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### ADHD and atopic diseases

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# Chapter 7

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THE TEMPORAL ORDER OF FLUCTUATIONS IN  
ATOPIC DISEASE SYMPTOMS AND ATTENTION-  
DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS:  
A PILOT STUDY

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## ABSTRACT

**Background** In a recent meta-analysis we found that atopic diseases, like asthma and allergic rhinitis, occur more frequently prior to the development of Attention-Deficit/Hyperactivity Disorder (ADHD). Our aim was to determine the temporal order of the association between fluctuations of atopic disease symptoms and ADHD symptoms in individual patients.

**Methods** In this observational study we performed a replicated time-series analysis of asthma and allergic rhinitis symptom fluctuation and ADHD symptom fluctuation. The study population consisted of 11 children in the age of 7-17 years with ADHD and comorbid asthma and/or allergic rhinitis. Data was collected through parents who filled in a daily online questionnaire during up to 50 days. In a vector autoregressive (VAR) model we investigated the causal dependency between atopic disease symptoms and ADHD symptoms in each individual participant, with sleeping problems, and medication use as covariates.

**Results** For 9 out of 11 participants a VAR model could be constructed. For a majority of the participants multiple significant associations were detected between atopic disease symptoms and ADHD symptoms. However, the results were heterogeneous, and both the direction, sign, and timing of the relationship between ADHD, atopy, sleep, and medication use varied.

**Conclusion** Time-series analysis is a potentially useful method to assess the temporal order of the association between atopy and ADHD. This study provides additional evidence that the symptom expression of atopy and ADHD are related. However, the connection between signs and symptoms of both diseases in children is heterogeneous within our study population.

## INTRODUCTION

Attention-deficit/hyperactivity disorder (ADHD) is a common neurobehavioral disorder with onset of symptoms before the age of 12 years<sup>1</sup>, characterized by behavioral symptoms of inattention, impulsivity, and/or hyperactivity that often lead to social impairments. ADHD is a multifactorial disorder associated with both genetic and environmental factors, including nutrition..<sup>2</sup>

Atopic diseases are also very common among children. These diseases are characterized by a hypersensitivity reaction initiated by the immune system, caused by specific allergens like pollen, dust mites, certain food components, or insect bites. The best well-known atopic diseases are (allergic) asthma, (atopic) eczema, and allergic rhinitis. In the Netherlands approximately 115,000 children have been diagnosed with asthma and it has been indicated that about 20-30% of children has a form of atopic disease.<sup>3</sup> ADHD and atopic diseases co-occur more often than would be expected on the basis of chance.<sup>4</sup> In view of this co-occurrence and the fact that ADHD and atopic diseases are both common diseases among children, the question has been raised whether there is a common causal pathway. Pelsser et al. studied the therapeutic potential of a low-allergen diet, for children with ADHD. They found that the diet resulted in a significant and relevant decrease of ADHD symptoms. The diet, however, was difficult to keep.<sup>5</sup>

Studies on the association between atopic diseases and ADHD have shown conflicting results in the strength of the association. However, almost all mention an increased risk in either the presence of an atopic disease in those with ADHD or an increased risk of the development of ADHD in people with an atopic disease.<sup>6</sup> However, there is large variability between the studies with regard to controlling for potential bias, adjustment for confounding factors, and assessment method of both diseases. It is unclear whether atopy is a risk factor for the development of ADHD and vice versa, or whether there is a more direct link between both disorders, i.e., a common cause. In epidemiological studies both a more frequent simultaneous onset of atopy and ADHD as well as a more frequent occurrence of atopy prior to the development of ADHD than would be expected by chance has been observed.<sup>4,7,8</sup> It is, however, not yet possible to draw any conclusions about causality.

Large cohorts with few measurement waves are only informative to detect general patterns, and are not suitable for the detection of dynamic relationships between symptoms on a patient level.<sup>9</sup> The expression of symptoms in both atopy and ADHD is among other things dependent on treatment efficiency, compliance to treatment, and external factors, which may cause symptom fluctuations in both diseases. Currently, treatment of both chronic disorders is often suboptimal, like undertreatment in atopic diseases<sup>10,11</sup> and possible overdiagnosis and overtreatment with medication in ADHD<sup>12</sup>. Daily fluctuation of symptoms are a hall-mark of both atopic diseases and ADHD. By studying these fluctuations over time within individuals and examining the dynamic association between atopic symptom fluctuations and ADHD symptom fluctuations, we aimed to determine the temporal order of the association between symptoms of atopic diseases and ADHD.

