. Because of this decrease in ICV, patients show a smaller brain volume in comparison to healthy subjects (O'Rahilly & Müller, 1992) (Kahn & Sommer, 2014). There is mostly loss in the volume

of gray matter, as can be seen in figure 1.A. Longitudinal studies show that white matter volume loss is present at the onset of psychosis, but does not progress further after the psychosis has emerged (Hulshoff Pol & Kahn, 2007). This means that the loss in white matter volume is more likely to be attributed to genetics, than to the consequences of psychosis. This finding is corresponding to twin studies that showed that decreases in white matter volume lead to an increased genetic risk in the development of schizophrenia (Hulshoff Pol et al., 2004). The decrease in gray matter volume was not observed before the onset of schizophrenia, and reduces even further during schizophrenia, so this overall reduction can be attributed as a consequence of schizophrenia. Abnormal brain development is already on-going long before the first psychosis, as seen in the reduced ICV and white matter. The shrunken matters, both white and gray, are not evenly dispersed throughout the brain. By the use of neuroimaging studies we know that reduced volume in gray matter is mostly seen in medial temporal, superior temporal, and prefrontal areas. These result from cortical thinning. In these regions episodic memory processing of auditory information and short-term memory/decision making are critically dependent (Wright et al., 2000). The smaller gotten gray volume results in cognitive dysfunction. Most white matter reductions are seen in association fibers, such as the uncinate and arcuate fasciculi (Kahn & Sommer, 2014). The uncinate fasciculus is a white matter association tract that connects parts of the limbic system to inferior parts of the frontal lobe. The tract forms a bi-directional pathway (Hasan et al., 2009). The arcuate fasciculus is a white matter association tract as well. It is a bundle of axons which connects Broca's area and Wernicke's area, and so forms a connection between the caudal temporal cortex and inferior frontal lobe (Carlson, 2021). It is common for both these fasciculi to be affected in psychiatric conditions. Problems with the arcuate fasciculus can lead to incoherent or nonsense speech, which is a symptom of psychosis. The decreases in white matter are also associated with reductions in oligodendrocytes, both in the superior frontal cortex (Hof et al., 2003) as well as in the bilateral hippocampus (Schmitt et al., 2008). This has been observed in post-mortem studies. These findings may suggest that white matter deficits in schizophrenia may be associated with the dysfunctioning of oligodendrocytes. In the next section, we will further look into this dysfunctioning of oligodendrocytes. In total we will look at three interacting pathophysiological mechanisms behind psychosis; increased pro-inflammatory status of the brain, disturbed glutamatergic neurotransmission and dopaminergic dysregulation. Oligodendrocytes are myelinating cells of the central nervous system and they express MHC-I antigens. MHC-I antigens are used by the cell to show other cells it has been infected. Because of this MHC-expression, they are linked to inflammation.

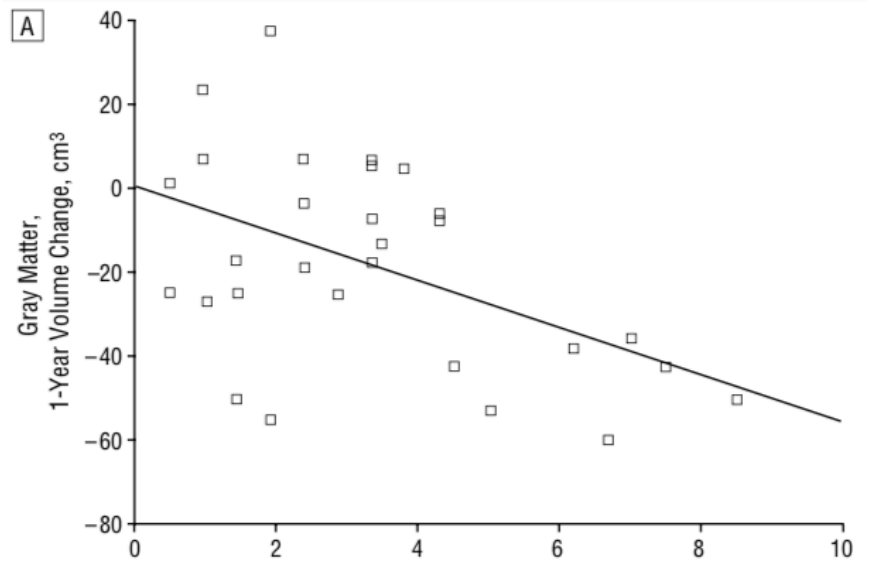

Figure 1.A In this graph there is a clear decline visible in the gray matter volume during a 1 year following of schizophrenia patients. On the y-axes you can see the gray matter volume change.

