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THE NEURAL CORRELATES OF INTERNET ADDICTION

Contextualized by a Comparison with ADHD

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Abstract

In everyday life, people are interacting with the Internet. The emergence of this phenomenon has been positively contributing to the rapid development of our society in the last decades. However, negative reports about excessive usage are coming to the surface and questions about potential negative consequences are being raised. Internet addiction (IA) has been suggested as a new type of disorder. There is a new field of research emerging with the aim to investigate its nature. This review compiles the most relevant literature on neuroimaging techniques used to identify the underlying neurobiological mechanisms of IA. Based on identified comorbidity between IA and attention-deficit hyperactivity disorder (ADHD), a comparison between the neural correlates of IA and ADHD is attempted, in order to illustrate the importance of bringing more attention to IA. The findings present structural, functional and neurochemical alterations in brain regions associated with emotional processing, cognitive control and reward processing. Similarities between the two disorders in terms of structural and functional alterations in regions associated with emotional processing and cognitive control are highlighted. Limitations regarding lack of consensus of the operational definition, narrow selection criteria of participants and a need for subcategories inside the term IA are pointed out. The thesis concludes that as of now the discovered alterations may be considered as biological markers underlying the disorder and IA is a field of research worthy of more attention.

Keywords: internet addiction, neuroscience, neuroimaging, comorbidity, ADHD

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Introduction

The Internet was invented not long ago and not many could imagine the enormous effect it would have on the world. The Internet has worked as an important tool in many aspects, allowing society to evolve at a rapid speed. On an individual level, the Internet is used by most of us, in many ways making our lives much more convenient. In later decades since our smartphones arrived and became available to an affordable price for many people, the Internet is even more present. Not only is it used in our free time for play activities such as games or social media, but also in most peoples work and at school. It is probably safe to say that it is being used daily, potentially several hours a day, by most of us. Aside from all the positive opportunities the Internet brings another question arise, the question about potential negative consequences.

Already in an early stage of the Internet, Young (1998) presented a study named "Internet Addiction: The Emergence of a New Clinical Disorder*"* as a result of anecdotal reports of people becoming addicted to internet use in the same way people becomes addicted to alcohol and drugs. The study aimed at investigating the existence of Internet Addiction (IA) and to what extent misuse of it could result in. Out of all the disorders listed in The Diagnostic and Statistical Manual of Mental Disorders—Fourth Edition, Pathological Gambling was the most alike and was used as a model to create a diagnostic questionnaire. IA could therefore be classified as an impulse-control disorder. The results of the study presented significant differences between the dependent and nondependent internet users in terms of behavioral and functional usage differences. More importantly, it showed that dependent internet users experienced occupational, relational and personal problems like those experienced by established addictions, such as alcoholism and pathological gambling (Young, 1998). Although Young pointed out the study's many limitations, this study showed the need for more research in this new area.

Furthermore, previously Young (1996) had published a case study to illustrate the potential problems of IA. It describes the situation of a 43-year-old female homemaker living with her husband and two daughters. After the first 3 months, she started to feel a need to use it more and more for her new-found internet-based chat room applications. She reported spending up to 50 to 60 hours per week interacting with others on various chat rooms. Eventually, she started to feel anxious, depressed and irritable (having no previous record of any psychiatric disorders) when not being in front of the computer. To avoid feeling withdrawal she stayed online for as much as possible. This behavior resulted in her quitting other social activities, resulting in fraction in all her relationships as well as quitting her

chores around the house. She did not see this as a problem at the time and refused to get treatment or reduce her internet use. As a result of this, her husband wanted a divorce and her two daughters felt ignored by her, resulting in a damaged relationship with them. This case paints a clear picture of what lacking control of one's Internet use could potentially result in.

The diagnosis of IA does not appear in any official diagnostic system, maybe due to the currently inconsistent view of what dimensions underlie the conceptualization of the disorder. According to Yau, Crowley, Mayes, and Potenza (2012) it could be argued that IA is a separate psychiatric disorder. They suggest it is either an addictive behavior or an impulse-control disorder. Furthermore, due to IA's heterogeneity (i.e the differences in the actual content one approaches when using the Internet), it engages different processing systems such as affective, behavioral and cognitive systems. Most recent views suggest it to be a compulsive-impulse spectrum disorder and simultaneously share characteristics with following addictive behaviors: 1) excessive use, a sense of loss of time and not considering one's basic drives, 2) withdrawal, experiencing negative feelings such as depression and anger when not having access to the internet, 3) tolerance, need for more usage and/or better equipment, and 4) negative repercussions, negative consequences such as worse performance in school or at work, social isolation, fatigue and arguments (Block, 2008). These are four proposed critical diagnostic criteria to make a diagnosis possible.

In order to help identify the prevalence of IA several self-report instruments have been developed. The most commonly used appears to be: 1) Young's Diagnostic Questionnaire (YDQ), which modified the criteria for Pathological Gambling, conceptualizing IA as a non-substance impulse-control disorder. Answering "yes" on five out of the following eight items "1. Is preoccupied with the Internet (think about previous online activity or anticipate next online session). 2. Needs to use the Internet with increased amounts of time in order to achieve satisfaction. 3. Has made unsuccessful efforts to control, cut back, or stop Internet use. 4. Is restless, moody, depressed, or irritable when attempting to cut down or stop Internet use. 5. Has stayed online longer than originally intended. 6. Has jeopardized or risked the loss of a significant relationship, job, educational or career opportunity because of the Internet. 7. Has lied to family members, therapist, or others to conceal the extent of involvement with the Internet. 8. Uses the Internet as a way of escaping from problems or of relieving a dysphoric mood (e.g., feelings of helplessness, guilt, anxiety, depression)" (Young, 1998, p. 238), are considered as having IA. 2) A modified version of YDQ. Item 1-5 (of the previously mentioned items) must be fulfilled. Also, additionally at least one of item 6-8 as well (Beard & Wolf, 2001). 3) Chen Internet Addiction Scale (CIAS), which is based on other traditional

addiction disorders (Chen, Weng, Su, Wu, & Yang, 2003) and 4) Young's Internet Addiction Test (YIAT), which seems to be the most commonly used of the assessments. It is constructed to evaluate the problematic use of areas like online games, social media, online porn and internet gambling. It consists of 20 self-report items. Because of the fact that IA can manifest in many different ways the test produces scores in 6 different areas to find out the most suitable treatment. The 6 areas are escape, compulsion, neglecting duties, anticipation, lack of control and social avoidance. The final score of the test evaluates the severity of the addiction ranging from none, mild, moderate to severe (Net Addiction, 2019).

Epidemiological studies on the prevalence of IA in the general population are lacking. Two studies have been conducted. The first was a telephone survey of 2513 adults that reported a prevalence rate of 0.7% (Aboujaoude, Koran, Gamel, Large, & Serpe, 2006) and the second was a postal survey using YDQ and reported a prevalence rate of 1%. Furthermore, the results showed that a higher YDQ-score correlated with reports of psychological impairments such as depression, anxiety, sleep disorder, substance abuse and suicidal ideations (Bakken, Wenzel, Götestam, Johansson, & Øren, 2009). Most of the epidemiological studies are conducted on either adolescents or students. Prevalence rates range from 1.0%-9.0% in European samples, 2.0-18.0% in Asian samples, to 6.0%-35.0% among university students (Spada, 2014).

There has been a comorbidity identified between IA and several psychiatric disorders. Comorbidity in this case means that IA has a higher than expected by chance associated symptoms with different psychiatric disorders. Several studies report associative symptoms between IA and disorders such as attention deficit hyperactivity disorder (ADHD) (Yoo et al., 2004), depressive disorders (Yen, Ko, Yen, Wu, & Yang, 2007), social anxiety disorder (Bernardi & Pallanti, 2009), substance use disorder (Ko et al., 2006) and hostility and aggressive behaviors (Yen et al., 2007). Ko, Yen, Yen, Chen, & Chen (2012) points out that the comorbidity suggests that there are underlying mechanisms contributing to the comorbidity. Furthermore, it is important to understand these mechanisms in order to develop accurate and effective treatments for both associative disorders. Additionally, Ko et al. (2012) mentions four possible mechanisms resulting in the comorbidity. 1) The psychiatric disorder contributes to or result in IA, 2) IA contributes to or result in psychiatric disorders, 3) Same underlying sociological, psychological or biological mechanisms are shared by both the psychiatric disorder and IA and 4) other factors result in over-estimation of the comorbidity (e.g. sampling, study design, analysis and assessment tools).

