ADHD and subthreshold symptoms in childhood and life outcomes at 40 years in a prospective birth-risk cohort

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ABSTRACT

We investigated ADHD symptoms and life outcomes in adulthood and their association with childhood ADHD and subthreshold symptoms in a prospectively followed cohort with perinatal risks. We identified participants with childhood ADHD (cADHD, $n = 37$), subthreshold symptoms defined as attention problems (cAP, $n = 64$), and no ADHD or cAP (Non-cAP, $n = 217$). We compared the groups and a control group with no perinatal risks ($n = 64$) on self-reported ADHD symptoms, executive dysfunction, and life outcomes in adulthood. At age 40, 21.6% of the cADHD, 6.3% of the cAP, 6.0% of the Non-cAP group, and 1.6% of the controls reached a screener cutoff for possible ADHD. The cADHD group had lower educational level, more ADHD symptoms and executive dysfunction, and higher rates of drug use than the other groups. Childhood ADHD associated with perinatal risks persists into midlife whereas childhood subthreshold ADHD symptoms in this cohort were not associated with negative outcomes in adulthood.

1. Introduction

Attention deficit/hyperactivity disorder (ADHD) has an estimated prevalence of 2–5% in adulthood (Kooij et al., 2010; Matte et al., 2015). The reports of persistence of ADHD from childhood to adulthood vary extensively with estimates ranging between 4% and 77% depending on the length of the follow-up and the definition of both childhood and adulthood ADHD (Faraone et al., 2006a; Sibley et al., 2016). Most longitudinal studies on ADHD only extend into adolescence or early adulthood, and prospective longitudinal studies continuing to the third and fourth decade are rare. The few studies extending beyond young adulthood have mostly consisted of clinic-referred boys (Klein et al., 2012; Satterfield et al., 2007). The persistence estimates for studies with a follow-up period of minimum 20 years range between 6% and 32% (Sibley et al., 2016). A recent cohort study over four decades found childhood-onset ADHD to continue into midlife in only 5% of cases (Moffitt et al., 2015).

Symptoms of ADHD form a continuum (Marcus and Barry, 2011). Focusing on subjects with an established diagnose thus excludes those

with symptoms below a diagnostic threshold from research and clinical scope (Faraone and Biederman, 2016). Although ADHD symptoms usually decline with age (Biederman et al., 2000; Faraone et al., 2006a), the individual course of symptoms varies throughout childhood and adulthood (Karam et al., 2017; Larsson et al., 2011). An individual might thus fulfill the diagnostic criteria at one point during their life and remain at a subthreshold level at another. Importantly, comorbid psychiatric disorders, such as substance use disorder and conduct disorder (Shankman et al., 2009), and adverse psychosocial outcomes (Norén Selinus et al., 2016) frequently associated with ADHD (Kooij et al., 2010), have also been found in adolescents and adults with previous subthreshold ADHD symptoms.

Adverse life outcomes and functional impairment associated with ADHD in adulthood are well established (Barkley et al., 2008; Biederman et al., 2006; Shaw et al., 2012). ADHD is linked to lower educational and occupational level (Biederman et al., 2012; Shaw et al., 2012), and higher rates of unemployment (Biederman et al., 2006). Moreover, the risk for comorbid psychiatric disorders is elevated (Kooij et al., 2010), including a high probability for substance use

disorder (Klein et al., 2012) and mood disorders (Biederman et al., 2012). Importantly, adults with a history of childhood ADHD exhibit adverse life outcomes and high levels of impairment even if ADHD symptoms are no longer severe (Caye et al., 2016; Moffitt et al., 2015). Dysfunction in executive functions has been proposed to be central in adult ADHD and partly explain these adverse outcomes (Adler et al., 2017; Barkley et al., 2008; Barkley and Fischer, 2011).

The long-term effects of early adverse events at birth on ADHD symptoms have been scarcely studied. In a recent review, low birth weight and preterm birth posed the greatest risk among perinatal complications for developing ADHD by age twelve (Serati et al., 2017). A longitudinal study to adolescence found complications in pregnancy and labor to be associated with ADHD symptoms throughout the follow-up period, with the association decreasing by age (Brinksma et al., 2017). Also, adults with ADHD symptoms have been reported to have a history of low birth weight or preterm birth more often than people with no ADHD symptoms (Halmøy et al., 2012; Strang-Karlsson et al., 2008).

