Summary

Attention-Deficit/Hyperactivity Disorder (ADHD) is a neuropsychiatric condition defined by a persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development. Although ADHD was originally considered a neurodevelopmental disorder occurring only in childhood, it is now well known that ADHD continues into adolescence, adulthood and even into old age. Despite the recognition of the persistence of the disorder into adulthood, there is much less research about ADHD in adults than in children. However, it is evident that adult ADHD is a prevalent and disabling disorder resulting in enormous societal costs. Taking this into consideration, more insight into the etiology and consequences of ADHD symptoms in adulthood is crucial in order to develop appropriate treatment and preventative strategies. The aims of this thesis are: (1) to gain more insight into etiological factors associated with adult ADHD; (2) to gain more insight into the association of ADHD symptom severity with the history and current presence of sleep problems, and into the association of the number of ADHD symptoms with axis I and II disorders in adults; and (3) to gain more insight into consequences of adult ADHD. To research these aims, data from the Netherlands Mental Health Survey and Incidence Study-2 (NEMESIS-2), the Netherlands Study on Depression and Anxiety (NESDA), the Netherlands Sleep Registry (NSR), and the PsyQ Program Adult ADHD were used.

Etiology of ADHD

In Chapter 3, we examined self-reported seasonal differences in the severity of ADHD symptoms in adults from the Dutch general population. We used data from 5,303 respondents participating in the second wave of the NEMESIS-2 study, a population-based study on mental health. As compared with participants who were assessed in autumn, the severity of ADHD symptoms was higher among participants who were assessed in spring or summer. Our observation suggests that researchers should pay attention to seasonal variations in ADHD symptom severity in the diagnostic process of ADHD in the adult general population.

In Chapter 4, we investigated whether ADHD is a dimensional trait in the Dutch general population by studying, amongst others, whether an increased number of ADHD symptoms was associated with higher exposure to genetic (i.e., parental psychopathology) and environmental risk factors (i.e., childhood abuse). A dimensional trait can be described using an iceberg metaphor: at the tip of the iceberg are the known cases with a full-blown disorder, representing one end of the dimension. The largest part of the iceberg is below the waterline, which depicts persons who have subclinical symptoms or are asymptomatic, representing the other end of the dimension. Data were used from N=5,303 respondents...
participating in the second wave of the NEMESIS-2 study. A dose-response relationship was found between the number of ADHD symptoms and exposure to these risk factors.

In Chapter 5, we studied whether ADHD symptoms were associated with dysregulation of stress-related biomarkers. Additionally, we examined whether ADHD symptoms interact with affective disorders in their association with dysregulated stress-related biomarkers. We analyzed data from 2307 subjects with and without affective disorders participating in NESDA. NESDA is an ongoing longitudinal cohort study on the predictors, course, and consequences of depressive and anxiety disorders. Some associations were observed between ADHD symptoms, the HPA-axis, and the pre-ejection period, but these were mostly driven by depressive and anxiety disorders. Furthermore, the results showed no evidence that ADHD symptomatology was associated with dysregulations in inflammatory markers and BDNF. Consequently, ADHD symptoms did not confer an added risk to the disturbances of stress-related biomarkers in an – already at-risk – population with affective disorders.

Comorbidity

Chapter 2 described a study whether current overall ADHD, inattention, or hyperactivity symptom severities were associated with the current presence and persistent history of sleep problems by using data from 942 adult participants from the NSR, an online platform for survey assessment. The most important finding was that ADHD severity, especially the severity of hyperactivity, was associated with both the current presence and persistent history of various sleep problems. This study stresses the importance of evaluating and treating sleep problems in persons with ADHD symptoms, in order to prevent serious health consequences in the long term.

As previously described, Chapter 4 used data from the NEMESIS-2 study in order to investigate whether ADHD is a dimensional trait in the adult general population. To further support this hypothesis, we investigated whether an increased number of ADHD symptoms was associated with higher comorbidity of psychiatric disorders. We observed a dose-response relationship between the number of ADHD symptoms and Axis I and II mental disorders, including mood, anxiety, substance use, antisocial personality (ASPD), and/or borderline personality disorder (BPD).
Consequences of ADHD

Chapter 4 also studied whether an increased number of ADHD symptoms was associated with higher mental and physical disability. We found a dose-response relationship between the number of ADHD symptoms and mental and physical disability, and that these associations were not driven by sociodemographics or psychiatric comorbidity. In summary, Chapter 4 showed that an increased number of ADHD symptoms was associated with higher comorbidity, exposure to risk factors, and disability. So, our study supported the notion that ADHD is a dimensional trait in the adult general population. Causal inferences are precluded by the cross-sectional nature of this study. Nevertheless, if subclinical ADHD symptoms are the cause of burden, treatment and/or indicated prevention aimed at persons with subclinical symptoms seems relevant in order to decrease the burden and to reduce the risk of progression to full-blown ADHD.

In Chapter 6, we examined whether circadian rhythm disruption is a mechanism linking ADHD symptoms to obesity. ADHD symptoms and two manifestations of circadian rhythm disruption: sleep problems and an unstable eating pattern (skipping breakfast and binge eating later in the day) were assessed in participants with obesity (n= 114), controls (n= 154), and adult ADHD patients (n= 202) from the PsyQ Program Adult ADHD. Both sleep duration and an unstable eating pattern mediated the association between ADHD symptoms and body mass index (BMI). Thus, our study supports the hypothesis that circadian rhythm disruption is a mechanism linking ADHD symptoms to obesity. Our result suggest that awareness and treatment of ADHD symptoms as well as circadian rhythm disruption is of importance in order to prevent additional weight gain or possibly even to facilitate weight loss.

Discussion

In Chapter 7, the general discussion, the main findings of the studies were summarized and discussed with implications for clinical or research practice. Furthermore, methodological considerations and suggestions for future research were addressed. It was concluded that seasonality, childhood abuse, parental psychopathology, and dysregulations in the HPA-axis may be etiological factors associated with adult ADHD. Furthermore, the severity of ADHD symptoms, especially the severity of hyperactivity symptoms, was associated with the current presence and persistent history of sleep problems, and an increased number of ADHD symptoms was associated with higher comorbidity of axis I and II disorders. Moreover, mental and physical disability and obesity may be consequences of adult ADHD.