Many studies have focused on this co-existence of psychiatric disorders with IA. It is certainly an important aspect to achieve an understanding of IA, but it also presents the risk of not understanding the actual underlying mechanisms of IA.

The amount of internet users has grown remarkably with 1019% between the years 2000-2019. 56.1% of the world's total population is using it (Internet World Stats, 2019) which probably makes it safe to say that further expansion of it will continue. Since reports are being presented of individuals negatively affected by using the Internet, resulting in IA, this is a scientific field worthy of more attention. It is important to understand the mechanisms of IA in order to develop accurate and effective preventive agents and treatments to help individuals in need of it.

Aim & Structure

The aim of this thesis is to investigate two different research questions. 1) what underlying neurobiological mechanisms of IA can be identified, and 2) are the underlying neurobiological mechanisms of IA similar or different from the underlying neurobiological mechanisms of ADHD. The purpose of this comparison is founded on Ko et al.'s (2012) suggestion that it is important to understand the underlying mechanisms of the comorbidity, in order to develop good preventative and effective treatments for IA. ADHD was chosen because it is the disorder with most associated symptoms. Furthermore, if shared alterations of brain regions between the two disorders are identified, it can possibly indicate a biological reason underlying the comorbidity as well as what severe risks excessive Internet use might result in (in terms of showing similar brain changes as an accepted disorder as ADHD). Highlighting the hypothesized similarities will contribute to making an argument for bringing more attention to this field of research. Hopefully, this thesis will contribute to enhancing our understanding of what effects the Internet has on our brain.

Literature from 2010 to 2019 was searched in the Web of Science using the keywords "internet addiction", "problematic internet use" together with "neuro*" and "neural*". Some inclusion criteria were used. The articles had to be 1) peer-reviewed, 2) in English and 3) not focused on Internet Gaming Disorder. The reason for the exclusion of literature focusing on Internet Gaming Disorder (IGD) was that it is a specific content of Internet use that already has been given some attention and, is mentioned in DSM for further investigation. A broader focus of Internet use in general, was therefore chosen. IGD is just a small part of all Internet usage, and its specific content can eventually have its own specific neurobiological mechanisms underlying it.

To discuss and answer these questions I start off with presenting background information consisting of general information about ADHD and how this disorder typically manifests in a behavioral context. Followed by presenting literature of the comorbidity between IA and ADHD which is the basis of which the second research question relies on. The background information will end with presenting what the literature tells us about underlying neurobiological mechanisms of ADHD, focusing on high-quality meta-analysis on structural and functional neural correlates of the disorder. Furthermore, the background will be followed by a chapter presenting 8 articles chosen from the Web of Science literature search. The presentation of these articles are arranged based on the neuroimaging technique used in the study. The neuroimaging techniques in focus will be MRI, fMRI, DTI, PET, and SPECT. Additionally, a discussion-section will follow consisting of a summary of the IA-findings, a comparison between IA and ADHD in terms of neurobiological markers, limitations, further directions and a conclusion of this thesis.

Background

Diagnostic Features of ADHD

According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (American Psychiatric Association [APA], 2013) ADHD consist of a persistent pattern of inattention and/or hyperactivity-impulsivity. The pattern interferes and affects the individuals functioning and development in a negative way. Inattention can manifest behaviorally by making it hard to keep up focus, being persistent and are disorganized easily wandering off task. Hyperactivity manifests as excessive motor activity in unappropriated settings. Impulsivity manifests as not thought through decision making, not taking into consideration possible negative consequences to oneself or others, and often occurs in social settings. This may reflect an inclination to quick rewards and an inability to delayed gratification (American Psychiatric Association [APA], 2013).

ADHD is classified as a neurodevelopmental disorder, meaning it starts in childhood. It has a requirement of several symptoms being present before the age of 12 in order to make the diagnosis. It is characterized by developmental deficits resulting in problems of occupational, academic, social and personal domains. It is prevalent in most cultures, approximately 5% of children and 2.5% of adults. Although, signs of the disorder can be hard to detect in different contexts, for example when the person is interacting one-on-one, receiving rewards for appropriate behavior, engaging in interesting activities, is in a novel

setting or has constant external stimulation via for example different kinds of screens (American Psychiatric Association [APA], 2013).

The Comorbidity of Internet Addiction and ADHD

Yoo et al. (2004) were the first to conduct a study to investigate the relationship between ADHD symptoms and IA. They recruited 535 participants being students from an elementary school. YIAT was used to evaluate the presence of the severity of IA. DuPaul's ADHD rating scale was used together with Child Behavior Checklists and was completed by teachers and parents to divide the participants into ADHD and non-ADHD groups. 0.9% of the total sample had definite IA and 14% had a probable IA. The ADHD-group had both a greater severity and prevalence of IA than the non-ADHD group. The IA group had more ADHD symptoms than the non-IA group. In other words, the results of the study showed significant positive correlations between the ADHD symptoms and IA, in both areas of inattention and hyperactivity-impulsivity (Yoo et al., 2004).

Bernardi and Pallanti (2009) found that 14% of adults with IA was diagnosed with ADHD. The sample size was however small with only 15 participants and a correlation between IA symptoms and ADHD could not be found. However, they discuss a hypothesis of why it seems like ADHD subjects are prone to use Internet in an excessive way, using the concept that Internet is more suited for ADHD subjects' cognitive and learning systems. This is because of Internets way in delivering information in a quicker, stronger and colored way than in real life. The ADHD subjects' lack of inhibitory control and strategic flexibility is also hypothesized to interfere with their self-regulation of the Internet (Bernardi & Pallanti, 2009).

Ko, Yen, Chen, Chen, and Yen (2008) also evaluated the association between ADHD and IA of Taiwanese college students via an interview study. Results showed that the IA-group were more likely to have ADHD than the control group and that ADHD is the most significant indicator among psychiatric disorder for IA. Furthermore, Ko et al. (2008) discuss possible explanations to the association and state that since ADHD is a preexisting disorder since childhood only two models most likely explains the association: 1) IA is secondary to adult ADHD or 2) IA and adult ADHD share some common factors. Different characteristics of ADHD subjects are hypothesized to make them more vulnerable to IA. They have a tendency to prefer immediate rewards instead of a larger delayed reward. The interactive alternatives on the Internet give them an immediate reward and a sense of control and are more satisfying to people with ADHD than other activities. Biological changes in the brain such as striatal dopamine release enhance concentration (in e.g. videogaming), leading to better performance and a sense of competence. This could make them want to engage for a

longer time avoiding the frustrations in the real world. Together with abnormal brain activity associated with inhibitory impairments could make it even harder to stop engaging in Internet activities. These mentioned factors could make people with ADHD progress towards IA and it is suggested that they are at a higher risk of IA (Ko et al., 2008).

The comorbidity of IA and ADHD is noticeable in several studies and often it is the most prevalent one out of all compared psychiatric disorders. One question arises, could the explanation for the common comorbidity be that the two disorders share similar underlying neurobiological mechanisms? Perhaps individuals suffering from IA have similar impaired brain activity as ADHD but to a smaller degree. So, through comparing the neural correlates of ADHD to those of IA, the understanding of underlying mechanisms of IA will increase.

The Neural Correlates of ADHD

In this chapter, an overview of neurobiological findings of ADHD will be presented. The aim is to show identified dysfunctions and alterations of the brain based on studies using different techniques. ADHD's neurobiology seems to be very complex. The chapter will focus on the major findings in the research area, focusing on findings in structural alterations and functional abnormalities.

Structural alterations. There seems to be evidence that ADHD is associated with changes in the volume of different structures of the brain. Reduced total and regional volume have been identified. Out of these alterations in terms of reduced volume, subcortical structures are the structures that showed the strongest correlations with volume changes (Albajara Sáenz, Villemonteix, & Massat, 2019).

