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THESIS

**Symptoms of attention-deficit/hyperactivity disorder  
and early cannabis use.**

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## **ABSTRACT**

In this study, the relation between attention-deficit/hyperactivity disorder (ADHD) symptoms and early cannabis use was examined. A database, with information from a questionnaire about multiple lifestyle aspects such as (psychosocial) health and behaviour, completed by 2<sup>nd</sup> and 3<sup>rd</sup> graders in secondary school (N=3166) was used. It was expected that adolescents with a high score on ADHD symptoms, measured by the Strengths and Difficulties Questionnaire, use more cannabis than their controls. Furthermore, ADHD symptoms were divided in hyperactivity/impulsivity (HI) and inattention (IN) symptoms, whereby the HI-group was expected to use more cannabis than controls, but the IN-group would not differ from the controls. Taking gender, symptoms of CD and the interaction between the latter two into account, a positive relation between ADHD symptoms and HI symptoms in adolescents and recent cannabis use was found. However, the effects found are small and decreased to insignificance when controlling for current smoking behaviour. Surprisingly, a negative effect for IN symptoms on recent cannabis use was found.

## **INTRODUCTION**

One of the most common and highly heritable childhood behavioural disorders in Europe and the United States is attention-deficit hyperactivity disorder (ADHD) (Coghill and Banaschewski, 2009; Faraone and Biederman, 1994). This clinical disorder is mostly characterized by impulsiveness, hyperactivity and inattention (Faraone and Biederman, 1998) and described in the Diagnostic and Statistical Manual for mental disorders, shortly DSM-IV TR (APA, 2000; see appendix B). These characteristics are especially apparent during childhood. The hyperactivity and impulsiveness frequently decreases following adolescence but the inattention often sustains during adulthood. During the course of ADHD there is a considerable probability of dropping out of school, conduct problems and developing substance abuse (Deelman, Eling, De Haan and Van Zomeren, 2007).

Theoretically, inattention, hyperactivity and impulsivity in ADHD may be due to underlying executive functioning, alerting, and orienting deficits (Swanson, 2003). In a widely applied model of Barkley (1997) five executive functions are distinguished, including response inhibition. In order to control verbal and motor behaviours, response inhibition delays and interrupts responses. Barkley proposed that this response inhibition is deficient in individuals with ADHD by a dysfunction of the prefrontal lobe. Poor attention regulation, impulsivity and hyperactivity may all secondary arise from poor prefrontal cortex regulation of behaviour and thought. Studies using functional and structural imaging also suggested abnormalities of the prefrontal cortex (Arnsten & Li, 2005; Eling, De Haan, Hijman & Schmand, 2003; Faraone & Biederman, 1998; Spencer, Biederman, Wilens & Faraone, 2002).

Gray (1981) was one of the first to link the neurotransmitter dopamine to a main characteristic of ADHD. He suggested that there are two conditioned systems in the brain that correspond to personality traits. One is the behavioural inhibition system and the other is the behavioural activation system, shortly referred as BIS and BAS. BAS is said to be modulated by dopamine, whereas BIS is modulated by serotonin. Novelty seeking behaviour, according to this system is one of the core features of BAS (Stuettgen, Hennig, Reuter & Netter, 2005) and is also seen as a main characteristic of ADHD (Purper-Ouakil, Cortese, Wohl, Aubron, Orejarena, Michel, et al., 2010). Cloninger (1987) described novelty as a tendency toward frequent exploratory activity and intense and exhilaration in response to novel or appetitive stimuli. This tendency could be translated in inappropriate classroom behaviour, extreme sports but also drug use and abuse, simply impulsivity.

Furthermore, the importance of dopamine for executive functioning is supported by the most effective pharmacological treatments of ADHD. Around 70% of the adolescents and

adults suffering from ADHD respond well to stimulant medication. The most used drug at the moment is methylphenidate which main characteristic is blocking dopamine transporters (Eling et al., 2003). Thereby it increases the levels of a.o. dopamine in the brain through reuptake inhibition of the monoamine transporters (e.g. dopamine, serotonin, norepinephrine) (Grilly, 2006). Multiple studies indicated weak cortical inhibitory control over subcortical systems as a possible explanation for ADHD. The inhibitory influences of frontal cortical activity on subcortical structures are possibly achieved through the effects of these stimulants on dopaminergic pathways (Faraone & Biederman, 1998).

Further evidence comes from animal studies. Viggiano and his colleagues (2004) found divergent dopamine transporter activity in the prefrontal cortex and striatum in spontaneously hypertensive rats, indicating these structures are involved in ADHD. Other studies confirming a relation between dopamine and ADHD are based on genes that regulate dopamine in the brain. Most widely confirmed is the link between the 7-repeat allele of the D<sub>4</sub> dopamine receptor gene (DRD4\*7) and ADHD (Arnsten & Li, 2005; Faraone & Biederman, 1998; Spencer et al., 2002; Swanson et al., 2000)

As mentioned above, there is considerable evidence for a link between ADHD and drug use. With respect to cannabis, this may be linked to the dopaminergic system. An influence of the main psychoactive component of cannabis, delta-9-tetrahydrocannabinol (THC), on endocannabinoid has been shown and evidence indicates that endocannabinoids are key-components in the regulation of dopamine neurotransmission (Chevalleyre, Talahashi, & Castillo, 2006). In addition, animal studies suggest that THC facilitates dopaminergic neurotransmission in several brain regions such as the striatum and prefrontal cortex (Kuepper, Morrison, van Os, Murray, Kenis & Henquet, 2010).