This study examines ADHD symptom development and life outcomes in a cohort with perinatal risks followed prospectively from birth. Our primary aim was to investigate whether ADHD symptoms and executive dysfunction were elevated at age 40 in subjects with childhood ADHD or subthreshold symptoms. Our secondary aim was to examine life outcomes including education, occupation, psychiatric symptoms, and drug and alcohol use in relation to childhood ADHD and subthreshold symptoms. We also evaluated medical factors that may contribute to ADHD symptoms at age 40 in subjects who did not have ADHD in childhood.

2. Methods

2.1. Participants

The participants are from a longitudinal research project (Perinatal Adverse Events and Special Trends in Cognitive Trajectory, PLASTIC-ITY) (Hokkanen et al., 2013). The prospective birth cohort (1196 infants) consists of individuals born in one maternity hospital in Helsinki in 1971–1974 (Michelsson et al., 1978). The participants had one or several pre-defined perinatal risks, such as low birth weight (see Table S1). Subjects who had severe disabilities (cerebral palsy, severe sensory deficits, intellectual disability), or died before the age of 5 were excluded (see Fig. 1) (Launes et al., 2014). A control group of 164 singletons with no perinatal risks born in the same hospital was also followed from childhood. For the latest follow-up at 40 years, risk cohort members and controls whose addresses were found in the Population Registry Center of Finland (*n* = 1061) were invited via mail, of whom 607 responded. We included subjects who had participated in both childhood follow-ups at ages 5 and 9 (risk cohort *n* = 318, control group *n* = 64). Brain MRI scans (see Table S2) were used to exclude participants due to traumatic brain injuries or strokes. Visual assessment of the images was performed by a specialist in neuroradiology (RV), who was blinded to all clinical parameters. Participation is illustrated in Fig. 1. The project was approved by Ethical Review Board of the Helsinki and Uusimaa hospital district (number 147/13/3/00/2013). Written informed consent was gathered from all participants.

2.2. Defining childhood symptom groups

The risk cohort participants were grouped into three different categories: childhood ADHD (cADHD *n* = 37), attention problems (cAP; *n* = 64) and no ADHD or attention problems (Non-cAP, *n* = 217). The cADHD group had a disorder identified earlier (Tervo et al., 2017), whereas in the cAP group symptoms were not severe enough to warrant an ADHD diagnosis. The cAP group had symptoms of either inattention or hyperactivity/ impulsivity or both. The control group (*n* = 64) had no perinatal risks, cADHD, or cAP. The childhood symptom grouping

was based on multiple study observations, informant reports, and assessments at 5 and 9 years of age (see Tables S3-S6). ADHD was not a diagnosis in use at the time of the childhood follow-up and was diagnosed retrospectively by the first principal investigator of the project (KM) using all the information described above (Hokkanen et al., 2013). Subthreshold symptoms were identified with a norm-based approach (Barkley et al., 2008; Sibley et al., 2016), in which scores of the controls were used to create threshold percentiles. The complete protocol for childhood symptom assessments is described in the supplementary materials.

2.3. Measures

Childhood socioeconomic status (SES) was defined as the highest median status of mother and father recorded in childhood assessments (0, 5, and 9 years). Four classes, based on occupational level, were originally used, but the two lowest categories were merged due to small numbers. Level 1 represents the highest SES class. Information on mother's education was collected in the latest follow-up and divided into three levels: basic, secondary and tertiary. Current information on ADHD symptoms and life outcomes was gathered through a questionnaire filled online or on paper, and during on-site neurological and neuropsychological evaluations in 2014–2016.