## METHODS

### Study design

We performed a replicated time-series analysis of asthma and allergic rhinitis symptom fluctuations and ADHD symptom fluctuations in individual patients. The time-series data were collected by means of a diary study in which one of the parents was asked to fill in the daily questionnaires, at a specific time of day, preferably at the end of the day between 8-9 pm, for 50 days. A short questionnaire form, applied in the form of a mobile phone application, was used to assess both the asthma and allergic rhinitis symptoms, and the ADHD symptoms. Co-variables like age, gender, sleep problems, and medication use were determined during inclusion or as part of the daily measurement. For each participant age, sex, and the ratings of for ADHD symptoms (26-item scale Swanson, Nolan, and Pelham Questionnaire (SNAP-26)), atopy (Control of Allergic Rhinitis and Asthma Test (CARAT)), and sleep (Children's Sleep Habits Questionnaire (CSHQ)) as rated by one of the parents in the week before the initiation of the study, were determined to describe the sample characteristics. To encourage compliance of filling in the daily questionnaire we provided a personal report of the results to each participant after the completion of minimal 30 time points.

### Study population

The study population consisted of 11 children in the age of 7-17 years in whom the diagnosis ADHD was established formally by a child psychiatrist, a child psychologist, or a pediatrician and who had a diagnosis of asthma or allergic rhinitis, as established by a physician. Children were excluded if they were diagnosed with any chronic disease other than atopic diseases or ADHD. Parents could not participate if they were not fluent in the Dutch language or were otherwise unable to fulfill the study procedures. Children and their parents were recruited by their pharmacists through the IADB.nl prescription database and the patient database of a medical center in Rotterdam. Participants were asked to continue care as usual throughout the study. Our local medical ethical committee waived the ethical approval for this observational study design.

### Measures

To assess the severity of ADHD symptoms we used the SNAP IV questionnaire. This validated questionnaire is based on the 18 DSM-IV ADHD items. The combined score of inattention and hyperactivity/impulsivity subscale scores was used as rating of ADHD symptoms (18 questions; total score range, 0-54). In addition, the separate inattention scores and hyperactivity/impulsivity scores were determined. The SNAP IV questionnaire is a frequently used tool in ADHD studies, for example the Multimodal Treatment Study of Children with ADHD<sup>14,15</sup>. To assess the asthma and allergic rhinitis symptom severity the adjusted Control of Allergic Rhinitis and Asthma Test (CARAT) was used (7 questions; total score range, 0-21). The CARAT questionnaire is a validated and consistent way to measure asthma and allergic rhinitis symptoms.<sup>17</sup> Currently, the Adapt Asthma application, which is based on the CARAT, is

already in use to monitor asthma and rhinitis symptoms<sup>18</sup>. In total, seven questions for atopy and eighteen questions for ADHD needed to be answered daily by the parents, with different response categories per question (see appendix I). The questions and answer options of both questionnaires were adapted for daily measurement by changing the phrasing and time periods the original questions were referring to.

### **Covariates**

To address the possible involvement of sleep problems in the fluctuations in ADHD and atopic symptom expression we added eight questions concerning assessment of waking up and daytime sleepiness selected from the Children's Sleep Habits Questionnaire (CSHQ) (8 questions; total score range, 7-31) to the daily diary. In addition, items on medication use of both ADHD and atopic medication were added to the daily diary (2 questions; total score range, 0-3) to account for the possible effects of fluctuations in medication use on symptom expression in the models.

### **Statistical analyses**

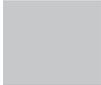
A vector autoregressive (VAR) model was used to investigate the dynamic associations between changes in atopy symptoms and changes in ADHD symptoms in each individual participant, and to examine the possible involvement of covariates in this association.<sup>19</sup> An important feature of the VAR model is the possibility to examine the temporal dynamics between multiple time series, which allows to study the temporal order of the association between atopy and ADHD symptoms accounting for potential bidirectional effects and effects of time-varying covariates like sleep problems and medication use.<sup>13,19</sup> An important feature of the VAR technique is the ability to investigate the temporal order of relationships between different variables by separating the dynamic longitudinal part from the simultaneous part of the associations between the variables.<sup>19</sup> In addition, the model allows to investigate and correct for potential feedback effects and bidirectionality.