THC acts as an agonist at the CB<sub>1</sub> cannabinoid receptor, which is only known to be expressed in the brain (CB<sub>2</sub> is expressed in peripheral tissues). CB<sub>1</sub> receptors are particularly present in high densities in the basal ganglia and cerebellum (but also prefrontal regions), which makes that cannabinoids have complex effects on psychomotor function (Iversen, 2003). Sañudo-Peña and colleagues (2000) found in rodents a triphasic effect of cannabinoids. Low doses of THC (0.2 mg/kg) tended to decrease locomotor activity. Doses of 1-2 mg/kg stimulated movements, while even higher doses (2.5 mg/kg) resulted in catalepsy. More specifically, it is suggested that the primary role of cannabinoids is to regulate levels of basal motor activity (Sañudo-Peña, Tsou & Walker, 1999).

Because of this perceived decrease in locomotor activity, cannabis use can be considered as part of self-medicated treatment to reduce hyperkinetic symptoms in ADHD. Fergusson and Boden (2008) already found a significant association between cannabis use and self-reported adult ADHD symptoms at age 25. Although, after controlling for the mediating effects of co-occurring other drug use the association decreased, resulting in a statistically insignificance.

Cannabis products are worldwide dominating the illicit drug market. According to the “gateway theory” in its original form, licit drug use involving alcohol and tobacco progresses into illicit drug use (Kandel & Faust, 1975). A further elaboration of this theory, by Pedersen and Skrondal in 1999, is based on studies reporting that the use of cannabis is typically initiated after using legal substances like cigarettes and alcohol, but before ecstasy and amphetamines (Golub & Johnson, 1994; Young, Mikulich, Godwin, Hardy, Martin, Zocolillo et al., 1995). Considering these findings, cannabis could be interpreted as a substance that is important in socialization to other illegal drugs and possible eventually to substance abuse. Although cannabis as a possible precursor for other illicit drug use, does not mean this will inevitably lead to drug abuse (Pedersen & Skrondal, 1999). The gateway theory is debated but remains an important basis for further research.

Overall, three mechanisms, cannabis use as a possible precursor for other illicit drug use (Golub & Johnson, 1994; Pedersen & Skrondal, 1999; Young et al., 1995), the suggested relation between cannabis use and symptoms of ADHD (Fergusson & Boden, 2008) and the early presentation of these symptoms (at least one before the age of seven), make it plausible that young adolescents with ADHD have an increased risk of (early) illicit drug use. As a preventive procedure, it is an option to make this group aware of the risks and disadvantages of using illicit substances, such as cannabis (Stein, 2010), by informing them before initiation.

As described above, there is a considerable chance of developing a substance use disorder during the course of ADHD. A study from two institutes concerning dependency treatment, shows that over 20% of the addicts has ADHD as a second diagnosis (Schubiner, Tzelepis, Milberger, Lockhart, Kruger, Kelley, et al., 2000). Furthermore, research by Fergusson and Horwood (1997) demonstrated a relationship between early onset of cannabis use and later substance abuse, but characteristics of those who choose to use cannabis should be taken into account. Since the first ADHD symptoms present themselves during early childhood and cannabis use is measurable at a young age as well, it is possible to look for a relation between

the two. The question whether or not adolescents with ADHD symptoms use more cannabis than their age related controls rises.

Besides de comorbidity of substance abuse, also comorbidity of Oppositional Defiant Disorder (ODD) or Conduct Disorder (CD) is frequently found in children and adolescents with ADHD (Angold, Costello and Erkanli, 1999). It is possible that primarily conduct problems are responsible for substance abuse, but not hyperactivity/impulsivity and inattention. In order to ascertain whether ADHD itself or just a dimension of this specific behavioural disorder is a precursor for cannabis use and eventually illegal substance abuse, it is necessary to distinguish the relationship of ADHD and CD with cannabis.

According tot the criteria of the DSM-IV TR (APA, 2000), there are three subtypes of ADHD, namely the combined type, the predominantly inattentive type and the predominately hyperactive-impulsive type. In a recently published longitudinal study, Elkins et al. (2007) investigated the role of ADHD, the combined type, as a risk factor for adolescent initiation and abuse of different substances, including cannabis. Furthermore, the subtypes of ADHD symptoms were considered when associating ADHD to substance initiation and abuses. The quantitative dimension of hyperactivity/impulsivity (HI) was distinguished from the inattention (IN) characteristics since this matches the other two subtypes of ADHD according to the DSM-IV TR (APA, 2000). CD was also taken in account. The results showed that although inattention significantly predicted illicit drug use, it's contribution mostly overlapped with those of hyperactivity and CD. Results showed that HI symptoms uniquely contributed to initiation of cannabis, as well as to cannabis use or dependence. Also age at initiation of illicit drug use was significantly predicted by a categorical diagnosis of ADHD. In addition, Elkins and her colleagues observed these findings even when controlling for CD. They suggest that a diagnosis of ADHD plays a role in initiating illicit drug use at younger ages, although less of a role in whether use escalates into abuse. Furthermore, it was concluded that HI and IN symptoms are primarily relevant in predicting substance initiation (Elkins et al., 2007; Kollins, McClernon & Fuemmeler, 2005)

Thus, to summarize there has been a lot of research considering the relation between early cannabis initiation, illicit drug use/abuse and ADHD, the results are not consistent. Some studies found that individuals with a history of ADHD compared with controls are more likely to develop substance use and substance related problems. Wilens and Biederman (2006) even found ADHD to accelerate the transition from substance abuse to dependence. Others did not find this relation or observed it to be mediated by CD (Clark, Parker & Lynch, 2010).