Makris et al. (2006) found a difference in cortical thickness of ADHD patients and healthy controls in several structures such as the cerebrum and prefrontal, lateral inferior parietal and cingulate regions. These regions are involved in the core and the circuitries of attentional and executive control systems of the brain. It is suggested that these areas could be considered as a biological marker for the attentional and executive deficiency in the disorder.

Ellison-Wright I, Ellison-Wright Z and Bullmore (2008) conducted a systematic search for studies using a voxel-based structural magnetic resonance imaging (MRI) studies of patients with ADHD and compared with control groups. No differences in regional gray matter increases were identified. Gray matter decreases were identified in the right putamen/globus pallidus region. These structures together with the caudate nucleus are a part of the corpus striatum. Lesions in right putamen in brain-damaged children who had no prior history of ADHD have been associated with the development of ADHD-symptoms (Herskovits et al., 1999). Corticostriatal circuits are said to involve signals from cortex to

caudate/putamen and back to the cortex through the globus pallidus and thalamus, mediating cognitive control. Substantia nigra signals with dopaminergic projections to the striatum, to allow the activity in the area (Ellison-Wright I et al., 2008). Furthermore, Proal et al. (2011) conducted a prospective study of 207 boys with ADHD, recruited at the age of 6-12 years and was followed-up at a mean age of 41.2 years. The comparison group consisted of all healthy subjects. The objective of the study was to compare differences in cortical thickness and gray matter decrease in regions being hypothesized to be involved in ADHD, using MRI and vertexwise cortical thickness analyses. The reports showed significant thinning of the cortex in the dorsal attentional network andlimbic areas. Also, a significant gray matter decrease in the right caudate, right thalamus and bilateral cerebellar hemispheres were identified. These affected areas all support processes involved in top-down control of attention, and regulation of emotion and motivation (Proal et al., 2011).

Abnormalities in white matter have also been found. Davenport, Karatekin, White and Lim (2010) used diffusion tensor imaging (DTI) to compare white matter integrity of ADHD-subjects (n = 14) with healthy controls (n = 26). All participants were adolescents. The integrity was indicated by fractional anisotropy (FA). The results showed significantly high FA in ADHD-patients in left inferior and right superior frontal regions, which could be associated with deficits in cognitive and behavioral aspects. Also, high FA was observed in bilateral frontostriatal tracts and lower FA in the left posterior fornix. Shaw et al. (2015) investigated if white matter tract microstructures had abnormalities as well. When comparing 75 ADHD-subjects with 74 healthy controls using DTI, they defined FA and also, measured diffusion perpendicular (radial) and parallel (axial) to the axon. The results showed that inattention (but not hyperactivity-impulsivity) was associated with lower FA in the left uncinate and inferior fronto-occipital fasciculi. The abnormalities identified were found in neural processing systems associated with ADHD. For example, systems involving attention control, emotion control and reward processing. Also, they found that the reason for the diffusivity in these tracts was due to radial rather than axial diffusivity and therefore suggested that altered myelination can be the reason for impaired connectivity in tracts regarding inferior fronto-occipital fasciculus and the uncinate fasciculus.

A cross-sectional meta-analysis was conducted by Hoogman et al. (2017) with a sample size of 3242 (1713 ADHD patients and 1529 controls). Several reductions in volume were identified. Reductions in the striatum, especially reduction in the caudate are the most consistent findings in ADHD patients, but also in the putamen and nucleus accumbens. The study confirms previous findings (Frodl & Skokauskas, 2012) of a reduction in these areas but

also acknowledges that the reduction is bilateral as well (Hoogman et al., 2017). Furthermore, alterations in smaller subcortical structures such as the amygdala and hippocampus were found. The Effects in these structures together with the accumbens have previously been identified but could not be replicated. This is hypothesized to be a result of the structures smaller volume and the lack of sufficient technique enough, to identify it. However, Hoogman et al. (2017) provide a more highly powered analysis making it possible. The amygdala seems to play an important role in ADHD. Alterations in the amygdala can result in having unemotional traits, problems in recognition of emotional stimuli and difficulties in emotional regulation in general (Aggleton, 1993). Unemotional traits, not being able to recognize emotional stimuli and problems with regulating one's emotions have all been linked to ADHD. Also, the volume of the amygdala has been associated with hyperactivity (Hoogman et al., 2017). The accumbens plays an important role in reward processing and seems to play a key role in ADHD-patients in terms of emotional and motivational dysfunction (Sonuga-Barke, Bitsakou, & Thompson, 2010). The smaller volume of the hippocampus and its association to ADHD is not as obvious as the previously mentioned brain regions since an impairment in long-term memory (the main function of the hippocampus; Burgess, Maguire, & O'Keefe, 2002) is not a common trait in ADHD-patients. However, studies have shown that the hippocampus may play a role in emotional and motivational processes as well (Shigemune et al., 2010) which is connected to dysfunctions in ADHD. Additionally, the decreases in brain volume were equal to decreases in those subjects who had been treated with psychostimulants medication, and, the findings could not be explained by comorbid disorders. No correlation between total brain volume and the severity of ADHD symptoms was found. The effects in volume size were biggest in childhood and pointed to a delayed peak in subcortical brain volume. Classification of ADHD as a disorder of brain maturation delay is suggested by the authors (Hoogman et al., 2017).

Functional alterations. Cortese et al. (2012) performed a meta-analysis on task-based functional MRI (fMRI) studies of ADHD patients. Seven neuronal systems were used as a reference to the identified brain dysfunctions found, being the default, dorsal and ventral attention, frontoparietal, limbic, sensorimotor and visual networks (Thomas Yeo et al., 2011). The results of children with ADHD showed dysfunctions in terms of hypoactivation in the frontal regions, right parietal and right temporal regions and putamen bilaterally. Hyperactivation was observed in the midcingulate cortex, posterior cingulate cortex, middle occipital gyrus, and right angular gyrus. It showed different results regarding adults.

Hypoactivation was significant in the middle frontal gyrus, precentral gyrus and right central sulcus. Hyperactivation was observed in the middle occipital, and right angular gyri.

In terms of the distribution of different activation in relation to neuronal networks in ADHD patients, adults showed 3% of hypoactivation in the somatomotor network and 97% hypoactivation in the frontoparietal network (Cortese et al., 2012). Hyperactivation was distributed with 26% located in the default mode network, 33% located in the dorsal attention network and 41% located in the visual network. In children the distribution was different however, hypoactivation was located 44% in the ventral attention and 39% in the parietal networks and hyperactivation was located 37% in the default network, 23% in the ventral attention and 22% in the somatomotor network. The different distribution of activation in different neuronal networks indicates that the pathology of ADHD may be due to the interrelationship of different networks (Cortese et al., 2012). Furthermore, in adults, almost all hypoactivated voxels were found in the frontoparietal systems which is consistent with the problems in executive functions of the disorder. The hypoactivated voxels in the somatomotor systems in adults compared to children were fewer, which is consistent with observations of the decline of motoric hyperactivity by age. The visual and dorsal attention systems showed more hyperactivated voxels in adults than in children, and it is hypothesized that these systems may be responsible for a compensatory effect in adults (Cortese et al., 2012).

These dysfunctions in specific neuronal networks may cause the impairment which could be the route of specific symptoms of ADHD. Neuroimaging findings do not seem to be able attributing the dysfunctions of the disorder to one specific lesion in the brain, however. Makris, Biederman, Monuteaux, and Seidman (2009) propose an explanation of the disorder as impairments in several neuroanatomical networks compared to healthy people. Four networks are proposed to be relevant to ADHD, moderating hyperactivity, inattention and executive function, impulsivity, and emotional self-regulation. Hyperactivity's network consists of connections between caudate, cerebellum, dorsal anterior cingular cortex, dorsolateral prefrontal cortex, and the supplementary motor area. Inattention and executive function consist of connections between the cerebellar hemisphere, dorsal anterior cingulate cortex, dorsolateral prefrontal cortex, inferior parietal lobule, and thalamus. Impulsivity consists of connections between cerebellar vermis, nucleus accumbens, orbital frontal cortex, and perigenual anterior cingulate cortex. Emotional self-regulation consists of connections between amygdala, cerebellar vermis, frontoorbital cortex, and perigenual anterior cingulate cortex (Makris et al., 2009).