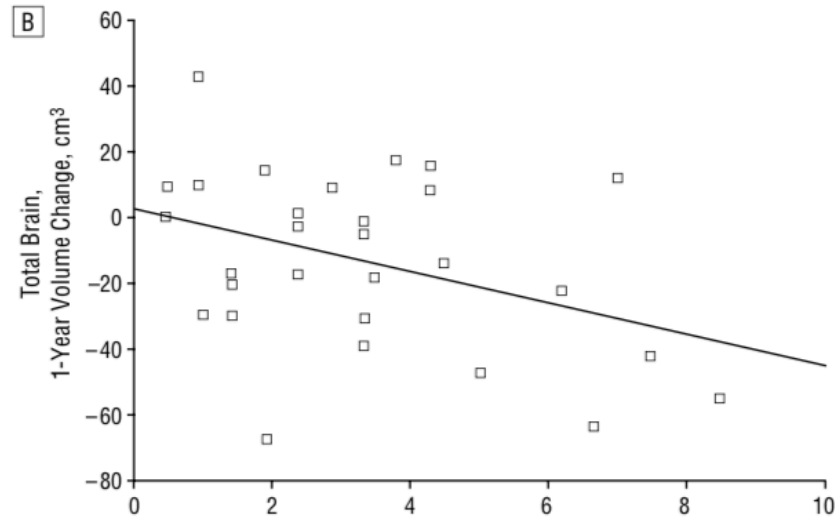

Figure 1.B In this graph there is a clear decline visible in total brain volume during a 1 year following of schizophrenia patients. On the y-axes you can see the total brain matter volume change.
Retrieved from Cahn et al.

Inflammation of the brain

The first possibly underlying schizophrenia symptoms are increased proinflammatory status. This hypothesis has been proposed already many years ago. One of the first to come up with this hypothesis was Stevens (Stevens, 1982). In his research he looked at post-mortem brains of schizophrenia patients and observed low-grade inflammation. This observation fed the

curiosity to the link between inflammation and schizophrenia. MHC regions seem to be involved in the susceptibility of schizophrenia (de Jong et al., 2012). MHC-I molecules have regulating effects on neurite outgrowth, synapse formation and function, homeostatic plasticity and activity-dependent synaptic refinement (McAllister, 2014). Due to all of this MHC-I molecules have direct effects on the development of the brain. With inflammation, microglial cells become activated. Activated microglial cells produce neurotoxic substances, such as free radicals and proinflammatory cytokines. These proinflammatory cytokines can damage neuronal and glial cells, which result in cognitive dysfunction and brain volume loss (Monji et al., 2009). Because of all this, inflammation can affect the brain development.