Current subjective ADHD symptoms were estimated with the World Health Organization Adult ADHD Self-Report Screening Scale, ASRS-v1.1 (Kessler et al., 2005). The ASRS screener measures inattention and hyperactivity according to DSM-IV criteria (American Psychiatric Association, 2000) with six questions. The wording of the questions was modified to fit the broader questionnaire. The general score of the ASRS (range 0–24) was analyzed and participants were grouped according to a cutoff point (scores at or above 14) (Kessler et al., 2007). In our sample, a cutoff point of two standard deviations above the control group mean, a cutoff point suggested in the literature (Barkley et al., 2008; Sibley et al., 2016), coincided with the recommended cutoff score of 14. Scores for hyperactivity and inattention were summed to assess ADHD symptom domains. There were 20 missing values in the screener, which were imputed with the average of the corresponding childhood group.

Executive dysfunction was assessed with the Behavior Rating Inventory - Adult version (BRIEF-A) (Roth et al., 2005). BRIEF-A self-report results in a General Executive Composite (GEC) and two indexes, Behavioral Regulation Index (BRI), and Metacognition Index (MI). The MI consists of scales Initiate, Working Memory, Plan/ Organize, Task Monitor, and Organization of Materials. The BRI is consists of scales Inhibit, Shift, Emotional Control, and Self-Monitor. The BRI assesses regulation of behavior and emotions, and the MI ability to plan and monitor activities. The raw score was compared to normative data in the manual and transformed into T-scores, with a threshold of $T \geq 65$ for elevated score (Roth et al., 2005).

Data on the participants' education, occupation, mental health, smoking, as well as alcohol and drug use were gathered with the questionnaire. Highest educational degree was classified into three levels: Basic (9 years), secondary (10–12 years) and tertiary education (13 + years). Grade average from comprehensive school (around age 16) was collected. The lowest possible grade is 4 and highest 10. Occupational status was recorded as currently employed or unemployed. Future work ability was assessed by asking the participants to estimate the number of years they would be able to continue working. Psychiatric symptoms were assessed using the short version of the Depression Anxiety Stress Scales (DASS-21) (Lovibond and Lovibond, 1995), which was translated and modified by transformation into a 5 item Likert scale. Alcohol use was assessed with the Finnish version of the Alcohol Use Disorders Test (AUDIT) (World Health Organization, 2001). Life-time drug use was asked separately for cannabis and other illicit drugs but combined for the analysis.