A VAR model consists of a set of regression equations, in which each of the variables is regressed on its own lagged values (autocorrelation) as well as the lagged values of the other variables (cross-lagged associations).<sup>19</sup> We built VAR models with two variables, atopy symptoms and ADHD symptoms. The variable sleep problems was added to the primary model as an endogenous variable. Medication use was added to the model as an endogenous variable if there was variation in medication use during the follow-up period. We first investigated the optimal lag number, used in each of the models (a lag = one day), according to a comparison of the final prediction error of each lag model. Subsequently, we compared four different types of VAR models (constant, trend, both, and none) to determine if a additional trend or intercept term is needed in the model, since VAR models assume stationarity. Then we selected the optimal model with the Akaike Information Criterion (AIC) based on the one with the smallest value of AIC, a measure of relative quality of the fitted model.

To assess the temporal order of the association between atopy and ADHD symptoms, and the possible involvement of sleep problems therein, we determined the independent cross-lagged associations between each variable. In addition, we assessed the contemporaneous correlations between symptoms of atopy, ADHD, and sleep problems per participant to determine the simultaneous associations between (or co-occurrence of) the expression of symptoms. These can be computed from the residuals of the VAR model.<sup>19</sup> In general, a p value  $\leq 0.05$  was considered to be statistically significant. Per individual model multiple diagnostic tests were performed to test for stability, residual autocorrelation, homoscedasticity, and normality of the model.<sup>20</sup> If one of these assumptions was not met, the model was adjusted until all assumptions were met.

Simulation studies have shown that for VAR modelling a minimum of 30 time points is needed, although larger numbers of observations yield more reliable results.<sup>20</sup> To allow for some missing data, we chose for a time-series length of 50 measurement points.

Missing values on the daily sum scores of ADHD, allergy, and sleep were dealt with using multiple imputation on the individual level<sup>21</sup>. The imputed disease ratings were then computed by taking the average scores generated in each imputation. ADHD ratings were calculated subsequently by summing up the separate inattentive score and hyperactive score.



## RESULTS

A description of the characteristics of our study sample is presented in table 1. The majority (72.7%) of the study population consisted of boys. All participants were between 7 and 16 years of age at the start of the study period. Per participant the overall ratings of ADHD symptoms (SNAP-26), atopy (CARAT), and sleep (CSHQ) are shown. Within our study sample more than 50% of the participants was diagnosed with both asthma and allergic rhinitis. The baseline ratings of inattention was higher compared to the score for hyperactivity/impulsivity ( $p=0.008$ ).

**Table 1.** Characteristics of the study sample (n=11).

Characteristics	Mean (SD)	Participants										
		1	2	3	4	5	6	7	8	9	10	11
Number of completed observations		39	48	46	49	30	5	30	22	43	44	42
Gender (female), n	3 (27.3%)	girl	boy	boy	boy	boy	boy	girl	girl	boy	boy	boy
Age	11.0 (2.5)	12	11	12	7	11	16	13	10	9	12	8
ADHD diagnosis		yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes
Asthma diagnosis		yes	no	no	yes	yes	yes	no	no	yes	no	yes
Allergic rhinitis diagnosis		yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes
SNAP-26 score Total	32.7 (13.4)	60	37	12	40	35	39	31	32	17	18	39
Inattention	17.0 (4.1)	19	17	11	18	17	23	20	15	9	17	21
Hyper/Impuls	10.7 (6.5)	18	11	1	20	15	8	9	15	7	0	14
CARAT score	8.3 (3.8)	7	6	7	12	17	4	11	4	8	8	7
CSHQ score	46.5 (8.8)	60	52	42	45	53	54	56	37	37	38	37
Overall sleep grade (0-10)	6.7 (2.1)	4	8	8	7	5	3	5	8	9	8	9

Abbreviation: SD, standard deviation; n, sample size; ADHD, attention-deficit/hyperactivity disorder; SNAP, Swanson Nolan and Pelham questionnaire; Hyper/Impuls, hyperactivity/impulsivity; CARAT, control of allergic rhinitis and asthma test; CSHQ, children’s sleep habits questionnaire.