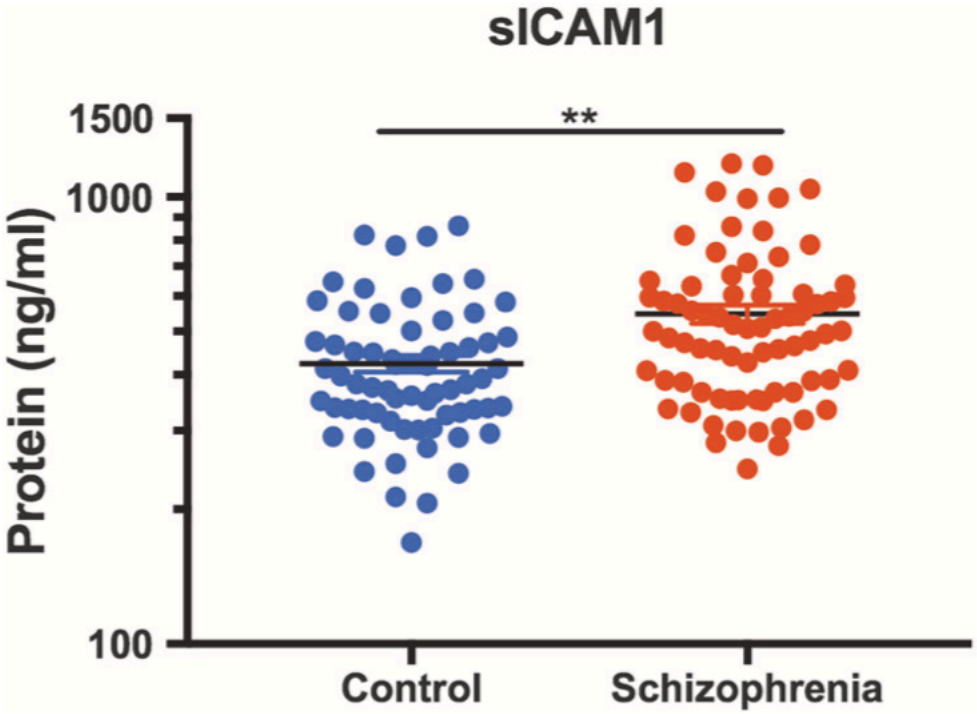

Figure 4. There is an increase visible in sICAM1 in the plasma of schizophrenia patients compared to control individuals. ICAM1 is a gene that is typically expressed on cells of the immune system. Since there is more sICAM1 in schizophrenia patients, there are more immune cells active, which in turn indicates inflammation.
Retrieved from Cai et al.
For the next underlying mechanism of psychosis we are going to take a look at glutamate

Role of glutamate

The second mechanism possibly underlying schizophrenia symptoms is glutamate dysfunctioning. For this reason, the effects of the dysfunctioning role will be discussed in this section. Some of the cognitive dysfunction in schizophrenia may be related to a disturbed neurotransmitter complex: the NMDAr/glutamate system (N-methyl-D-aspartate receptor) (Anticevic et al., 2012). It has been hypothesized that the NMDA receptor, located between the

primary and secondary glutamatergic cortical neurons, constitutes the main deficit underlying schizophrenia (Kahn & Sommer, 2014). Poor functioning of the NMDA receptor results in less effective GABA-ergic (gamma-amino-buteric-acid) interneurons, which in turn results in insufficient inhibition of the secondary glutamatergic neurons. Disinhibition of these neurons allows them to fire more, but in turn less synchronously. This directly affects excessive firing of dopaminergic neurons in the mesolimbic system (Thomas L. Schwartz et al., 2012). The functioning is based on previous research that has been done with NMDA receptor antagonists, such as ketamine. These antagonists were found to induce hallucinations and delusions (Thomas L. Schwartz et al., 2012). To summarize, decreased activation of the NMDA receptor results in an increase in striatal dopamine release, which in turn induces psychotic symptoms (Adell et al., 2011). In conclusion; a dysfunctioning glutamate system results in an increase in dopamine. The next section is going to explain the effects of this increase in dopamine.

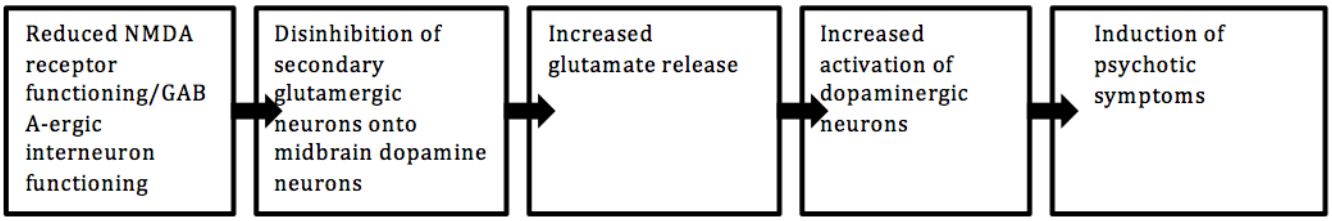

Figure 3. Step-By-Step series of what happens with a dysfunctioning glutamate system.