Functional studies seem to report effected fronto-subcortical systems as a part of the psychopathology of ADHD (Charney, Buxbaum, Sklar, & Nestler, 2013). Also, the most consistent findings appear to be less activity of the inferior frontostriatal, temporoparietal and cerebellar areas when performing a test that involves attention and inhibitory control. It appears as when ADHD-patients are trying to perform a task their brain activates different compensatory networks and it is trying to perform it in a less effective way. Instead of using the executive function parts of the brain in a cognitive task, they use the motor, visual and spatial processing areas. One treatment of ADHD is to prevent this from happening, ordering stimulants to the patient in order to activate the hypoactivated areas making it function as a more normal functioning brain. Research is not sure why these brain regions malfunction but point out that the most plausible explanation for the miswiring of the ADHD-brain is a result of genetic factors and environmental influences during fetal development (Charney et al., 2013).

The Neurobiological Findings of IA

This section will present the results of the literature search on the Web of Science. Studies found and chosen to be presented, are based on the fact that they met the inclusion criteria. Studies will be presented based on the imaging technique being used in the study.

Magnetic Resonance Imaging (MRI)

Zhou et al. (2011) investigated gray matter density changes using voxel-based morphometry (VBM) analysis in adolescents with IA using structural MRI. VBM is a time-saving technique used to compare different groups of people on brain volume in an effective way. It does not measure specific regions of the brain but instead focuses on group differences in gray matter tissues across the whole brain (Ashburner & Friston, 2000). The IA subjects consisted of two females and sixteen males with a mean age of 17.23 ± 2.60. YDQ was used to classify participants as internet addicted or not. The control group consisted of fifteen healthy participants. These subjects were age and gender-matched with the IA group. The results showed that the IA group had lower gray matter volume compared to the control group in the left anterior cingulate cortex, left posterior cingulate cortex, left lingulate gyrus and the left insula (Zhou et al., 2011).

The cingulate gyrus is an important part of the limbic system which is responsible for controlling different emotional states such as motivation, emotions and motor control. This region also provides a pathway from the thalamus to the hippocampus and is hypothesized to help focus attention to emotional stimuli and regulate aggressive behavior. But it is also a part

of a bigger default system of cortical regions. Dysfunctions within this system may result in disturbance of emotional behavior (Mayberg, 1997). The insula seems to play an important part in different addictions. Dysfunctions of the insula in terms of lesions and/or hypoactivity underlies addiction and is necessary for the explicit motivation to take different substances (Naqvi, Rudrauf, Damasio, & Bechara, 2007). This theory is also strengthened by two different studies, the first one showing that cocaine users have decreased gray matter density in the insula (Franklin et al., 2002) and the second one showing that patients with schizophrenia have a tendency to have a higher number of cigarette smoking compared to healthy subjects, hypothesized being because of a reduced gray matter density in the insula (Crespo-Facorro et al., 2000). According to Zhou et al. (2011) all these areas where reduction of gray matter was identified in the IA group, are linked together by regions responsible for emotional behavior. These areas should affect the functioning of these regions and are supported by the often occurring behavioral and emotional problems reported from IA patients (Yuhua & Du Yasong, 2006). Furthermore, Zhou et al. (2011) state that the change in the visual associative area left lingulate gyrus was a relatively new finding, although it had been seen in patients with schizophrenia earlier. They could not interpret the meaning of this finding.

Diffusion Tensor Imaging (DTI)

Yuan et al. (2011) enhanced the understanding of IA by conducting a study to see the effects of IA on the microstructural integrity of certain neuronal pathways, as well as to investigate these microstructural changes in relation to the actual duration of the addiction. They used an optimized VBM technique to see the morphology of the brain in IA subjects compared to controls and used diffusion tensor imaging (DTI) to study changes in white matter fractional anisotropy (FA), to finally link the changes to the duration of IA. 18 (12 males and 6 females, mean age 19.4 ± 3.1) student participants were recruited and diagnosed with IA according to the modified YDQ. All participants were gender-matched with healthy controls (mean age 19.56 ± 2.8; Yuan et al., 2011

The VBM results showed decreased gray matter volume in IA-subjects compared to controls in the regions of the bilateral dorsolateral prefrontal cortex, the right supplementary motor area, the right orbitofrontal cortex, the cerebellum and the left rostral anterior cingulate cortex (Yuan et al., 2011). No regions showed an increase in gray matter volume. The dorsolateral prefrontal cortex, left rostral anterior cingulate cortex and, the right supplementary motor area showed a negative correlation with the amount of months of IA, which implies that the atrophy of these brain regions becomes worse with the length of

internet usage. The DTI results showed white matter changes in terms of enhanced FA value in IA-subject compared to controls in the left posterior limb of the internal capsule and a reduced FA value in the right parahippocampal gyrus. A positive correlation was found between the FA value and duration of IA in the left posterior limb of the internal capsule but not in the right parahippocampal gyrus (Yuan et al., 2011).

The authors of the study suggest that these changes of structural abnormalities are probably associated with a decrease in cognitive control (Yuan et al., 2011). Cognitive control can be understood as a process suppressing incorrect responses and being able to filter out information from different simultaneously stimuli to allow the correct response in different demanding tasks and environments (Botvinick, Braver, Barch, Carter, & Cohen, 2001). Previous studies have shown that the bilateral dorsolateral prefrontal cortex and the rostral anterior cingulate cortex plays a key part in cognitive control (Krawczyk, 2002). The orbito-frontal cortex is also involved in cognitive control in the way that it is assessing the motivational importance of a stimulus, followed by deciding proper behavior to meet desired outcomes in response to the stimuli (Rolls, 2000). Also, the orbitofrontal cortex is highly connected with regions of the brain involved in motivational behavior and reward processing such as the striatum and limbic regions, therefore involved in integrating these signals (Groenewegen & Uylings, 2000). The supplementary motor area plays an important part in deciding whether to execute a response or inhibit an inappropriate response (Simmonds, Pekar, & Mostofsky, 2008). The cerebellums part in higher cognitive functions is also recognized as mentioned above. Yuan et al. (2011) suggest that the atrophy in mentioned brain regions may at least play a part in the dysfunctions of cognitive control and goal-directed behavior in Internet addicts. Also, they can serve as an explanation for some of the symptoms reported by them.

The DTI and measuring of FA value in white matter showed enhanced FA in the left posterior limb of the internal capsule. The internal capsule is a region that separates the thalamus and caudate nucleus from the lenticular nucleus which contains many incoming and outgoing fibers (Wakana, Jiang, Nagae-Poetscher, Van Zijl, & Mori, 2004). The primary motor cortex is important in for example finger movement and motor imagery and sends its signals through the internal capsule (Schnitzler, Salenius, Salmelin, Jousmäki, & Hari, 1997). Yuan et al. (2011) hypothesize that the change of the white matter structure in the internal capsule is a result of the amount of repetition of mouse clicking and keyboard taping in internet addicts and explains the positive correlation with the duration of the addiction. Furthermore, since signaling between the frontal and subcortical regions travels through the

internal capsule and modulates cognitive functioning and behaviors, abnormalities in these tracts can affect these functions. Regarding the parahippocampal gyrus, it anatomically surrounds the hippocampus and is involved in encoding and retrieval of memory (Wagner et al., 1998). It receives sensory signals and provides it to the hippocampus which is involved in cognitive functions, memory, and emotional regulation. Yuan et al. (2011) suggest that the parahippocampal's abnormalities can explain the deficits in working memory of Internet addicts, since working memory is important in cognitive control due to its function of temporary storage and manipulation of information (Engle & Kane, 2004).