Based on this literature, the aim of this study is to investigate the relationship between cannabis use and ADHD symptoms in young adolescents.

This report is based on a large study executed by the Municipal Health Services. The data consists among others of self-reported cannabis use and symptoms of ADHD (hyperactivity/impulsivity and inattention) measured by the Strengths and Difficulties Questionnaire (SDQ). Based on the literature discussed above and the three subtypes of the developmental disorder ADHD as described in the DSM-IV TR, the first hypothesis: *Adolescents with both hyperactivity/impulsivity and inattention symptoms use more cannabis than their age-related control group.* When dividing the symptoms in groups consistent with the other two subtypes, there is a relation between hyperactivity/impulsivity symptoms and cannabis use expected, but not for cannabis use and inattention symptoms. These hypotheses are described as follows: 1) *Adolescents with hyperactivity and impulsivity symptoms use more cannabis than their age-related control group* and 2) *adolescents with inattention symptoms do not use more cannabis than their age-related control group.* Because of the proposed influence of CD on cannabis use, symptoms in accordance with this disorder and their relation with cannabis use are also investigated. Findings might be of interest for developing interference programs addressed to risk groups for early cannabis initiation.

## **METHODS**

Participants between 12 and 16 years old were recruited from second and third grade students of secondary school. A total of 3166 adolescents completed a 13 parts counting questionnaire, including the Strengths and Difficulties Questionnaire (SDQ) which is a brief behavioural screening questionnaire. The SDQ is designed to give an indication of psychopathology and to detect adolescents with heightened risks of developing emotional and conduct problems. It is a self-rating instrument and includes twenty-five statements equally divided between five scales: emotional symptoms, conduct problems, hyperactivity/inattention, peer relationship problems and prosocial behaviour. The list measures, on a three point Likert scale, the conformity of the participant with the statements. The scores on the items are added up per scale and each scale has its own standard to determine whether or not a score is above normal (see appendix C). According to the Dutch commission for examination matters (COTAN), in 2007 the SDQ is found sufficient reliable and the concept validation is satisfactory as well. More investigation is required to judge criterion validity (Achenbach, Becker, Döpfner, Heiervang, Roessner, Steinhausen et al., 2008; Goedhart, Treffers & Van Widenfelt, 2003).

The scale hyperactivity/inattention was used to measure ADHD symptoms, whereas the scale concerning conduct problems was used to control for CD since this is an often seen comorbidity in children with ADHD.

Furthermore, the participants answered some questions about tobacco and cannabis use. Concerning these substances, first participants reported per substance if they have ever used it during their lifetime. When confirming cannabis use, participants are asked whether they used cannabis in the last 4 weeks. Regarding the use of tobacco, participants current smoking behaviour is questioned. Recent use of tobacco is used as a confounding variable for predicting recent cannabis use.

## **STATISTICAL ANALYSIS**

The statistical analyses were done using the Statistical Package for the Social Science 17.0 (SPSS). First the data was explored using descriptive statistics to look for mean age, education level and ethnicity. In order to split up the hyperactivity/inattention scale of the SDQ and determine whether a score is high or low, a median-split is performed on the statements concerning these ADHD symptoms. Furthermore the data is checked for normal distribution by plotting the data in a histogram with a normality curve on top of it and using a standard test of normality, the Kolmogorov-Smirnov test.

For testing the gender differences in score on the subscales of the SDQ for hyperactive/inattention and for conduct problems, a Mann-Whitney test as well as an independent sample t-test was used. Possible differences between cannabis using and non-using adolescents in high or low scores on the subscales of the SDQ are investigated by performing a Chi-Square test.

Because of the big sample size and absence of suitable non-parametrical tests to control for the effect of gender and CD on (current) cannabis use, a logistic regression was applied to measure the effect of ADHD symptoms on (current) cannabis use. Current smoking behaviour is added to the model in a further analysis to assess whether this may result in a possible improvement of the suggested model on cannabis use.

## **RESULTS**

### *Group characteristics*

In total there were 3166 participants in this study, with half of the sample (50%) male and an average age of 14.4 years (SD .83) with a range of 12 up to 16 years of age. All participants were second or third class high school students. Table 1 shows more details about the



participants' distribution of educational levels. The country of birth of most (92%) of the participants is The Netherlands, see table 2 for more details concerning ethnicity. Therefore no corrections for ethnicity have been applied.

Because cannabis use in the last 4 weeks was used as an indicator of current cannabis use as it seems a more reliable measure of current cannabis use than lifetime prevalence. Overall 7% of the participants had used cannabis in the last 4 weeks. Cannabis using and non-using groups were compared for gender differences. In the group with recent cannabis usage there were significantly more boys (60%) than girls,  $\chi^2(1, N=3137) = 10.056, p=.002$ . There was no gender difference between the non-users.

### *SDQ score*

The distribution of the SDQ-score on the hyperactivity/inattention and conduct problems subscales are both significantly non-normal,  $D(3089)=.15, p<.001$  and  $D(3061)=.22, p<.001$ , but distributed as predicted by the standard of the questionnaire to determine whether or not a score is considered normal or high (Figure 1 & 2), meaning approximately 20% of the sample scores in the borderline and abnormal band. Based on the standard enclosed in the questionnaire, a low score on the SDQ scale measuring symptoms of CD is smaller than four and as a consequence a score higher than three is categorised as high. Likewise categorisation of the SDQ subscale measuring ADHD symptoms resulted in a score smaller than six indicated as low. Scores higher than five are categorised as high. Cut-off scores for defining a score as high or low on the HI and the IN scales are determined by performing a median-split on the score obtained on the statements concerning these symptoms. The cut-off score for HI is determined on three and on two for IN. No significant differences were found for gender concerning ADHD symptoms with either a two-tailed independent sample t-test,  $t(3072)=.490, p<.624$ , or a Mann-Whitney U test,  $z=-.44, p=.661$ . The score on the subscale measuring symptoms of CD did show a significant gender difference,  $t(2989)=9.418, p<.001$  and  $z=-9.22, p<.000$ , with boys receiving higher scores than girls.