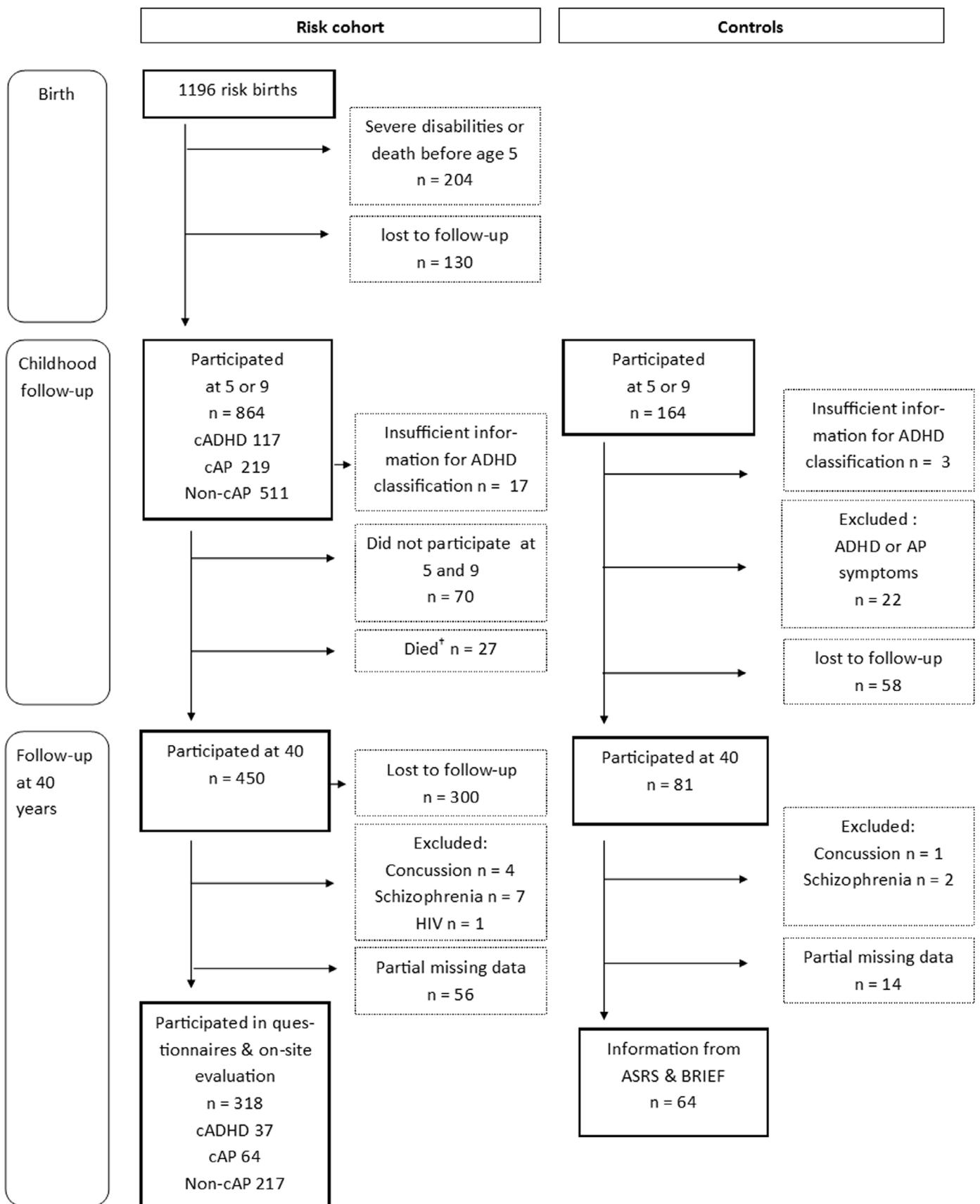All subjects underwent a semi-structured medical and

Fig. 1. Flow chart of the participants. [†]Died after childhood follow-ups.

socioeconomic history interview by a neurologist with 25 years of clinical experience (JL), who was not blinded to the birth data. We had access to purchases of reimbursed prescription medicines provided by the Social Insurance Institution of Finland, ICD-8 and ICD-9 codes of discharge from public hospitals since 1980 and from 2002 onwards also from outpatient care, provided by the National Institute for Health and Welfare THL. All medical data were systematically reviewed by JL and a list of adulthood concomitant conditions was compiled. Conditions related to mental health, sleep disorders, and neurological conditions were reviewed in evaluating possible underlying factors for ADHD symptoms in adulthood.

2.4. Statistical analyses

Statistical analyses were conducted using IBM SPSS software, version 24. Means and standard deviations were calculated for all continuous variables and percentages for categorical variables. Chi-square test was used to compare proportions in contingency tables. Logarithmic transformations were applied when necessary to make distributions of variables less skewed and were used to conduct univariate ANOVA analyses. Kruskall-Wallis analysis of variance, Mann-Whitney-U two sample tests, and rank analysis of covariance (Quade, 1967) were used when assumptions for parametric tests were not met. Logistic regression analysis was used to predict outcome and calculate odds ratios for ASRS screener cutoff group. Holm-Bonferroni corrections were applied to all pairwise analyses due to multiple comparisons. Effect sizes were estimated with Cramer's V for contingency tables and partial eta squared for continuous variables.

3. Results

Demographic characteristics and test statistics for the childhood symptom groups are shown in Table 1. The groups differed on gender, age, and childhood SES. Gender and childhood SES were used as covariates in all analyses of outcome measures. Age was not included as a covariate because the range in all groups was narrow (39 to 45 years) and the effect size was small.