Lin et al. (2012) conducted a study with the same interest of investigating the white matter integrity in adolescents of Internet addicts, without doing assumptions about where to find these potential abnormalities in the white matter structure. 15 (13 males and 2 females, mean age 17.01 ± 2.50) were included in the IA-group and compared with 14 age and gender-matched healthy control subjects. The IA-group were diagnosed with IA according to the modified YDQ. The results showed that no brain region had a lower FA value in the control group compared to the IA group. However, the IA group had significantly lower FA value and showed deficits in white matter integrity in following brain regions: commissural fibers of the corpus callosum, association fibers in the inferior frontal-occipital fasciculus, projection fibers containing corona radiation, internal capsule and external capsule, cingulum and orbito-frontal regions. Furthermore, the analysis showed that the deficits of the white matter mainly consisted of radial diffusivity which is hypothesized being a result of demyelination (Lin et al., 2012).

Orbito-frontal regions are involved in emotional processing in addiction and play a big role in symptoms associated with addiction such as maladaptive decision-making, compulsive and repetitive behaviors and craving (Schoenbaum, Roesch, & Stalnaker, 2006). This region has many connections with motor, sensory, prefrontal and limbic regions (Öngür & Price, 2000). The anterior cingulate cortex is highly connected to the frontal lobes and is as previously mentioned highly involved in emotional processing, cognitive control, and craving (Goldstein & Volkow, 2002). The largest white matter tract in the brain is corpus callosum and is placed in the center of the brain and is responsible for connecting the two hemispheres together (De Lacoste, Kirkpatrick, & Ross, 1985). Abnormalities in the microstructure of the white matter were found here as well. Lin et al. (2012) suggest that the alterations in the internal capsule may be a representation of abnormalities in the subcortical circuits of reward and emotional processing. The pathway of the internal capsule connects thalamus/striatum and the frontal cortical regions. Furthermore, the external capsule connects the striatum with

ventral and medial parts of the prefrontal cortex. The corona radiata is connecting the internal capsule to the cerebral cortex and is involved in connectivity between frontal, occipital, parietal and temporal lobes. Alterations in all these mentioned fiber tracts are all consistent with previous findings of affected fiber tracts of those patients suffering from different kind of addictions (Lin et al., 2012). Since radial diffusivity is a reflection of the integrity and thickness of the myelin sheath and axial diffusivity is a reflection of the structure and integrity of the axon (Song et al., 2002), Lin et al. (2012) humbly conclude that the abnormalities in the fiber tracts are mainly due to impaired myelin sheaths.

Functional Magnetic Resonance Imaging (fMRI)

Dong, Huang and Du (2011) conducted a study of how IA subjects process reward and punishment in a neurobiological sense compared to healthy controls. Recruited IA subjects were 14 males, and they were age-matched with 13 healthy control subjects. All IA subjects were diagnosed according to YIAT, with a larger than normal (80 compared to 50 points) threshold score. The study was constructed to measure the participants' brain activity using fMRI during a problematic guessing task in which they experienced monetary gain and loss. The task lasted one session with a total of 245 trials. The backside of two playing cards was shown on a monitor and participants had to choose between the two cards by pushing a button. Then, the cards were turned over and, presented randomly either a win or a loss of 10 dollars. Participants started with 50 dollars and were informed that they would keep the remaining balance at the end of the task. The results showed a difference in the neural circuitry underlying reward and punishment. The IA subjects had increased activity in the orbitofrontal cortex during win conditions and decreased activity in the anterior cingulate cortex during loose conditions, compared to control subjects. Additionally, a positive correlation was found between YIAT and the activation of the orbitofrontal cortex (Dong et al., 2011).

It is suggested that the hyperactivation of the orbitofrontal cortex may be due to a higher sensitivity to rewards of the IA patients (Dong et al., 2011). The suggestion is based on the fact that the orbitofrontal cortex is associated with value-guided behavior (Rangel, Camerer, & Montague, 2008) and its activation during pleasant touch and rewarding (Rolls & Larry, 2009). In addiction the reward circuitry is hypothesized to play a crucial role in terms of the development and maintenance of the disorder. Also, addicts have a deficient reward system which is believed to be the reason for why addicts try to compensate through engaging in for example drug use or pathological gambling, in order to maintain wanted homeostasis in the dopamine levels of the reward circuitry (Robbins & Everitt, 1999). However, the findings

of hyperactivation in Internet addicts are inconsistent with the previous findings in other addiction groups, where hypoactivation of the same brain region was the most consistent finding (Dong et al., 2011). Monetary loss in IA compared to healthy controls was associated with a decreased activity in the anterior cingulate cortex. This brain region is a part of a network involved in aversive processing, emotional response to pain and empathy for pain (Vogt & Sikes, 2000). Petrovic et al. (2008) also found that activation of this brain region rose in line with unpleasantness ratings for losses and that it functioned causally in regulating the hedonic experience of losses. Dong et al. (2011) speculate that this can explain why Internet addicts show less response to monetary loss and it could indicate why Internet addicts choose to engage in Internet activities without being concerned about potential consequences in different domains of life.

Liu et al. (2010) conducted a study using fMRI to localize functional characteristics during resting state in IA patients using a regional homogeneity method (ReHo). This method was chosen because according to the authors it produces a clearer understanding when interpreting the results of which brain regions are involved.

A total of 38 participants between 18-22 years of age were recruited. 19 (11 males and 8 females) were diagnosed with IA according to YDQ, and 19 sex-matched healthy controls. (Liu et al., 2010). The results showed an increased synchronization among most brain regions in Internet addicts compared to controls, and abnormalities in regional homogeneity. The synchronizations were enhanced in the cerebellum, brainstem, bilateral parahippocampus, right frontal lobe, right cingulate gyrus, left precuneus, right inferior temporal gyrus, middle temporal gyrus, left superior temporal gyrus, right middle occipital gyrus, right postcentral gyrus and left superior frontal gyrus. The synchronization among brainstem, cerebellum, occipital lobe, frontal lobe, and limbic lobe may be relevant to reward pathways (Liu et al., 2010). Aside from the cerebellums' most paid attention functions of balance and movement, studies report it has some higher cognitive functions, for example planning actions and emotions. The connectivity between the cerebellum and the rest of the brain helps in cognitive activity and the processing of emotions. The cerebellum, cingulate gyrus, mesencephalon and parahippocampal gyrus are parts of the reward pathway, and the enhancement in connectivity between them indicates an enhanced reward pathway in Internet addicts. The major functions of the temporal regions are the regulation of sense perception, also the processing of auditory and visual stimuli via the primary and secondary associated cortex. The increased connectivity in the parietal and temporal regions are considered to perhaps be a result of the behavior of the Internet addicts, in terms of constant visual stimuli from the screen and

frequent exposure to sounds (Liu et al., 2010). The constant stimulation over a long period of time is hypothesized to make these regions easily excited and be the reason for the enhanced connectivity. The connectivity in the frontal lobe and parietal lobe showed advanced enhancement compared to a normal person. The cortex of the frontal lobe (which is the essential brain region for impulse control) is the most complex and evolved region of the cortex which receives signals via nerve fibers from the different lobes, sensory cortex, limbic cortex including parahippocampal gyrus and cingulate gyrus (which produce efferent signals to the striatum and pons). The researchers conclude that based on their study and current literature at the time, concrete sensory experiences such as color and spatial/positional/space perception are formed in the parietal lobe (conducted via certain visual and auditory pathways). Furthermore, these are signaled to the frontal lobe for planning, execution and decision making. The frequent activation of these regions in the Internet addicts results in an enhanced synchronization of these regions as seen in the fMRI and it may be associated with reward pathways. However, further studies are needed to confirm the findings (Liu et al., 2010).