Role of dopamine

The last mechanism possibly underlying schizophrenia symptoms is dopaminergic dysfunction, which will now be discussed. As previously mentioned, psychosis is linked to the over activity of the neurotransmitter dopamine. Patients show increased presynaptic dopamine in the associative and limbic striatum (Kesby et al., 2018), and increased basal dopamine synthesis capacity and release capacity (Howes et al., 2013). Increased striatal dopamine synthesis may be the common pathway to psychotic symptoms (Howes & Kapur, 2009). Changes in dopamine function within the associative striatum most likely add to the misappropriation of salience to certain stimuli, which is a big aspect of hallucinations/delusions and psychosis (Winton-Brown et al., 2014). The dopaminergic aberrations are greatest within dorsal regions of the striatum (McCutcheon et al., 2017). The major locus of dopaminergic dysfunction is presynaptic rather than postsynaptic (Kahn & Sommer, 2014). The overall conclusion of an increase in dopamine is that it can result in the experience of hallucinations and delusions. We will now take a deeper look at what exactly are those hallucinations and delusions.

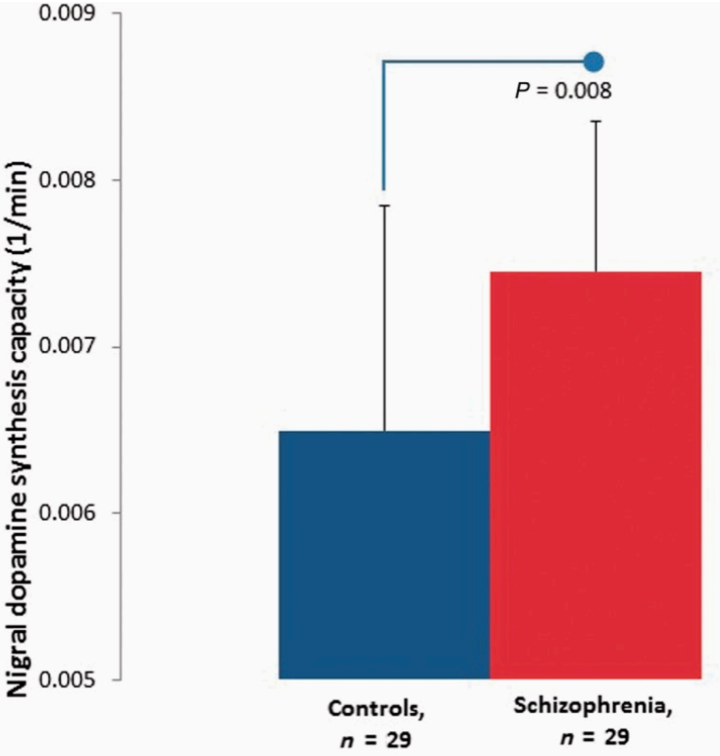

Figure 2. In this graph you can see a difference in the mean dopamine synthesis capacity between schizophrenia patients and healthy individuals. Schizophrenia patients have a higher synthesis capacity for dopamine (here in the substantia nigra) compared with control subjects Retrieved from Howes et al.

Hallucinations

As previously mentioned, hallucinations are something you experience when having a psychotic episode. Hallucinations are defined as sensory perceptions, occurring in the absence of corresponding external or somatic stimuli and they are described according to the sensory domain in which it occurs (Arciniegas, 2015). Hallucinations are recognizable by increased activity in primary and secondary sensory cortices, specifically in the left idle temporal gyrus, left superior temporal gyrus, and left inferior frontal gyrus (Knott et al., 2020). The lucidity of the hallucinations is connected to activity in the ventral striatum, hippocampus, and the anterior cingulate cortex (ACC). These areas are involved in the emotional circuitry of humans. Thus, emotions are linked to the abnormal activity in sensory cortices during psychosis. Abnormally internally generated sensory experiences, together with abnormal emotional processing result in hallucinations and thus create a link between emotions and the lucidity of hallucinations.
They can occur in different forms; auditory, visual or tactile. Auditory hallucinations are most common in psychosis. Auditory hallucinations are associated with the dysfunction of the temporal lobe and altered connectivity between the hippocampus and thalamus (Amad et al., 2013). Visual hallucinations are associated with the dysfunction of the occipital lobe, striatum and thalamus. Tactile hallucinations are associated with wrong integration of tactile sensory neural signals to the primary and secondary somatosensory cortex. Tactile sensory neuronal

signals are generated in the spinal cord and thalamus, (Gallace et al., 2010). During all hallucinations, there is a decrease in brain activity since the brain isn't receiving information properly anymore.