The participating risk cohort and controls ($n = 382$) were compared to non-participants (cohort 300, controls 58, total $n = 358$). Fewer men participated in the follow-up [46.9% vs. 59.5%; $\chi^2(1), = 11.85$, $p = .001$, $V = 0.13$]. There were no differences in birth risks (all p values > 0.3), or childhood SES between the participants and non-participants ($p = .21$). The participants and non-participants differed on childhood group status ($\chi^2(3), = 12.18, p = .007$). There were more participants than non-participants in the Non-cAP group [56.8% vs 45.8%, $\chi^2(1) = 8.95$, $p = .017$, $V = 0.11$]. In the cAP group, fewer subjects participated in the follow-up [16.8% vs. 24.9%, $\chi^2(1) = 7.40$, $p = .033$, $V = 0.10$].

The childhood symptom groups differed on level of education, grade average, subjective future work ability, and drug use (Table 1). The groups also differed on ASRS total and hyperactive scores (Table 2). The groups differed on reaching a cutoff score on ASRS ($\chi^2(3), = 15.83$, $p = .001$, $V = 0.20$, Fig. 2). In pairwise comparisons, a higher proportion of the cADHD group reached the cutoff than of the Non-cAP, ($p = .007$) and control ($p = .004$) groups. In total, 53.8% (14 out of 26) of those reaching the ASRS cutoff did not belong to the cADHD or cAP groups and hence did not have ADHD or subthreshold symptoms in childhood (Fig. 2). The BRIEF-A GEC and Index scores, as well as some Scale scores differed between the childhood symptom groups (Table 2). The groups differed on reaching a cutoff for elevated symptoms on the BRIEF-A GEC [$\chi^2(3), = 13.21, p = .004, V = 0.19$], see Fig. 2. More participants in the cADHD group exceeded the cutoff than in the Non-cAP ($p = .026$) and control groups ($p = .006$). The bivariate correlation for BRIEF-A GEC T score and ASRS total score was 0.65, $p < .001$.

Current medications were drugs primarily indicated for treating arterial hypertension ($n = 39$), depression ($n = 37$), psychosis ($n = 7$), and asthma ($n = 25$). Antidepressive and antipsychotic medications were also used for several off-label indications, e.g. sleep disturbance,

Table 1
Demographic characteristics and life outcomes at 40 years in childhood ADHD and attention problem groups.

Characteristic	Childhood group cADHD (1) $N = 37$ n (%) or $M \pm SD$	cAP (2) $N = 64$ n (%) or $M \pm SD$	Non-cAP (3) $N = 217$ n (%) or $M \pm SD$	Controls (4) $N = 64$ n (%) or $M \pm SD$	χ^2/F	p	V/η^2	Pairwise comparison
Sex (male)	24 (64.9)	35 (54.7)	93 (42.9)	27 (42.2)	8.35	**.039**	.15	
Age at follow-up	42.1 ± 1.27	41.8 ± 1.24	42.3 ± 1.27	41.6 ± 1.27	12.92	**.005**	.026	3 > 4*
SES in childhood					19.28	**.004**	.16	
Level 1	5 (13.5)	17 (26.6)	47 (21.7)	26 (40.6)				4 > 1,3*
Level 2	11 (29.7)	11 (17.2)	64 (29.5)	20 (31.3)				
Level 3	21 (56.8)	36 (56.3)	106 (48.8)	18 (28.1)				2 > 4**; 1,3 > 4*
Mother's education ($n = 365$)					3.69	.72	.07	
Basic	10 (29.4)	23 (37.7)	69 (33.2)	15 (24.2)				
Secondary	20 (58.8)	28 (45.9)	106 (51.0)	36 (58.1)				
Tertiary	4 (11.8)	10 (16.4)	33 (15.9)	11 (17.7)				
Occupational Status (employed)	32 (86.5)	58 (90.6)	204 (94.0)	61 (95.3)	3.79	.29	.10	
Subjective work ability (years)	19.77 ± 4.67	20.89 ± 4.69	21.27 ± 4.35	22.47 ± 3.64	3.31	**.020**	.03	4 > 1*
Education					53.45	**< 0.001**	.26	
Basic	14 (37.8)	6 (9.4)	11 (5.1)	1 (1.6)				1 > 3,4***; 1 > 2**
Secondary	16 (43.2)	37 (57.8)	118 (54.4)	30 (46.9)				
Tertiary	7 (18.9)	21 (32.8)	88 (40.6)	33 (51.6)				4 > 1**
Grade average[†]	6.58 ± 1.10	7.50 ± 1.12	7.76 ± 1.24	8.10 ± 1.31	37.44	**< 0.001**	.09	3,4 > 1***; 2 > 1**
Smoking (yes)	10 (27.0)	19 (29.7)	38 (17.5)	9 (14.1)	7.18	.07	.14	
Drug use	10 (27.0)	4 (6.3)	19 (8.8)	5 (7.8)	13.70	**.003**	.15	1 > 3**; 1 > 2,4*
Alcohol use (Audit)	8.17 ± 5.64	6.13 ± 3.95	6.53 ± 4.63	5.94 ± 2.78	0.97	.41	.01	
DASS-21 total score	24.88 ± 15.93	18.74 ± 14.03	17.56 ± 12.35	17.98 ± 12.54	2.39	.07	.02	