**Estimation of the VAR model**

Out of the 11 participants, two participants (#6 and #8) did not have enough observations (n<30) completed during the data collection and no analyses were performed for these participants. Considering the percentage of the missing measurements per participant, we obtained five imputed datasets for participant 1, 2, 3, 4, 9, 10, and 11, and ten imputed datasets for participant 5 and 7. In all models an optimal lag of one day was selected to be optimal. The model of four of the remaining ten participants were log-transformed for either the score of atopy (participant 10 and 11) or for both atopy and sleep (participant 2 and 3), because the residuals of the VAR model did not meet the normality assumption. Participant 5 showed an increasing trend in ADHD symptoms during the study period (regression coefficient (B)= 0.22, p-value=0.008), while participant 2 and 9 showed a decreasing trend in ADHD symptoms (B= -0.19, p=0.011; B= 0.10, p= 0.002).

**Temporal order of the relationship between atopy, ADHD, and sleep**

Both the temporal direction as well as the sign (positive or negative) and size of the effect varied between the participants. Three out of the ten participants showed a significant (p<0.05) cross-lagged association between one of the symptom variables ( table 2). In participant 1 an increase in expression of atopic symptoms preceded a worsening in ADHD

symptoms ( $B=3.59$ ;  $p=0.004$ ) and sleep ( $B=0.71$ ;  $p=0.023$ ), while increases in sleep were followed by decreases in ADHD symptoms. In participant 10 an increase in ADHD symptoms in this participant was followed by an increase in symptoms of atopy ( $B=0.12$ ;  $p=0.007$ ). In contrast to the other participants, in participants 11 a negative association was detected in which an increase in ADHD symptoms were preceded by a decrease in atopic symptoms ( $B=-1.25$ ;  $p=0.048$ ).

**Table 2.** Significant and trend 1-day cross-lagged associations.

Patient ID	Atopy → ADHD		Sleep → ADHD		ADHD → Atopy		Sleep → Atopy		ADHD → Sleep		Atopy → Sleep	
	B	P value	B	P value	B	P value	B	P value	B	P value	B	P value
1	3.59	0.004	-1.51	0.013							0.71	0.023
2*			-9.27	0.075								
3*												
4					-0.13	0.056						
5												
6	x	x	x	x	x	x	x	x	x	x	x	x
7												
8	x	x	x	x	x	x	x	x	x	x	x	x
9	0.40	0.052			0.22	0.051						
10*					0.12	0.007						
11*	-1.25	0.048					-0.07	0.058				

Abbreviations: → dynamic effect; atopy, sum score of atopic symptoms; ADHD, sum score of attention-deficit/hyperactivity disorder symptoms; sleep, sum score of sleep problems; B, unstandardized regression coefficient.

\*Cross-lagged associations are adjusted for ADHD medication use (participant 2, 3, 10, and 11) and allergic medication use (participant 10).

### Contemporaneous associations

In addition to the temporal order of the association between symptoms of atopy, ADHD, and sleep problems we also addressed the co-occurrence of the expression of symptoms of the different diseases. Table 3 shows an overview of the contemporaneous associations between atopy, ADHD, and sleep. Both atopy and ADHD, sleep and ADHD, and sleep and atopy were contemporaneously associated in a number of participants. Most often, the effect was positive but sometimes it was negative.

### Variation in medication use

In four participants the medication use related to ADHD (participants 2, 3, 10, and 11) and allergy (participant 10) varied during the study period. We included these variables as an extra endogenous parameters in the model. When adjusting for medication use the significant cross-lagged associations remained significant. In addition, participant 10 showed a significant cross-lagged association between sleep ( $B=0.14$ ;  $p=0.048$ ) and ADHD medication: an increase in sleep problems was followed by an increase in ADHD medication. In participant 10 also a trend negative cross-lagged association was detected between ADHD-related medication use and sleep problems ( $B=-0.66$ ;  $p=0.096$ ); increases in ADHD-related medication was followed by decreases in sleep problems.

When looking at the contemporaneous association between medication use and the symptom expression of the different diseases we detected a negative association between ADHD medication and atopy ( $r=-0.29$ ;  $p=0.042$ ) and sleep ( $r=-0.36$ ;  $p=0.010$ ) in participant 2. In addition, we observed a negative association between sleep and ADHD medication ( $r=-0.29$ ;  $p=0.044$ ) in participant 10.