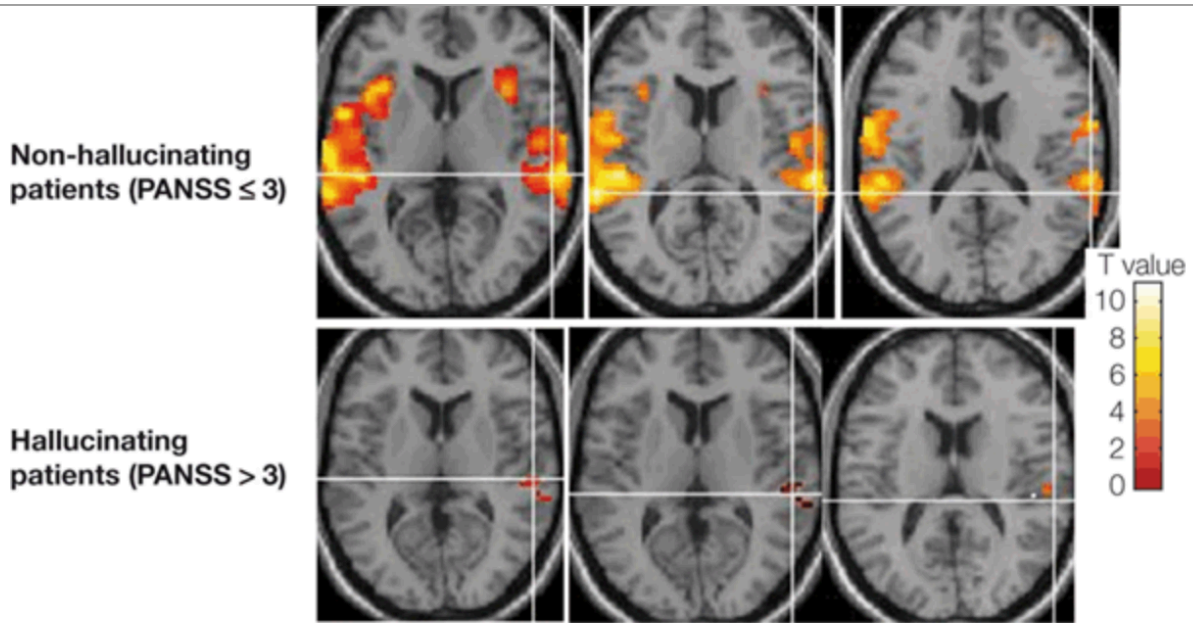

Figure 5. fMRI scan of non-hallucinating patients compared to hallucinating patients. There is more visible brain activity in the scans of non-hallucinating patients compared to hallucinating patients. This is because the brains of hallucinating patients are dysfunctioning and integrating signals incorrect.
Retrieved from Hugdahl et al.

Delusions

The other symptom of psychosis are delusions. Delusions are defined as fixed false beliefs. Delusions are based on incorrect/false inferences about reality. This can be external to, or about the person experiencing the delusion. Delusions are fixed despite possible presentation of evidence that contradicts the beliefs and proves otherwise. There are multiple different types of delusions known today. Most delusions are divided into two categories; ordinary and bizarre. Ordinary delusions are derived from misinterpreted everyday-like experiences. Ordinary delusions are usually understood, but not accepted by other members of the person's culture (Arciniegas, 2015). For example one believes that all his savings have been given to pirates, even thought the bank states otherwise. Bizarre delusions involve phenomena that are physically impossible, and other people would find implausible. For example being kidnapped by aliens. These delusions are considered unrealistic. Hallucinations and delusions are mostly considered 'unpleasant' to experience. To help people who are suffering from this, a form of therapeutics has been made, called antipsychotics. The next section will explain how these therapeutics work and help to supress psychotic symptoms.

Antipsychotics:

Hallucinations and delusions are associated with hyperdopaminergic neurotransmission, which particularly takes place in the mesolimbic dopamine pathway (Li et al., 2016). Excessive dopamine signalling in the associative and limbic striatum can directly lead to psychotic symptoms (Abi-Dargham et al., 2000). To prevent this effect, treatment is needed which will stop the hyperdopaminergic neurotransmission. Psychosis is usually treated with the help of pharmaceutics. These medicines are in pill form and called antipsychotics. Antipsychotics are most commonly dopamine D2 receptor antagonists. They are used to reduce the hyperdopaminergic neurotransmission and attenuate the expression of psychotic symptoms. This treatment for psychosis has been used for more than 50 years already. New possible treatments can be in the correction for NMDA receptor hypofunction or to reduce the increased proinflammatory status of the brain. Antipsychotics work to reduce dopamine levels in the brain. Something that is also connected to dopamine levels in the brain is SD. To get there, we will first take a look at what exactly is SD.