### *SDQ score and cannabis use*

The participants' scores on the subscales of the SDQ were divided in "high" or "low" by the standard of the questionnaire and if not available, by a median-split. A chi-square test showed that adolescents with a high score on the hyperactivity/inattention subscale use more cannabis than adolescents with a low score on this subscale,  $\chi^2(1)=11.344, p<.001$ . The group scoring

high on HI used more cannabis than the low scoring group,  $\chi^2(1)=18.000, p<.000$ , but this was not the case for the group scoring high on IN  $\chi^2(1)=.236, p=.330$ .

Differences in recent cannabis use in relation to conduct problems were investigated by performing a chi-square test. Adolescents scoring high on the subscale measuring symptoms of CD, used significantly more cannabis than adolescents with a low score,  $\chi^2(1)=8.960, p<.002$ .

After adjusting the effect of ADHD symptoms on recent cannabis use for gender, symptoms of CD and interaction of the latter two by applying a logistic regression analysis, the model improved with  $\chi^2(1)=5.529, p=.019$  to  $\chi^2(4)=32.070, p=.000$ . Adolescents with a high score on ADHD symptoms have 1.435 ( $p=.018$ ) times the odds more chance to have used cannabis in the last 4 weeks. It should be noted that the interaction of gender and symptoms of CD were stronger predictors for recent cannabis use,  $\text{Exp}(B)=3.845, p=.019$  (Table 4a, model 1),

Adjusting the effect of symptoms of IN or HI on recent cannabis use for gender, symptoms of CD and their interaction, improved the model with  $\chi^2(2)=10.513, p=.005$  to  $\chi^2(5)=37.054, p=.000$ . This resulted in an insignificant effect for IN on recent cannabis use. The effect of a high score on HI on recent cannabis use however was still significant but very small,  $\text{Exp}(B)=1.600, p=.009$ . Again, this effect is overshadowed by the effect of the interaction between gender and symptoms of CD,  $\text{Exp}(B)=3.774, p=.021$  (Table 4b, model 1).

### *Smoking and cannabis use*

As a final step, current tobacco use is added to the model as a covariate. The model improved to  $\chi^2(5)=443.719, p=.000$ . The main relation found is between current smoking behaviour and recent cannabis use,  $\text{Exp}(B)=25.494, p=.000$ . Furthermore, previously found significant effects, including the relation between ADHD symptoms in general and recent cannabis use, turned out insignificant in this full model (Table 4a, model 2).

Adding smoking as a covariate to the model investigating the effect of symptoms of IN or HI on recent cannabis use, resulted in an improvement of the model to  $\chi^2(6)=445.580, p=.000$ . The association between HI and recent cannabis use decreased, resulting in a statistically insignificance. The association between IN and recent cannabis use however increased, resulting in a significant negative effect,  $\text{Exp}(B)=-.603, p=.032$ . Again, smoking is found as the main association with recent cannabis use,  $\text{Exp}(B)=25.917, p=.000$  (Table 4b, model 2).

## **DISCUSSION**

This study was conducted to investigate the relation between adolescents with symptoms of ADHD (viz. hyperactivity, impulsivity and inattention) and cannabis use. To improve the suggested model, symptoms of conduct disorder and current smoking behaviour of tobacco were added as covariates. Second and third graders from secondary school in The Netherlands (the central district) were subdivided in either scoring high or low on ADHD symptoms. Adolescents scoring low were used as controls and therefore compared to the high scoring group. Adolescents with hyperactivity, impulsivity and inattention symptoms were expected to use more cannabis than their age-related control group. This expected difference was found, even when controlling for gender and symptoms of CD, indicating that ADHD symptoms en CD symptoms make (partially) separate contributions to the risk of early illegal substance (e.g. cannabis) use. However, after controlling for current tobacco use, the association decreased to a statistically insignificance.

Because of the dimensional character of ADHD, the symptoms were also subdivided in HI and IN in accordance with the diagnostic criteria of the other two subtypes of ADHD as described in the DSM-IV (APA, 2000). Based on earlier research (Elkins et al., 2007), symptoms of HI were expected to be predictive for early drug use. This relation was found and was stronger than the relation between ADHD and cannabis use. Again, the association decreased to a very small effect when controlling for gender and CD symptoms. Possibly the overlap between HI and CD symptoms and the often observed comorbidity (Angold et al., 1999; Clark et al., 2010) is able to explain the decrease in association between HI scores and cannabis use. Adding use of tobacco to the model resulted in an insignificant effect of HI on cannabis use, meaning the use of tobacco must be seen as a predictor for cannabis use instead of HI symptoms. It is highly suggestible that there is a positive relation between HI symptoms and smoking behaviour and use of tobacco as a predictor for cannabis use therefore makes HI symptoms indirectly a predictor for cannabis use.

Concerning inattention, adolescents scoring high on these symptoms were not expected to use more cannabis than their age-related controls. Indeed, no effect for IN on cannabis use was found. Surprisingly, IN symptoms showed a negative relation with cannabis use when controlling for smoking behaviour. This suggests that the adolescents with (mainly) IN symptoms run a smaller risk on early cannabis initiation than their controls.