**Table 3.** Contemporaneous significant and trend associations between symptoms of atopy, ADHD, and sleep problems.

Patient ID	Atopy&ADHD		Sleep&ADHD		Sleep&Atopy	
	r	P value	r	P value	r	P value
1						
2*	-0.29	0.093	-0.24	0.045	0.40	0.004
3*						
4			0.26	0.067		
5					-0.70	<0.001
6	x	x	x	x	x	x
7	0.28	0.080			0.27	0.093
8	x	x	x	x	x	x
9						
10*	0.31	0.032	-0.45	0.001		
11*						

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; r, correlation coefficient.\*Cross-lagged associations are adjusted for ADHD medication use (participant 2, 3, 10, and 11) and allergic medication use (participant 10).

### Differentiating inattention and hyperactivity/impulsivity

When stratifying the ADHD sum score into separate scores of inattention and hyperactivity/impulsivity similar results were observed. A notable difference was that the cross-lagged effect of sleep on ADHD symptoms in participant 2 appeared to be driven by an effect on hyperactivity/impulsivity symptoms. The same applied to the effect of ADHD on atopic symptoms in participant 4, which was also driven by an effect on hyperactivity/impulsivity symptoms. The opposite was true for the cross-lagged effect of ADHD symptoms on atopic symptoms in participant 10, which was driven by symptoms of inattention.

A separate cross-lagged association appeared in participant 3 for the effect of inattention on sleep ( $B=0.02$ ;  $p=0.072$ ). Also a separate positive effect of inattention on hyperactivity/impulsivity symptoms ( $B=0.38$ ;  $p=0.010$ ) and a negative effect of hyperactivity/impulsivity on inattention ( $B=-0.42$ ;  $p=0.034$ ) was observed in participant 7.

As regards the contemporaneous associations between the different symptoms also similar results were observed as in the original analyses. The contemporaneous association between atopy and ADHD, and sleep and ADHD in participant 10 was driven by symptoms of inattention. In comparison with table 3, new associations were found between atopy and inattention ( $r=0.40$ ;  $p=0.005$ ), and sleep and inattention ( $r=0.37$ ;  $p=0.010$ ) in participant 4, sleep and inattention ( $r=0.46$ ;  $p=0.002$ ) in participant 7, and sleep and hyperactivity/impulsivity ( $r=-0.37$ ;  $p=0.010$ ) in participant 9. The majority of the participants (#1, 2, 4, 5, 7, 11) showed a positive association between contemporaneous symptoms of inattention and hyperactivity/impulsivity.

## DISCUSSION

To our knowledge this is the first study using time-series analysis to examine the temporal order of the association between atopic disease symptoms and ADHD symptoms. For a majority of the participants multiple significant associations were detected between atopic disease symptoms and ADHD symptoms. However, the results were heterogeneous, and both the direction, sign, and timing of the relationship between ADHD, atopy, sleep, and medication use varied. In other words, the observed associations were not consistent across the participants.

Looking at the ADHD symptoms as outcome, our analysis showed a relationship between symptoms of allergy or sleeping problems and ADHD symptoms in some of the participants. The association of atopy and ADHD differed in sign between the participants. However, the negative association between sleep problems and ADHD was consistent. When looking at atopic symptoms as the outcome, only one participant showed a lagged significant association of ADHD on allergy symptoms. When assessing the more direct contemporaneous relationship, our analyses showed an association in six participants between ADHD symptoms or ADHD medication use, allergy, and/or sleep problems. The associations differed in both sign and strength. Participant 3 was the only participant who did not show a significant lagged or a direct effect between symptoms of allergy, sleep problems, and symptoms of ADHD.

Based on different group-based observational studies the association between atopy and ADHD is weak to moderate<sup>4,22</sup>. Although the association between symptom patterns in some participants does correspond with these between-subject results, in just as much participants a relationship between ADHD and atopy is absent or even reversed from what would be expected based on the literature of between-subject results. This could be explained by the fact that both atopic disease and ADHD are complex and heterogeneous diseases, and both diseases can vary in etiology and treatment, which leads to different patterns of symptoms expression.<sup>23,24</sup> Another reason may be that our series were rather short, which has limited our power. Future studies should preferably collect longer series. In general, the heterogeneity of our study results can be interpreted as one of the reasons that the effect size of the association between atopy and ADHD in group-based studies is considered to be weak. In a heterogeneous population, in which the association between atopy and ADHD is not present in every individual the group-based association between the two diseases can be diluted, while the association between the diseases can still be significant at an individual level. This is illustrated by our results in which the cross-lagged association of atopy and subsequent ADHD symptoms is reversed in participant 1 compared to participant 11, while both show a significant association between the diseases. A similar pattern is evident when comparing the between-subjects correlation and the within-subject correlation, representing the correlation over individuals and over time, respectively. Participant 5 and 7 both scored relatively high on the baseline score of atopy and sleep compared to the other participants, while at an individual level over time atopy and sleep were negatively correlated in participant 5 and positively correlated in participant 7.