Hong et al. (2013) investigated whole-brain functional connectivity in adolescents diagnosed with IA, compared to healthy subjects, using resting-state fMRI. The author's predictions were to find the most prominent alterations in cortico-striatal circuits, based on neurobiological findings of other addictions. 12 right-handed males diagnosed with IA in accordance with YIAT participated in the study, together with 11 gender and IQ-matched healthy control subjects. Hong et al. (2013) mapped the difference in functional connectivity between 90 distinct cortical and subcortical brain regions. The results showed the identification of a single network that showed significantly decreased connectivity. This network had 59 links and involved 38 different brain regions. 24% of the connections involved links between frontal and subcortical regions, and 27% involved links between subcortical and parietal areas, a small involvement of insula included. Among these 59 links, 25 were connections between the hemispheres and 34 were connections inside one of the hemispheres, which point to both long-range and short-range connections being involved. Hong et al. (2013) point out it is surprising finding such a wide effected network in a disorder that is fairly new. To increase the understanding of which subcortical regions that were involved in this finding they separately examined the connectivity between each subcortical region and each cortical lobe. This examination showed involvement of the putamen, hippocampus, and globus pallidus. The bilateral putamen was the most involved subcortical region and showed decreased connectivity with all cerebral lobes. The putamen is a part of the

striatum and striatum is a part of the subcortical structures. The putamen is a subcortical structure mainly associated with motor activity (Jueptner, Frith, Brooks, Frackowiak, & Passingham, 1997). The putamen has not frequently been identified in addiction disorders, an explanation for identifying it in this study could be due to the impairment of cognitive processes together with the caudate in IA, creating dysfunction in reward-processes (Volkow, Fowler, & Wang, 2003). It is hypothesized that the decreased connectivity in the IA group of the putamen is due to repetitive behavior such as frequent mouse and keyboard use (Hong et al., 2013). The putamen is also known to modulate different neurotransmitters including dopamine, also, an altered striatal dopaminergic function has been identified as a key neurological mechanism in addiction disorders (Goldstein & Volkow, 2011). Hong et al. (2013) suggest that the decreased functional connectivity observed can be due to the altered striatal dopaminergic function since the putamen is a key modulator. The study could not find any brain region with increased connectivity in the IA group compared to the control group. The authors suggest, that the fact that their analysis identified decreased connectivity in these cortico-subcortical systems, it is very likely that it is a part of the pathology of IA. Especially, the affected subcortical regions since these neurobiological mechanisms are shared with other addictive disorders (Hong et al., 2013). Furthermore, they make a point of highlighting that IA is diagnosed as a behavioral addiction and could be considered as a pure addiction free from long-term drug effects. Therefore, the interpretation of the result can give a more targeted model on how to study addiction in general.

Positron-Emission Tomography (PET)

Kim et al. (2011) conducted a study to test if people with IA had a decreased dopaminergic receptor availability in striatal brain regions, on the basis that IA shares the same neurocognitive mechanisms as other addiction disorders. The study used Positron-Emission Tomography (PET) to assess dopaminergic receptor availability using a radioligand that binds to dopamine receptors without any other neurochemical reactions. The IA group consisted of 5 males (age: 22.60 ± 1.16) diagnosed in accordance with YIAT and the control group consisted of 7 age-matched males. Kim et al. (2011) targeted specific brain regions, in which they assessed D2 receptor availability. The predetermined regions were the dorsal caudate, dorsal putamen and the ventral striatum, all regions being a part of the striatum. The results showed significantly reduced binding potential of the radioligand in the IA group compared to the control group, situated in the left dorsal caudate, left dorsal putamen and right dorsal caudate. A trend of decreased BP in the right putamen was also identified. No difference could be identified between the groups in the left ventral striatum and right ventral

striatum. Furthermore, Kim et al. (2011) tested if the dopamine D2 receptor availability could be associated with the duration of the Internet addiction. Significant negative correlations were found between scores of YIAT and measures of the radioligands BPs in the left dorsal caudate, left dorsal putamen and right dorsal putamen. In other words, a higher reduction of D2 receptor availability pointed to higher severity of the addiction.

Reduced D2 receptor availability in the reward-pathway is a mentioned explanation in reward deficiency syndrome, and people diagnosed with it describe an increase in need of excitement and stimulation (Comings & Blum, 2000). Engaging in Internet activities may stimulate the reward pathway. One study pointed out that feelings of excitement and pleasure from using the Internet was mentioned as experienced feelings of Internet addicts while using it, and, was suggested as a key predictor of IA (Chou & Hsiao, 2000). Based on these studies Kim et al. (2011) hypothesize that Internet addicts may use the Internet to stimulate the hypodopaminergic reward pathway. Furthermore, the failure to identify differences between the groups in the ventral striatum is hypothesized by the authors to be explained by the PET imaging limitations in detecting statistically significant differences in small areas of the brain. This shortcoming occurred even though they predicted to find it, based on previous findings that nucleus accumbens of the striatum are impaired in the processing of rewarding properties of a stimulus (Robbins & Everitt, 1992). Kim et al. (2011) conclude that their findings are consistent with previously findings of hypodopaminergic activity in the dorsal striatal regions of other addictions.

Single-Photon Emission Computed Tomography (SPECT)

Hou et al. (2012) conducted a study to investigate if striatal dopamine transporter (DAT) levels were altered in individuals with IA compared to healthy controls, based on the hypothesis that altered availability of DAT is associated with the pathogenesis of IA. DAT is a protein working in the presynaptic terminal with the mission of dopamine reuptake into the presynaptic neuron, making it a key modulator of striatal synaptic dopamine levels (Schultz, 1998). They used SPECT as an imaging technique.

Participants consisted of 5 males (age: 20.40 ± 2.30 years old) in the IA group being diagnosed according to YDQ. Thecontrol group consisted of 9 age-matched healthy control subjects (Hou et al., 2012). Results of the SPECT images showed that the bilateral corpus striatum of the control subjects was panda-eye formed and DAT was symmetrically distributed. However, images of the Internet addicts brains showed asymmetrical shapes of the bilateral corpus striatum and being smaller in size. The values of the volume, weight and the ratio between corpus striatum/whole brain were significantly decreased. Also, a significant

decrease in the radioligand binding to the DAT in the striatum compared to the control group. Hou et al. (2012) further speculate that the reduced stats of DAT found in their study may indicate neurological damage of the dopaminergic neural system in the bilateral corpus striatum probably caused by IA. Their conclusion is drawn based on the result of their study together with knowledge from the literature at the time. DATs have been used as markers for dopamine terminals, also they play an important role in the regulation of dopamine levels in the synaptic cleft of the striatum (Schultz, 1998). Hou et al. (2012) speculate that a reduction of striatal dopamine terminals may be a result of a reduction of neuron membrane DATs, or of impairment in the dopaminergic system of the brain, which has been seen in other substance-related addictions (Jia, Wang, Liu, & Wu, 2005). Furthermore, since an earlier study shows that participants reported feelings of euphoria and high (when experiencing reward) simultaneously as they had an increase of extracellular dopamine levels in the striatum (Volkow, Fowler, Wang, Baler, & Telang, 2009), and that a study has shown an increase of dopamine levels in the striatum while engaging in video games (Koepp et al., 1998), Hou et al. (2012) speculate that Internet addicts also may experience these mentioned feelings when dopamine levels rise in the striatum. However, having increased levels of dopamine over a long period of time in the striatum have been showed to create a reduction of dopamine terminals (LaVoie & Hastings, 1999) as well as abnormalities of dopaminergic cell bodies (Kish et al., 2001). Taken this together, Hou et al. (2012) arrive at the earlier mentioned conclusion and additionally say that the present study shows the objective proofs that long-term use of the Internet may cause serious problems, although some limitations of the study should be considered for a complete interpretation of the results.

Discussion

The aim of this thesis was to investigate two different research questions. 1) what underlying neurobiological mechanisms of IA can be identified, and 2) are the underlying neurobiological mechanisms of IA similar or different from the underlying neurobiological mechanisms of ADHD. The purpose of this comparison is founded on Ko et al.'s (2012) suggestion that it is important to understand the underlying mechanisms of the comorbidity, in order to develop good preventative and effective treatments for IA. This discussion section will aim to firstly, present a summary of the identified neural correlates of IA, secondly, present a comparison between neural correlates of IA and ADHD, and thirdly, discuss limitations and, -further directions and end with a conclusion.

Summary of Research on the Neural Correlates of IA

We considered two studies that used the neuroimaging technique MRI to identify structural changes in the brain of IA subjects and, several different regions were identified. A lower gray matter volume was identified by Zhou et al. (2011) in the left anterior cingulate cortex, left posterior cingulate cortex, left lingulate gyrus and the left insula. Also, identified alterations were found in the bilateral dorsolateral prefrontal cortex, the right supplementary motor area, the right orbitofrontal cortex, cerebellum and the left rostral anterior cingulate cortex by Yuan et al. (2011). No regions showed an increase in gray matter volume. Furthermore, a negative correlation was shown with the dorsolateral prefrontal cortex, left rostral anterior cingulate cortex, right supplementary motor area and the duration of IA.