cADHD, childhood ADHD; cAP, childhood attention problem; Non-cAP, no childhood ADHD or attention problems; SES, socioeconomic status; Audit, Alcohol Use Disorders Test; DASS, Depression Anxiety Stress Scales.

[†] Grade average in comprehensive school.

* $p < .05$.

** $p < .01$.

*** $p < .001$.

Table 2
ADHD and executive functions symptom scores at 40.

| | Childhood group | | | | | | | |
| | cADHD (1) $N = 37$ $M \pm SD$ n (%) | cAP (2) $N = 64$ $M \pm SD$ n (%) | Non-cAP (3) $N = 217$ $M \pm SD$ n (%) | Controls (4) $N = 64$ $M \pm SD$ n (%) | F | p | η^2 | Pairwise comparison |
Variable								
ASRS Tot	9.43 ± 5.06	6.30 ± 4.51	6.20 ± 4.09	6.69 ± 3.49	5.45	**.001**	.041	1 > 3***; 1 > 4**
ASRS Hyp	3.16 ± 2.24	1.98 ± 1.79	1.69 ± 1.72	2.0 ± 1.83	5.37	**.001**	.041	1 > 3***
ASRS Inat	6.27 ± 4.03	4.53 ± 3.29	4.52 ± 3.15	4.69 ± 2.70	2.49	.06	.019	
BRIEF-A GEC	56.89 ± 10.99	51.33 ± 9.20	50.74 ± 9.45	49.42 ± 7.53	4.67	**.003**	.036	1 > 3,4**; 1 > 2*
BRIEF-A BRI	56.16 ± 12.25	49.91 ± 10.68	49.93 ± 9.61	48.09 ± 8.37	4.94	**.002**	.038	1 > 3,4**; 1 > 2*
Inhibit	54.84 ± 8.74	49.55 ± 9.62	48.46 ± 8.03	46.77 ± 6.67	7.11	**< 0.001**	.054	1 > 3,4***; 1 > 2**
Shift	55.78 ± 12.83	49.70 ± 9.82	51.34 ± 10.11	50.03 ± 10.43	2.84	**.038**	.022	1 > 2*
EC	54.35 ± 12.48	50.41 ± 10.79	50.72 ± 10.48	49.28 ± 9.69	2.23	.09	.017	
Self-M	55.43 ± 11.59	49.56 ± 11.02	48.69 ± 9.22	47.27 ± 8.0	4.75	**.003**	.037	1 > 3,4**; 1 > 2*
BRIEF-A MI	56.76 ± 9.88	52.39 ± 8.72	51.43 ± 9.45	50.70 ± 7.49	3.44	**.017**	.027	1 > 3,4*
Initiate	56.65 ± 12.80	53.70 ± 10.46	52.24 ± 10.29	52.16 ± 8.66	1.23	.3	.01	
WM	61.54 ± 11.84	54.86 ± 12.04	54.73 ± 10.70	53.44 ± 9.45	4.54	**.004**	.035	1 > 2,3,4***
Plan	55.54 ± 8.72	50.31 ± 8.26	49.59 ± 8.61	48.95 ± 8.38	5.07	**.002**	.039	1 > 3,4**; 1 > 2*
TM	56.11 ± 9.09	52.84 ± 8.22	52.76 ± 9.60	52.17 ± 8.48	1.53	.21	.012	
OM	50.51 ± 10.53	50.16 ± 10.10	48.62 ± 9.75	48.05 ± 8.91	0.74	.53	.006	