The results of the current study and those described by Elkins et al. (2007) and Kollins et al. (2005) suggest that, because of the differences in predictive values of HI and IN, these dimensional predictors can be considered as more precise and therefore better indicators than

a categorical diagnosis of ADHD. However, it should be noted that HI and IN as independent predictors are based on a minimum of statements, resulting in a small range of possible scores. This makes it hard to measure extreme symptoms.

Furthermore, the impact of the reported difficulties (e.g. duration, interference with daily functioning, caused distress) was not taken into account when dividing the adolescents in the high- or low scoring group. Because of that, it is not possible to draw strong inferences about the degree of the ADHD symptoms, which is necessary for generalising the findings to the group of adolescents with actual ADHD (in order to be diagnosed with ADHD it has to interfere with daily functioning e.g. in school) (Appendix B).

Another limitation of this study is that the data-set is based on the reliability of the informant. According to Goedhart et al. (2003), for optimal reliability of reported behaviour, the SDQ should preferably be completed by a teacher. A less desirable but still sufficient option is completion of the questionnaire by parents of the adolescent. Self-report is the least desirable option to obtain information of behaviour components as measured by the SDQ. Despite the undesirability of self-report concerning the SDQ, self-report on cannabis use is more reliable (but not completely), than report by teachers or parents (Buchan, Dennis, Tims, Diamond, 2002).

### *Future studies*

Based on the indication that there is a relation between symptoms of ADHD and early cannabis use, in future research it is essential to extend the questionnaire concerning the dimensional predictors (namely HI and IN) because of the possible lack of subtlety in discrimination between high and low scores. Smoking behaviour is taken into account when investigating the relation of ADHD symptoms and recent cannabis use. Other substance such as alcohol but also illegal (hard)drugs are plausible confounders when examining cannabis use. Also the increased administration of methylphenidates leads to a point for interesting future investigation. Does it protect from or increases future (illegal) substance use or abuse? Longitudinal studies might provide more information on the causal relation en development of cannabis use in adolescents.

## **CONCLUSION**

A relation between ADHD symptoms and HI symptoms in adolescents and recent cannabis use is found in this study, even when taking gender, symptoms of CD and the interaction between the latter two into account. However, the effects found are small and decreased to

insignificance when controlling for current smoking behaviour. With HI symptoms as predictors for smoking behaviour (Elkins et al., 2007; Kollins et al., 2005) and use of tobacco as a predictor for cannabis use, it is suggestible that both HI symptoms and tobacco use are predictors for cannabis use. As predicted, at first no significant effect for IN on recent cannabis use is found. However, when adding current tobacco use to the model, a negative effect of IN symptoms on recent cannabis use occurred, suggesting adolescents with IN symptoms run a smaller risk on early cannabis use than their age related controls. Further investigations should focus on further exploring the effects of different symptoms on early cannabis use.

## REFERENCE LIST

Achenbach, T.M., Becker, A., Döpfner, M., Heiervang, E., Roessner, V., Steinhausen, H. and Rothenberger, A., (2008). Multicultural assessment of child and adolescent psychopathology with ASEBA and SDQ instruments: research findings, applications, and future directions. *Child Psychology and Psychiatry* 49, 251-275.

American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision*. Washington, DC, American Psychiatric Association, 2000.

Angold, A., Costello, J. and Erkanli, A. (1999). Comorbidity. *Journal of Child Psychology and Psychiatry* 40, 57-87.

Arnsten, A.F.T. (2007). Catecholamine and second messenger influences on prefrontal cortical networks of “representational knowledge”: A rational bridge between genetics and the symptoms of mental illness. *Cerebral Cortex* 17, 6-15.

Arnsten, A.F.T. and Li, B. (2005) Neurobiology of executive functions: Catecholamine influences on prefrontal cortical functions. *Biological Psychiatry* 57, 1377-1384.

Barkley, R.A. (1997). *ADHD and the nature of self-control*, New York, NY: Guilford.

Eling, P., De Haan, E., Hijman, R. and Schmand, B. (2003). *Cognitieve neuropsychiatrie*. Amsterdam: Boom.

Buchan, B.J., Dennis, M.L., Tims, M.T. and Diamond, G.S. (2002). Cannabis use: consistency and validity of self-report, on-site urine testing and laboratory testing. *Addiction* 97, 98-108.

Chevalyere, V., Talahashi, K.A. and Castillo, P.E. (2006). Endocannabinoid-mediated synaptic plasticity in the CNS. *Annual review of Neuroscience* 29, 37-76.

Clark, D.B., Parker, A.M. and Lynch, K.G. (1999). Psychopathology and substance-related problems during early adolescence: A survival analysis. *Journal of Clinical Child & Adolescent Psychology* 28, 333-341.

Cloninger, C.R. (1987). Neurogenetic adaptive mechanisms in alcoholism. *Science* 236, 410-416.

Coghill, D. & Banaschewski, T. (2009). The genetics of attention-deficit/hyperactivity disorder. *Expert review of neurotherapeutics* Oct 9, 1547-65.

Deelman, B., Eling, P., De Haan, E. and Van Zomeren, E. (2007). *Klinische neuropsychologie*. Uitgeverij Boom: Amsterdam; 417-436.

Eling, P., De Haan, E., Hijman, R. and Schmand, B. (2003). *Cognitive neuropsychiatrie*. Uitgeverij Boom: Amsterdam: 286-314.