Three studies used fMRI to investigate the functional connectivity of the IA brain. Dong et al. (2011) had IA subjects perform a problematic guessing task containing gain and loss results. They identified increased activity in the orbitofrontal cortex during win conditions and decreased activity in the anterior cingulate cortex during loss conditions. Also, a positive correlation between YIAT and the activation of the orbitofrontal cortex was identified. Liu et al. (2010) identified an increased synchronization among most brain regions when using resting state fMRI. Increased activity was found in the cerebellum, brainstem, bilateral parahippocampus, right frontal lobe, right cingulate gyrus, left precuneus, right inferior temporal gyrus, middle temporal gyrus, left superior temporal gyrus, right middle occipital gyrus, right postcentral gyrus and left superior frontal gyrus. Hong et al. (2013) mapped the difference in functional connectivity between 90 distinct cortical and subcortical regions. A single network showing significantly decreased connectivity, consisting of 38 different brain regions was identified where connections between subcortical regions and frontal/parietal regions seemed to be most involved. Both short-range and long-range connections between the hemispheres were involved. Further examination of connectivity between each subcortical region and each cortical lobe showed a major involvement of the subcortical structures the putamen, hippocampus and globus pallidus.

We also considered two studies that used DTI to investigate white matter integrity. Yuan et al. (2011) identified white matter changes in terms of enhanced FA value in the left posterior limb of the internal capsule and a reduced FA value in the right parahippocampal gyrus. A positive correlation was found between the FA value and the duration of IA in the left posterior limb of the internal capsule. Lin et al. (2012) identified a lower FA value in the corpus callosum, inferior frontal occipital fasciculus, corona radiation, internal capsule,

external capsule cingulum, and orbitofrontal regions. Further examination showed that the deficits in white matter integrity mainly consisted of radial diffusivity (i.e. demyelination).

One study (Kim et al., 2011) used PET to study the dopaminergic receptor availability in striatal brain regions, specifically identifying abnormalities in dopamine D2 receptors. Significantly reduced BP of the used radioligand was identified in the left dorsal caudate, left dorsal putamen and right dorsal caudate. Also, a trend of reduced BP in the right putamen was found. Furthermore, negative correlations were found between YIAT and BP in the left dorsal caudate, left dorsal putamen and right dorsal putamen.

One study (Hou et al., 2012) used SPECT to research if striatal DAT levels were altered. They identified a difference in images of the bilateral corpus striatum in terms of asymmetrical shapes, smaller size and the volume, weight, and ratio (between corpus striatum/whole brain) were significantly decreased. Also, a significant decrease in radioligand bindings to DAT.

When all findings are taken together it seems as if IA has some underlying neurobiological mechanisms constituting the existence of the disorder. This thesis considered eight separate studies, together showing some similar, but also different, and in one case conflicting results. However, it seems that some of the symptoms showed by IA subjects can be logically explained by thinking about the affected brain regions functions in healthy conditions. In other words, the alterations of these regions may cause the symptoms. Plausible parallels have been drawn throughout the text between these affected brain regions and symptoms of IA. In accordance with Young's (1998) diagnostic questions, some of them regard symptoms of failure in controlling one's negative emotions such as feeling restless, moody or depressed. Alterations of brain structures associated with emotional behavior have been identified and may be considered as biological markers for the impaired emotional processing of an IA subject. One can speculate that impairment of emotional regions could explain why internet addicts choose to engage in excessive use and not care about the potential consequences of this behavior.

Alterations of cingulate gyrus (important part of the limbic system) in structural (Zhou et al., 2011; Yuan et al., 2011), in functional connectivity (Dong et al., 2011; Liu et al., 2010) and in white matter integrity (Lin et al., 2012), as well as structural alterations in insula (Zhou et al., 2011) and in prefrontal areas, all indicate the biological markers associated with disturbed emotional processing. Furthermore, several altered brain regions have been identified which are associated with impaired cognitive control. These alterations are in line with other diagnostic questions of Young's (Young, 1998). They regard the ability to control

one's behavior (for example not being able to control usage time, cutting back in usage time, totally stop usage time or in other words using the internet more than one intended to do). One can speculate that brain regions associated with goal-directed behavior, impulse- and cognitive control plays an important part in not being able to control ones' usage time. Different kinds of visual and auditory stimuli reach us constantly and constant decision-making takes place when differentiating between these stimuli. The lack in the ability to suppress responses to this information overload, as well as evaluating the motivational importance of the stimuli, in order to allow the correct response (for example, not engaging in usage) may play a key role in experiencing IA. Alterations of brain regions associated with these cognitive abilities were identified in orbitofrontal cortex in structural connectivity (Yuan et al., 2011), functional connectivity (Dong et al., 2011; Hong et al., 2013) and in white matter integrity (Lin et al., 2012). Also, prefrontal regions in structural (Zhou et al., 2011; Yuan et al., 2011), functional connectivity (Liu et al., 2010; Hong et al., 2013). Also, the supplementary motor area (Yuan et al., 2011) and cerebellum (Yuan et al., 2011). Additionally, the functional connectivity alterations identified of parahippocampal gyrus (Yuan et al., 2011) which provides the hippocampus with signals, and alterations of these fiber tracts can also affect cognitive control since working memory is an important part of cognitive control.

It seems that one important aspect of the pathology of IA is alterations of the reward pathway system. Alterations in functional connectivity among the cerebellum, cingulate gyrus, mesencephalon, and parahippocampal gyrus are parts of the reward pathway (Liu et al., 2010) and the enhancement in connectivity between them indicates an enhanced reward pathway in Internet addicts. Also, the alterations identified in the fiber tracts of the internal capsule, external capsule, and the corona radiata connect with reward pathways (Lin et al., 2012) which consequently adds on to the suggestion of altered reward circuitry. Furthermore, Hong et al. (2013) identified the putamen as one of the most involved subcortical structures in enhanced functional connectivity. The putamen's role in motor activity and modulation of neurotransmitters (for example dopamine) also point to an altered dopaminergic function. Furthermore, this literature review included PET and SPECT studies which suggested a decreased dopamine D2 receptor availability in the caudate and the putamen (Kim et al., 2011; also, a correlation between the availability of receptors with the duration of IA). And, a decreased number of DATs were found in the bilateral corpus striatum (Hou et al., 2012). These findings further show an altered reward circuitry in the IA subject's brain. As discussed in the text, other addictions have deficient reward systems and one possible suggestion for

why Internet addicts engage in excessive use is that it helps to maintain homeostasis in the dopamine levels of the reward circuitry. Dopamine is a key neurotransmitter of the reward circuitry and high levels of this neurotransmitter in the system may create pleasant feelings. Prone that engaging in Internet activities releases dopamine and create good feelings (Koepp et al., 1998), and that increased levels of dopamine over a long period of time in this system leads to a reduction of dopamine terminals and abnormalities in dopaminergic cell bodies (LaVoie & Hastings, 1999); Kish et al., 2001). This supposedly points in the direction of a possible explanation to why Internet addicts feel an urge to engage. In other words, in order to balance the deficient dopamine levels of the reward circuitry. This idea would explain several symptoms of being diagnosed according to YDQ. For example, why internet addicts are preoccupied with the internet, why they develop increased tolerance (as dopamine levels decreases with time) and why they experience bad emotions when not using the Internet. Also, why Internet addicts prioritize Internet activities in front of other important tasks in life, making them risk negative consequences in different domains in life.

Comparison of the Neural Correlates Between ADHD and IA

A comparison between the underlying neurological mechanisms of ADHD and IA, in terms of similar structural and functional alterations, will be presented in this section. The purpose of this comparison is to make an argument for the importance of bringing more attention to IA. ADHD is a well-established psychiatric disorder. Highlighting similar alterations of brain regions between these disorders may create an understanding of the increased attention needed for IA.