cADHD, childhood ADHD; cAP, childhood attention problem; Non-cAP, no childhood ADHD or attention problems; ASRS, Adult ADHD Self-Report Screening Scale; ASRS Tot, ASRS total score; ASRS Hyp, ASRS hyperactive score, ASRS Inat, ASRS inattention score; GEC, general executive composite; BRI, behavioral regulation index; MI, metacognitive index; EC, emotional control; Self-M, self-monitor; WM, working memory; TM, task monitor; OM, organization of materials; * $p < .05$, ** $p < .01$, *** $p < .001$. All BRIEF-A descriptive data are presented as T-scores.
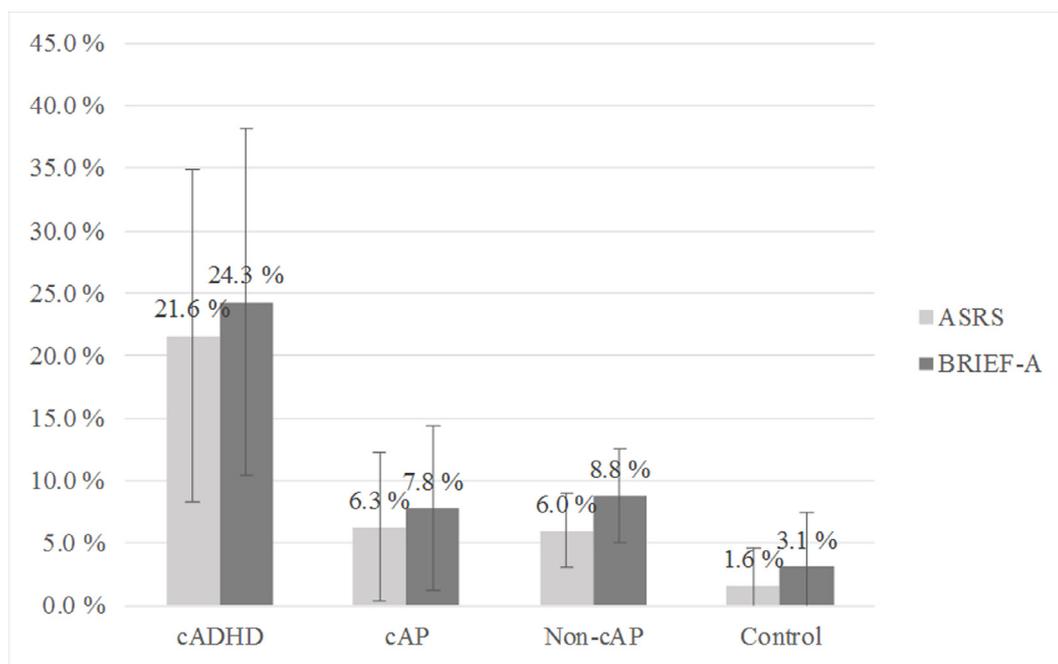

Fig. 2. Percentage of subjects reaching a cutoff on measures of ADHD symptoms and executive dysfunction in childhood groups with 95% confidence intervals. cADHD, childhood ADHD; cAP, childhood attention problem; Non-cAP, no childhood ADHD or attention problems; ASRS, Adult ADHD Self-Report Screening Scale, score ≥ 14; cADHD $n = 8$, cAP $n = 4$, Non-cAP $n = 13$, Control $n = 1$. BRIEF-A, Behavior Rating Inventory of Executive Functions, Adult, GEC T score ≥ 65: cADHD $n = 9$, cAP $n = 5$, Non-cAP $n = 19$, Control $n = 2$.

migraine and pain. Additionally, 37 subjects had medications for endocrine disorders, rheumatoid arthritis, Crohn's disease and epilepsy. There was no difference between the study groups in current medication for depression [$\chi^2(3) = 1.04$, $p = .79$, Mean rank for cADHD 198.8, cAP 193.9, Non-cAP 190.6, controls 187.9]. None of the participants had medication for ADHD either currently or in childhood.