Elkins, I.J., McGue, M. and Iacono, W.G. (2007). Prospective effects of attention-deficit/hyperactivity disorder, conduct disorder, and sex on adolescent substance use and abuse. *Archives of General Psychiatry* 64, 10.

Faraone, S.V. & Biederman, J. (1994). Genetics of attention-deficit hyperactivity disorder. *Child and adolescent Psychiatry of Clin North AM* 3, 285-301.

Faraone, S.V. & Biederman, J. (1998). Neurobiology of attention-deficit hyperactivity disorder. *Biologic Psychiatry* 44, 951-958.

Fergusson, D.M. and Boden, M. (2008). Cannabis use and adult ADHD symptoms. *Drug and Alcohol Dependence* 95, 90-96.

Goedhart, A., Treffers, F. and Widenfelt, B. (2003). Vragen naar psychische problemen bij kinderen en adolescenten: de Strengths and Difficulties Questionnaire. *Maandblad Geestelijke Volksgezondheid*. 58, 1018-1035.

Golub, A. and Johnson, B.D. (1994). Cohort differences in drug-use pathways to crack among current crack abusers in New York City. *Criminal Justice and Behavior* 21, 403-422.

Gray, J. A. (1981). A critique of Eysenck's theory of personality. In H. J. Eysenck (Ed.), *A model for personality* (pp. 246–276). New York: Springer.

Grilly, D.M. (2006). *Drugs and human behaviour*. Pearson Education: Boston, 183-224.

Iversen, L. (2003). Cannabis and the brain. *Brain* 126, 1252-1270.

Junger-Tas J., van der Laan, P.H. and Kruisink M. (1992). *Ontwikkeling van de jeugdcriminaliteit en de justitiele jeugdbescherming: periode 1980-1990*. Arnhem, The Netherlands: Gouda Quint.

Kandel, D.B. and Faust, R. (1975). Sequence and stages in patterns adolescent drug use. *Archives of General Psychiatry* 32, 923-932.

Kollins, S.H., McClernon, F.J. and Fuemmeler, B.F. (2005). Association between smoking and Attention-Deficit/Hyperactivity Disorder symptoms in a population-based sample of young adults. *Archives of General Psychiatry* 62, 1142-1147.

Kuepper, R., Morrison, P.D., van Os, J., Murray, R.M., Kenis, G. and Henquet, C. (2010). Does dopamine mediate the psychosis-inducing effects of cannabis? A review and integration of findings across disciplines. *Schizophrenia Research* 121, 107-117.

Pedersen, W. and Skrandal, A. (1999). Ecstasy and new patterns of drug use: a normal population study. *Addiction* 94, 1695-1706.

Pedersen, W., Mastekaasa, A. and Wichstrøm, L. (2001). Conduct problems and early cannabis initiation: a longitudinal study of gender differences. *Addiction* 96, 415-431.

Purper-Ouakil, D., Cortese, S., Wohl, M., Aubron, V., Orejarena, S., Michel, G., Asch, M., Mouren, M. and Gorwood, P. (2010). Temperament and character dimensions associated with clinical characteristics and treatment outcome in attention-deficit/hyperactivity disorder boys. *Comprehensive Psychiatry* 51, 286-292.

Sañudo-Peña, M.C., Romero, J., Seale, G.E., Fernandex-Ruiz, J.J. and Walker, J.M. (2000). Activational role of cannabinoids on movement. *European journal of Pharmacology* 391, 267-274.

Sañudo-Peña, M.C., Tsou, K. and Walker, J.M. (1999). Motor actions of cannabinoids in the basal ganglia output nuclei. *Life Sciences* 65, 703-713.

Schubiner, H., Tzelepis, A., Milberger, S., Lockhart, N., Kruger, M., Kelley, B.J. and Schoener, E.P. (2000). Prevalence of attention-deficit/hyperactivity disorder and conduct disorder among substance abusers. *Journal of Clinical Psychiatry* 61, 244-251.

Spencer, T.J., Biederman, J., Wilens, T.E. and Faraone, S.V. (2002) Overview and neurobiology of Attention-Deficit/Hyperactivity Disorder. *Journal of Clinical Psychiatry* 63, 2-9.

Stein, J. (2010). Early cannabis use may contribute to psychosis-related outcomes in young adults. *Arch Gen Psychiatry* 67, 440-447.

Stuettgen, M.C., Hennig, J., Reuter, M. and Netter, P. (2005). Novelty seeking but not BAS is associated with high dopamine as indicated by a neurotransmitter challenge test using mazindol as a challenge substance. *Personality and Individual Differences* 38, 1597-1608.

Swanson, J.M. (2003). Role of executive function in ADHD. *Journal of Clinical Psychiatry* 64, 35-39.

Swanson, J.M., Flodman, P., Kennedy, J., Spence, M.A., Moyzis, R., Schuck, S. ... Posner, M. (2000). Dopamine genes and ADHD. *Neuroscience and biobehavioral reviews* 24, 21-25.

Viggiano, D., Vallone, D. and Sadile, A. (2004). Dysfunctions in dopamine systems and ADHD: Evidence from animal and modelling. *Neural Plasticity* 11, 97-104.

Wilens, T.E. and Biederman, J. (2006). Alcohol, drugs, and attention-deficit/hyperactivity disorder: a model for the study of addictions in youth. *Journal of Psychopharmacology* 20, 580.

Widenfelt van, B.M., Goedhart, A.W., Treffers, P.D. and Goodman, R. (2003). Dutch version of the Strengths and Difficulties Questionnaire (SDQ). *Eur Child Adolesc Psychiatry* 12, 281-289.