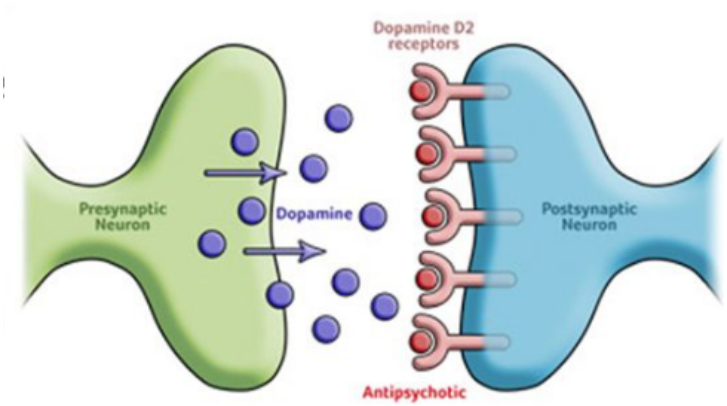

Figure 6. The antipsychotic drugs (dark red) reduce dopamine uptake by blocking the dopamine D2 receptors (light red) of the postsynaptic neuron. Because of this there is a decrease in dopamine transport since the receptors are already full.
Retrieved from Marshall Charles.

What is sleep deprivation

Sleep is something we all need. Despite this word-wide need for sleep, we still do not completely understand the physiological function of sleep. Sleep is regulated by circadian rhythms present in the hypothalamus. Sleep consists of two phases; NREM (non-rapid-eye-movement) and REM (rapid-eye-movement). Sleep is essential for proper functioning of the brain. Sleep plays a role in fostering connections among neuronal networks (Alkadhi et al., 2013). It is implicated in brain plasticity and mood regulation. Insufficient sleep can result in some serious consequences. Not only adults are affected by sleep loss, also adolescents and children can suffer from it (Fredriksen et al., 2004) (Meijer et al., 2000). Multiple factors in today's society may have an influence on the decrease in sleep. First of all is the use of artificial lighting. Artificial lighting has an effect on the body's biological clock and disturbs this, resulting

in a decreased production of melatonin, which in turn leads to a decrease in sleep. Another factor is the growing demand for productivity that belongs to the era we live in now. Our 24-h economy requires people to work in shifts. Shift-work negatively affects sleep since it disturbs the body's natural circadian rhythm as well. The night's rest of a shift worker is on average reduced by 2-4 hours and shift work as a whole is associated with severe sleepiness (Akerstedt, 2003). The last factor is that we easily sacrifice sleep to cope with our social demands and daily interests. Acute SD is associated with a decline in cognitive performance, such as imparted attention and working memory. There is also a negative effect on long-term memory, decision-making and vigilance (Alhola et al., 2007). Chronic SD may induce neurobiological changes that can accumulate over time and result in serious health complaints. Acute SD has been identified as a risk factor for various disorders such as cardiovascular diseases (Nagai et al., 2010) and psychiatric disorders (Riemann, 2003). To create an ever better understanding of SD, we will look into its neurobiology.

Neurobiology SD:

The effect SD has on the brain is not exactly known yet since different studies come to different conclusions. The study of Van Der Borght et al., suggests that cell proliferation does not change by SD, whilst the study of Grassi Zucconi et al., suggests that SD upregulates hippocampal neurogenesis. SD does change the metabolism of the brain. The metabolic rate in the thalamic, parietal, temporal and prefrontal regions are reduced during prolonged sleep loss (Thomas et al., 2000)(Thomas, 2003). The prefrontal cortex is most affected by sleep loss, since this region is responsible for alertness, attention, and higher-order cognitive processes, all which decline during SD. The study of Thomas et al., suggests that SD targets the prefrontal and thalamic regions together as a functional network, since they showed positive correlation during a 72h SD period. SD also results in memory deficits, specifically hippocampus-dependent memories. This is because SD impairs hippocampal cAMP and mTOR signalling. This ultimately causes spine loss of CA1 neurons. CA1 neurons are located in the hippocampus, and the hippocampus is in turn responsible for learning and memory. (Havekes & Abel, 2017). In total SD has multiple effects on the brain, just like psychosis as previously mentioned. The two will be linked together in the next section.