Several structural alterations of ADHD were identified. First of all, there was a decrease in cortical thickness in the cerebrum, prefrontal-, parietal-, and cingulate regions. These regions were suggested as biological markers for attentional and executive deficiency in ADHD (Makris et al., 2006). Furthermore, thinning of the critical thickness in limbic areas and attentional networks has been observed (Proal et al., 2011). Gray matter decrease in the right putamen/globus pallidus region (parts of the corpus striatum; Ellison-Wright et al., 2008). Hoogman et al. (2017) found reductions in the volume of the striatum, especially in the caudate but also in the putamen and nucleus accumbens. Also, alterations in subcortical structures as the amygdala and hippocampus were found. Both IA and ADHD seem to share some similar structural alterations, in regions associated with emotional processing, such as limbic areas, specifically the cingulate regions. In ADHD the amygdala seems to play a big part in the disorder, being associated with emotional processes, but it has not been identified as altered in IA. The volume of the amygdala has been associated with hyperactivity in

ADHD (Hoogman et al., 2017), which is not a reported symptom of IA. In IA, the insula was identified as altered, but not in ADHD. The insula is more associated with addiction in general. Also, the cerebellum seems to be altered in both disorders as well as the prefrontal regions. Alterations of both areas are associated with deficiencies in cognitive control and attentional deficiencies, being characteristic symptoms of both disorders.

Although structural alterations of areas such as the putamen, caudate, globus pallidus region, nucleus accumbens, and hippocampus are identified in ADHD, such alterations do not seem to be identified in the structural studies of IA. However, alterations of these brain regions have been identified in fMRI, DTI, PET and SPECT studies of IA. This may imply that the two disorders share at least some alterations in these brain regions as well. Alterations of the putamen were identified in several different contexts in the IA studies. Furthermore, lesions in the right putamen in brain-damaged children who had no prior history of ADHD, have been associated with the development of ADHD-symptoms (Herskovits et al., 1999). This may imply that alterations of the putamen in IA can explain some of the similarities between the two disorders.

Several functional alterations have also been identified in both ADHD and IA. In ADHD adult subjects, 97% of the hypoactivation was identified inside a frontoparietal network (Cortese et al., 2012). Hypoactivation in this network can explain problems with executive functions, such as cognitive control (shared with IA). IA also seems to have hypoactivation of this frontoparietal network. The dysfunctions of the disorder do not seem to be able to be attributed to one specific lesion in the brain but instead consist of impairments of several neuroanatomical networks. In terms of shared symptoms between the two disorders, some involved networks may be considered as an explanation for those. Out of the four mentioned networks (Makris et al., 2009), the one's moderating attention- and executive functions, and emotional self-regulation seems like the most plausible to be shared. Inattention and executive function consist of hyperactivated connections between the cerebellar hemisphere, dorsal anterior cingulate cortex, dorsolateral prefrontal cortex, inferior parietal lobule and thalamus. Also, emotional self-regulation consists of hyperactivated connections between the amygdala, cerebellar vermis, frontoorbital cortex and anterior cingulate cortex (Makris et al., 2009). In terms of altered brain regions, IA share increased altered connections between the cerebellum, prefrontal regions, cingulate regions, orbitofrontal regions (Liu et al., 2010). However, in the fMRI studies, the results are somewhat inconsistent. Some show hyperactivation and some show hypoactivation regarding the same brain regions, and conclusions are difficult to be drawn. It is obvious though that in

Internet addicts compared to healthy controls, significant differences exist in terms of functional connectivity. It is hard to detect a consistent pattern, especially in seeing clear similarities in functional connectivity. However, the same brain regions seem to be involved in both disorders.

Limitations and Further Directions

IA is for now only a suggested disorder and the field of research seems to be constrained by many different limitations which probably complicates the process to make it an established and accepted disorder. This section points out some of these limitations and simultaneously suggests future directions to increase the chances for improvement inside this research field. Also, limitations of this thesis, in general, are discussed.

This field of research is not built on one singular model describing IA. Several different models exist and inconsistencies among them is a fact. For example, of the included studies in this thesis, at least three different assessment tools of IA are being used for diagnosing the participants as Internet addicts. The lack of consensus of the diagnostic model underlying IA should be considered as a possible shortcoming.

Regarding the sample being used in most of the studies, it is generally a very small number of participants. Inconsistencies due to multiple studies with a small sample size should also be considered as a problem of the field. Furthermore, most of the studies are conducted in East Asia and consist of Eastern individuals. This fact is creating a problem of not being able to generalize the findings across cultures. Also, the selection criteria of participants have mainly been focused on young/adolescents males which aggravate the generalizability furthermore.

The conceptualization of IA as a broad and general term including all Internet activities as the same seems to be a faulty approach. When using the Internet there are many activities available, different from each other. This fact can adventure generalizability. It could be the case that Internet activities different from each other have different underlying neurological mechanisms. However, this possibility has not been considered in most studies. And, if the neural correlates are different, different approaches are likely to be necessary to develop correct preventative measures and treatments. The only separation being made is between IGD and IA.

Regarding the neuroimaging technique approach, it can only describe different correlations between brain regions and IA. It can not be used to create causality inferences and it leaves out a potential causal explanation of the findings. However, it seems as if it can

function as a good tool to map out the disorder and be used in the creation of a better, clearer model of IA.

Further limitations regarding the research approach of this thesis must be lifted. Firstly, this thesis only covers a small part of the existing literature in the field of research. Therefore, any major conclusions should be avoided, although the thesis does present an approximate view of where IA stands in its development of understanding its neural correlates at the moment. Secondly, making a comparison between ADHD and IA, with the approached used, has only a limited value. Comparing identified alterations in brain regions only gives a small indication of potential shared mechanisms, due to the complexity of the brain. More advanced approaches are needed to present more substantial correlations between the two.

Further directions for research in IA should be focused to reach a consensus in the operational definition of IA. Selection criteria for the participants have to make a broader approach and attempt to include participants with different ethnic and cultural backgrounds. Also, an aim to include a wider age-range and better gender-ratio to increase the generalizability of the findings is needed. It would be interesting to see longitudinal studies to increase the understanding of the development of IA, as well as the changes occurring correlated with the duration of IA. Also, a development of subcategories based on the kind of activity the individual engages in when using the Internet. This can potentially lead to more accurate preventative measures and treatments.

Conclusion

Although the research field of IA consists of many limitations, the existing literature of underlying neurological mechanisms seems to have identified some relevant and interesting findings with the use of neuroimaging techniques.

In conclusion, this thesis shows that MRI, fMRI, DTI, PET and SPECT studies have revealed several structural, functional and neurochemical alterations of the IA brain. These alterations are found in areas associated with emotional processing (the cingulate gyrus and insula), cognitive control (orbitofrontal regions, supplementary motor area, parahippocampal gyrus and prefrontal regions) and reward processing. A decreased dopamine D2 receptor availability in the corpus striatum and a decreased number of DATs in the corpus striatum was identified, both hypothesized being related to a deficient reward processing system. These identified regions and their functions are logically discussed to be in line with typical diagnostic questions being used in relation to IA. The alterations in the identified brain regions can be considered as a broad aim for biological markers of IA, as of now.

Structural and functional comparisons between ADHD and IA were made. Similarities in affected brain regions of emotional processing, attention and cognitive control were highlighted while pointing out the major limitations of the simple comparison being made. Also, limitations and further directions have been discussed, stressing the importance of reaching a consensus on the operational definition of IA, creating subcategories inside the term of IA. As well as expanding the selection criteria when conducting studies.

Lastly, this thesis concludes that neuroimaging studies on IA show that excessive use of the Internet leads to neurological alterations of the brain. Due to these alterations, the symptoms reported of those suffering from IA and a showed similarity with an accepted psychiatric disorder as ADHD (in terms of alterations of brain regions), IA is worthy of more attention. Moreover, the usage of the Internet is continuously increasing. Younger generations are introduced to it early in life and as of now, we use it in a reckless way, in terms of not knowing how it might affect us negatively. It is of great ethical importance to increase the understanding of the Internet to prevent potential negative societal implications.

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