Young, S.E., Mikulich, S.K., Godwin, M.B., Hardy, J., Martin, C.L., Zocolillo, M.S. and Crowley, T.J. (1995). Treated delinquent boys' use: onset, pattern, relationship to conduct and mood disorders. *Drug and Alcohol Dependence* 37, 149-162.



## APPENDIX A

Table 1

*Frequency of Participants per Education Level*

	All participants N= 3166	Cannabis users* n= 217	Non-users n= 2920
VMBO TL	496	19 (3.9%)	469 (96.1%)
VMBO rest	703	29 (4.2%)	666 (95.8%)
HAVO	432	57 (13.3%)	373 (86.7%)
HAVO/VWO	336	19 (5.7%)	315 (94.3%)
VWO	1144	91 (8.0%)	1047 (92.0%)
Missing	55	2 (3.8%)	50 (96.2%)

\* Used cannabis in the last 4 weeks.

Table 2

*Frequency of Participants per Ethnicity*

	All participants n = 3166	Cannabis users* n = 217	Non-users n = 2920
Netherlands	2906	198 (6.9%)	2683 (93.1%)
Suriname	16	3 (18.8%)	13 (81.2%)
Netherlands Antilles	5	0 (0.0%)	5 (100%)
Aruba	1	0 (0.0%)	1 (100%)
Turkey	27	0 (0.0%)	26 (100%)
Morocco	59	3 (5.2%)	55 (84.8%)
Other	111	9 (8.3%)	100 (91.7%)
Missing	41	4 (9.8%)	37 (91.2%)

\* Used cannabis in the last 4 weeks.

Table 3

*Frequency of Participants per Ethnicity*

	All participants n = 3166	Cannabis users* n = 217	Non-users n = 2920
Netherlands	2906	198 (6.9%)	2683 (93.1%)
Suriname	16	3 (18.8%)	13 (81.2%)
Netherlands Antilles	5	0 (0.0%)	5 (100%)
Aruba	1	0 (0.0%)	1 (100%)
Turkey	27	0 (0.0%)	26 (100%)
Morocco	59	3 (5.2%)	55 (84.8%)
Other	111	9 (8.3%)	100 (91.7%)
Missing	41	4 (9.8%)	37 (91.2%)

\* Used cannabis in the last 4 weeks.

Table 4a

*Estimated parameters of logistic regression models for the log odds of recent cannabis use among 2<sup>nd</sup> and 3<sup>rd</sup> graders in secondary school with ADHD symptoms*

	Model 1		Model 2	
	B (SE)	Exp b	B (SE)	Exp b
Gender	-1.668* (.554)	.189	-1.530* (.585)	.216
CD symptoms	.106 (.262)	1.112	.127 (.298)	1.136
ADHD symptoms	.361* (.158)	1.435	.039 (.175)	1.040
CD symptoms * gender	1.347* (.575)	3.854	.924 (.611)	2.519
Smoking			3.238** (.168)	25.494
Constant	-2.592** (.232)	.075	-3.512** (.277)	.030
Nagelkerke pseudo R <sup>2</sup>	.026		.341	

Note: a significant *B* is also a significant *Exp b*.

<sup>a</sup> Model 1:  $\chi^2(4)=32.070$ ,  $p=.000$ , Model 2:  $\chi^2(5)=443.719$ ,  $p=.000$

<sup>b</sup> \*  $p<.005$ , \*\*  $p<.001$ .

**Table 4b**

*Estimated parameters of logistic regression models for the log odds of recent cannabis use among 2<sup>nd</sup> and 3<sup>rd</sup> graders in secondary school with HI or IN symptoms*

	Model 1		Model 2	
	B (SE)	Exp b	B (SE)	Exp b
Gender	-1.663* (.555)	.189	-1.469* (.585)	.230
CD symptoms	.066 (.318)	1.086	.392 (.362)	1.479
HI symptoms	.470* (.179)	1.600	.043 (.205)	1.044
IN symptoms	-.243 (.203)	.232	-.506* (.235)	.603
CD symptoms * gender	1.328* (.576)	3.774	.839 (.611)	2.314
Smoking			3.255** (.170)	25.917
Constant	-2.515** (.240)	.081	-3.344** (.284)	.035
Nagelkerke pseudo R <sup>2</sup>	.030		.345	

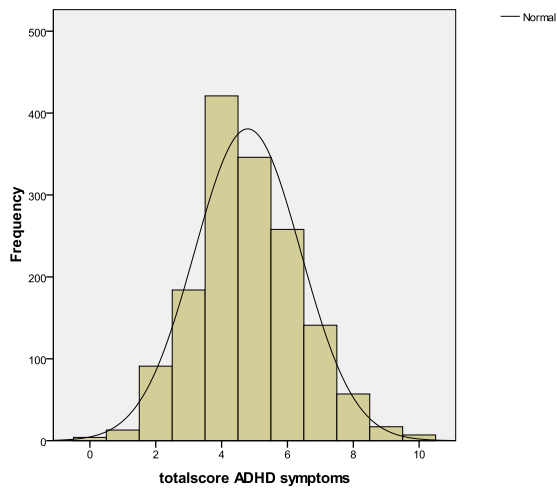
Note: a significant *B* is also a significant Exp *b*.