### **Clinical Relevance**

A recent study showed that treatment of allergic rhinitis decreased ADHD ratings significantly compared with the change of ADHD ratings in healthy controls and children with pure ADHD.<sup>25</sup> In our study, in only one participant increases in allergic symptoms were followed by subsequent increases in ADHD symptoms, suggesting that a specific treatment of the atopic symptoms might perhaps improve the symptoms of ADHD in this individual. On the contrary, treatment of ADHD might be beneficial for the symptoms of allergy of participant 10, because increases in ADHD symptoms were followed by increases in allergic symptoms in this participant. Participants 4 (inattention), 7, and 10 showed a contemporaneous positive association between allergic and ADHD symptoms, in which an improvement of atopic symptoms could potentially benefit the participant by also improving the ADHD symptom expression, and vice versa. Because of a direct relationship between sleep and inattention in participant 3, and a contemporaneous positive association between ADHD and sleep in participants 4, 7 (inattention), and 10, these participants might perhaps benefit from improving their sleep for amelioration of their ADHD symptoms .

Taking into account the group-based cross-sectional and prospective association between atopy and ADHD in the literature<sup>4</sup>, it might be expected that this study would show a more consistent direct or lagged effect between ADHD and atopy. Because no such consistent relationship was established in this study it is possible that the association between atopy and ADHD partly exists because of an indirect mechanism, like genetic predisposition, or that the temporal association of cause and effect is stretched over a longer period of time. While a general group-based approach of treating atopy to improve ADHD symptoms, and vice versa, will not necessarily benefit the whole group, individualized assessment of interdisciplinary treatment of both diseases could benefit individual patients.

### **Strengths and Limitations**

Our findings should be interpreted in the light of the strengths and limitations. To our knowledge, this was the first study which examined symptom fluctuations of both allergy, ADHD, and sleep problems on a daily basis. This allowed us to observe the concurrent as well as the temporal relationships between the different variables. Although our study population was heterogeneous, a limitation was the small sample size of the study, which limits the generalizability of the results. However, due to the multiple repeated measurement points per patients it was possible to examine each individual participant in detail and to explore the possible temporal order of the association between atopy and ADHD. Combining both study types, with repeated measurements of symptom expression of both atopy and ADHD in a large cohort, would benefit the study of the association between both diseases.

Another limitation has been the limited study period. The participants were followed daily for a maximum of 50 days, but the effects of the symptom expression of one of the diseases could accumulate over time to have a larger and more significant effect on the long term.<sup>26,27</sup> For example, weekly measurements over a longer period of time could reveal

a more consistent association between the symptom expression of both diseases. Multiple pathophysiological hypotheses have been raised to explain the possible comorbidity between atopic diseases and ADHD.<sup>28</sup> Among other things, chronic stress and chronic inflammation have been raised as possible connections between atopy and ADHD. Because of the limited study period it was not possible to measure these possible effects.

## **CONCLUSION**

Time-series analysis is a potentially useful method to assess the temporal order of the association between atopy and ADHD. This study provides additional evidence that the symptom expression of atopy and ADHD are related. However, the connection between sign and symptoms of both diseases in children is heterogeneous and differs in both sign, direction, and strength within our study population. Personalized treatment needs of children with both an atopic disease and ADHD should be assessed at an individual basis to possibly improve the care of this patient group.

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## APPENDIX I

### Vragenlijst voor de dagboekstudie naar ADHD en atopische symptoom expressie

De volgende vragen en stellingen gaan over symptomen van ADHD, symptomen van allergie en slaapproblemen. Alle vragen hebben betrekking op uw kind. Bij het beantwoorden van de vragen verzoeken wij u om terug te denken aan hoe het de **afgelopen dag** met uw kind is gegaan. Selecteer daarvoor het rondje dat van toepassing is.