Link between psychosis and SD

To be able to give an answer to the question on what the effect sleep deprivation has on the induction of hallucinations and psychosis, we need to form a link between the two.
Psychosis, and so hallucinations, are associated with an increase in dopamine, mainly in the associative and limbic striatum. There is an increase in the overall basal dopamine synthesis. Psychotic patients show reduced brain activity. There is also a decrease in the gray matter volume within the medial temporal, superior temporal, prefrontal cortex and anterior cingulate gyrus and disrupted white matter integrity. SD works mainly on the brain metabolism, which it decreases. With SD, there is a decrease in the cerebral metabolism within the prefrontal,

thalamic, parietal and temporal regions. Psychosis is closely linked with prefrontal dysfunction. Prefrontal dysfunction can occur when a person is sleep deprived and so can lead to the onset of hallucinations. As mentioned before, psychotic patients show reduced brain activity. Reduced brain activity is linked to a decrease in brain metabolism, which occurs when a person is sleep deprived. During psychosis there are changes in dopamine function within the associative striatum that add to the misappropriation of salience to certain stimuli. A sleep deprived person also tends to have misappropriation of salience to certain stimuli because their prefrontal cortex is affected by SD, which leads to reduced cognitive functioning.

Discussion/Conclusion

To answer the question on what the effect of sleep deprivation is on the induction of hallucinations and psychosis, we have looked at the neurobiology of psychosis, and that of SD and linked the two together. Psychotic symptoms such as hallucinations and delusions arise in the associative and limbic striatum, due to an increase in dopamine. Because of this increase, there are misappropriations of salience to certain stimuli. From personal experiences you might know that when you are tired, you also respond less to stimuli in comparison to when you feel fully rested. Psychotic patients show reduced brain activity, a phenomenon also observed in sleep-deprived persons. SD leads to prefrontal dysfunction, and in turn prefrontal dysfunction can lead to the onset of hallucinations and delusions. Reductions in sleep are directly followed by an increase in psychotic symptom severity. For further research it is important to understand which systems and brain regions are most involved in the onset of psychosis. This may help to identify the core neurobiological features of psychosis. Since psychosis is the result of a network dysfunction, including a variety of brain regions. Impairment at any level can already result in psychotic symptoms. For the sleep deprived brain it is also important to understand which systems and brain regions are most involved, since SD also includes disruption within multiple brain regions. Further research in SD is difficult since it is unethical to leave a person sleep deprived for over 48h. To obtain information about people with extreme sleep-loss, exceeding this 48h, you need to examine older studies. These studies are not always trustworthy anymore. For the research on psychosis, most studies are focused on schizophrenia patients. Schizophrenia patients do experience hallucinations and delusions, just what happens during psychosis, but not everyone that has had a psychosis is a schizophrenia patient. There is no causal relationship between psychosis and schizophrenia. More research into people solely experiencing psychosis can be done. Also, there are multiple possible treatments for schizophrenia available, including different types of therapies, whilst for psychosis almost solely antipsychotics are prescribed. My personal opinion on this topic is that we need to find a way to reduce stress in society. Our world should not be based on a 24-h economy anymore. Sleep needs to become a priority again instead of the reasons for voluntary sleep loss. Also, informing people better about all the risks that come with decreased sleep seems like a good idea to make people aware of its threats. This can for example be done in high school, but especially in work environments where people are known to work overtime. The amount op people in shift work should also be minimalized to the very few, since this kind of work is particularly bad for

your sleep cycle. Hopefully by creating some awareness about the dangers of missing sleep, and the benefits of sleeping good, people will make it a primary issue. Sleeping well has many benefits for your health, and a better overall health leads to a better mental state and in total a happier life. A better health will save in health care costs as well. The main conclusion of this review is that psychotic symptoms can develop with increasing time awake. These symptoms are likely to resolve after a period of sleep. Further research can be done in the identification of the systems and brain regions involving psychosis and SD, as well as in the identification of factors that may contribute to the prevention of psychotic symptoms, and in different treatment options for people solely suffering from psychosis.

Afterword

For the making of this review, I would like to thank R. Havekes for his supervision and feedback. During the writing process I have learned a lot of new things about psychosis and sleep deprivation. Overall it was a very informative experience.

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