<sup>a</sup> Model 1:  $\chi^2(4)=37.045$ ,  $p=.000$ , Model 2:  $\chi^2(5)=448.580$ ,  $p=.000$

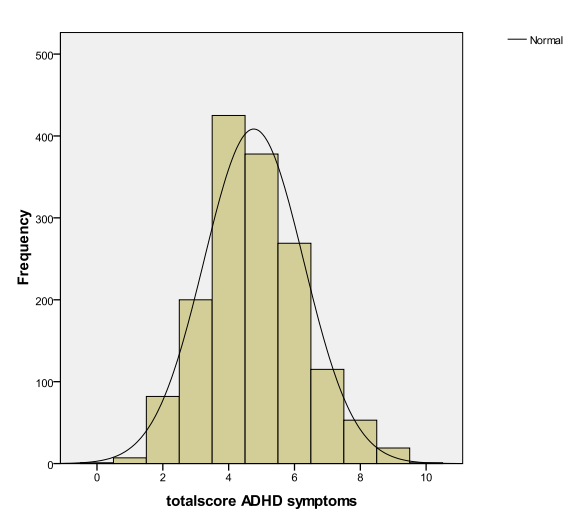
<sup>b</sup> \*  $p<.005$ , \*\*  $p<.001$ .

**Figure 1**

*Histogram with Normal curve of Frequency Total Score on SDQ hyperactivity/inattention subscale*



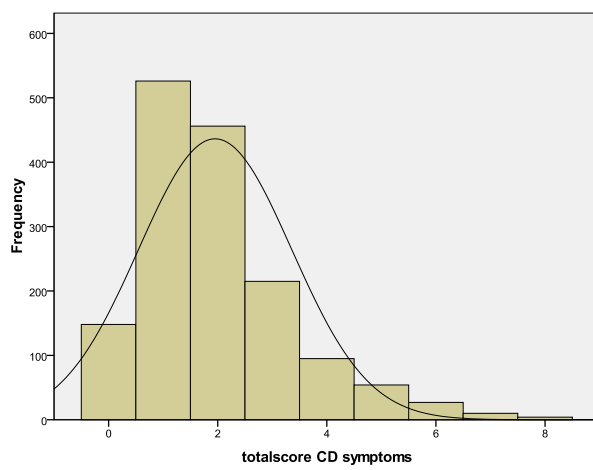
a) Boys



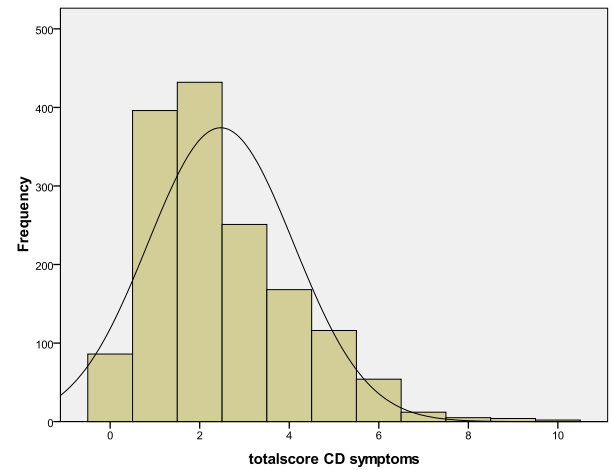
b) Girls

**Figure 2**

*Histogram with Normal curve of Frequency Total Score on SDQ conduct problems subscale*



a) Boys



b) Girls

## **APPENDIX B**

### DSM-IV Criteria for ADHD

#### **I. Either A or B:**

- A. Six or more of the following symptoms of inattention have been present for at least 6 months to a point that is inappropriate for developmental level:**

##### **Inattention**

1. Often does not give close attention to details or makes careless mistakes in schoolwork, work, or other activities.
2. Often has trouble keeping attention on tasks or play activities.
3. Often does not seem to listen when spoken to directly.
4. Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (not due to oppositional behavior or failure to understand instructions).
5. Often has trouble organizing activities.
6. Often avoids, dislikes, or doesn't want to do things that take a lot of mental effort for a long period of time (such as schoolwork or homework).
7. Often loses things needed for tasks and activities (e.g. toys, school assignments, pencils, books, or tools).
8. Is often easily distracted.
9. Is often forgetful in daily activities.

- B. Six or more of the following symptoms of hyperactivity-impulsivity have been present for at least 6 months to an extent that is disruptive and inappropriate for developmental level:**

##### **Hyperactivity**

1. Often fidgets with hands or feet or squirms in seat when sitting still is expected.
2. Often gets up from seat when remaining in seat is expected.
3. Often excessively runs about or climbs when and where it is not appropriate (adolescents or adults may feel very restless).
4. Often has trouble playing or doing leisure activities quietly.
5. Is often "on the go" or often acts as if "driven by a motor".
6. Often talks excessively.

## **Impulsivity**

7. Often blurts out answers before questions have been finished.
8. Often has trouble waiting one's turn.
9. Often interrupts or intrudes on others (e.g., butts into conversations or games).

**II.** Some symptoms that cause impairment were present before age 7 years.

**III.** Some impairment from the symptoms is present in two or more settings (e.g. at school/work and at home).

**IV.** There must be clear evidence of clinically significant impairment in social, school, or work functioning.

**V.** The symptoms do not happen only during the course of a Pervasive Developmental Disorder, Schizophrenia, or other Psychotic Disorder. The symptoms are not better accounted for by another mental disorder (e.g. Mood Disorder, Anxiety Disorder, Dissociative Disorder, or a Personality Disorder).

### **Based on these criteria, three types of ADHD are identified:**

IA. ADHD, *Combined Type*: if both criteria IA and IB are met for the past 6 months.

IB. ADHD, *Predominantly Inattentive Type*: if criterion IA is met but criterion IB is not met for the past six months.

IC. ADHD, *Predominantly Hyperactive-Impulsive Type*: if Criterion IB is met but Criterion IA is not met for the past six months.