Datum: \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

ID nummer: \_\_\_\_\_

#### Slaapgedrag

Mijn kind:	Helemaal mee oneens (1)	Mee oneens	Neutraal	Mee eens	Helemaal mee eens (5)
1. werd (van)zelf wakker.(r)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. werd wakker met een slecht humeur.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. had moeite vanochtend uit bed te komen.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Had vanochtend lang de tijd nodig om goed wakker te worden.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. lijkt vermoeid.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Mijn kind leek vandaag erg slaperig of is in slaap gevallen tijdens het volgende (kruis alles aan waarbij bovenstaande is voorgevallen):

	Niet slaperig (1)	Erg slaperig	Viel in slaap (3)
6. TV kijken	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Autorit	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

8. Hoe beoordeelt u de slaap van uw kind de afgelopen nacht op een schaal van 0 tot 10? (omcirkel het juiste getal)

0	1	2	3	4	5	6	7	8	9	10
Slechts denkbare slaap										Best denkbare slaap

## Allergie

Hoe vaak heeft uw kind, vanwege zijn/haar allergische neusklachten en/of astma, vandaag last gehad van:

	Niet (0)	Nauwelijks	Een deel van de dag	(Bijna) de hele dag (3)
1. Verstopte neus?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Niezen?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Jeuk aan de neus?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Loopneus?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Benauwdheid/Kortademigheid?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Piepende ademhaling?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7's Nachts wakker worden?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Hoe vaak moest uw kind vandaag, vanwege allergische neusklachten en/of astma:

	Mijn kind heeft vandaag <u>geen</u> medicijnen gebruikt (0)	Mijn kind heeft vandaag <u>een lagere dosis</u> medicijnen gebruikt	Mijn kind heeft vandaag <u>de normale dosis</u> medicijnen gebruikt	Mijn kind heeft vandaag <u>een hogere dosis</u> medicijnen gebruikt (3)
8. Zijn/haar medicijnen extra gebruiken?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

## ADHD

Wilt u bij elke vraag aangeven in welke mate u het daarmee eens bent of niet? Het gaat om het gedrag van uw kind **vandaag**.

	Helemaal niet (0)	Enigszins	Behoorlijk	Heel duidelijk (3)
1. Slaagt er niet in voldoende aandacht te geven aan details of maakt achteloos fouten in schoolwerk of taken.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Heeft moeite de aandacht bij taken of spel te houden.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Lijkt niet te luisteren als hij/zij direct aangesproken wordt.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Volgt aanwijzingen niet op en slaagt er niet in schoolwerk, karweitjes af te maken of verplichtingen na te komen.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Heeft moeite met het organiseren van taken en activiteiten.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Vermijdt, heeft een afkeer van of is onwillig zich bezig te houden met taken die een langdurige geestelijke inspanning vereisen.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Raakt dingen kwijt die nodig zijn voor taken of bezigheden (bijvoorbeeld speelgoed, huiswerk, potloden of boeken).	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Wordt afgeleid door uitwendige prikkels.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. Is vergeetachtig bij dagelijkse bezigheden.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10. Beweegt onrustig met handen of voeten, of draait in zijn/haar stoel.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11. Staat op in de klas of in andere situaties waar verwacht wordt dat men op zijn plaats blijft zitten.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
12. Rent rond of klimt overal op in situaties waarin dit ongepast is.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
13. Kan moeilijk rustig spelen of zich bezig houden met ontspannende activiteiten.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
14. Is "in de weer" of "draaft maar door".	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
15. Praat aan een stuk door.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
16. Gooit het antwoord er al uit voordat de vragen afgemaakt zijn.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

	Helemaal niet	Enigszins	Behoorlijk	Heel duidelijk
17. Heeft moeite op zijn/haar beurt te wachten.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
18. Verstoot bezigheden van anderen of dringt zich op (bijvoorbeeld mengt zich zomaar in gesprekken of spelletjes).	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Hoe vaak heeft uw kind vandaag, vanwege ADHD:

	Mijn kind heeft vandaag <u>geen</u> medicijnen gebruikt (0)	Mijn kind heeft vandaag een <u>lagere dosis</u> medicijnen gebruikt	Mijn kind heeft vandaag de <u>normale dosis</u> medicijnen gebruikt	Mijn kind heeft vandaag een <u>hogere dosis</u> medicijnen gebruikt (3)
8. Zijn/haar medicijnen gebruikt?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

## Overig

7

Opmerkingen:

# PART III

The association of atopy and  
attention-deficit/hyperactivity  
disorder among adults.