Adulthood concomitant conditions related to mental health, sleep disorders, and neurological conditions were found in 10/26 (38.5%) participants exceeding the cutoff on ASRS and in 62/356 participants (17.4%) in the remaining cohort [$\chi^2(1) = 7.02$, $p = .008$, $V = 0.14$]. Conditions were equally distributed across the childhood symptom

groups [$\chi^2(3) = 4.37$, $p = .22$, $V = 0.11$]. In those exceeding the ASRS cutoff, two conditions were found in the cADHD, three in the cAP, four in the Non-cAP, and one in the control group. Higher DASS-21 score and belonging to the cADHD group predicted reaching the ASRS cutoff in logistic regression analysis (Table 3). The full model was significant compared to a model with constant only [$\chi^2(12) = 68.80$, $p < .001$].

4. Discussion

In this prospective cohort study of 382 participants over four decades we found childhood ADHD to be associated with higher rates of

Table 3
Predictors for reaching a cutoff on the ASRS screener.

Predictor	B	SE	Adjusted OR	95% CI	p
Sex (male)	0.25	0.59	1.29	0.41–4.08	.67
Childhood SES[†]					
Level 2	0.69	0.75	1.99	0.46–8.70	.36
Level 3	0.36	0.81	1.43	0.30–6.95	.66
Education[‡]					
Basic	−1.08	0.99	0.34	0.05–2.34	.27
Secondary	−0.10	0.63	0.91	0.27–3.11	.88
Smoking (yes)	1.01	0.58	2.75	0.88–8.62	.08
Audit score	−0.05	0.05	0.95	0.86–1.05	.32
Drug use (yes)	−0.49	0.83	0.62	0.12–3.13	.56
DASS-21	0.12	0.02	1.13	1.08–1.18	**< 0.001**
Childhood group					
cADHD	3.25	1.26	25.81	2.20–302.47	**.010**
cAP	1.37	1.27	3.94	0.32–47.79	.28
Non-cAP	1.90	1.15	6.71	0.70–64.22	.10

SES, socioeconomic status; Audit, Alcohol Use Disorders Test; DASS-21, Depression Anxiety Stress Scales; cADHD, childhood ADHD; cAP, childhood attention problem; Non-cAP, no childhood ADHD or attention problems; CI, confidence interval.

[†] compared to Level 1.
[‡] compared to Tertiary.

ADHD symptoms, executive dysfunction, and educational under-achievement at age 40 compared to those who had subthreshold or no symptoms in childhood. Childhood subthreshold symptoms were not associated with elevated symptoms or negative outcomes in adulthood.

In addition to reporting more ADHD symptoms at age 40 than the other groups, one fifth of the cADHD group reached a cutoff for possible ADHD. ADHD symptoms appear to persist in adulthood, as a follow-up of the same cohort at age 30 also showed higher rates of ADHD symptoms in the cADHD group compared to controls (Tervo et al., 2017). Previous estimates of ADHD persistence from longitudinal studies with individuals aged 30 or older (Sibley et al., 2016) have yielded comparable results, suggesting that severe ADHD symptoms continue beyond young adulthood among those with childhood ADHD. Still, most individuals with cADHD (78%) in our study no longer had elevated symptoms. This estimate is highly similar to results reported in two other longitudinal studies with adults over the age 30, where 74–78% of subjects with childhood ADHD did not fulfill the diagnostic criteria in adulthood (Klein et al., 2012; Mannuzza et al., 2011). The estimate in the present study is lower compared to another longitudinal cohort study, where 95% of subjects with childhood ADHD did not have ADHD in adulthood (Moffitt et al., 2015). Even though different assessment methods and definitions of ADHD were used in these and the present study, the percentage of symptom-free individuals is of the same magnitude. Thus, while there is a group of adults with childhood ADHD who still have evident ADHD symptoms, for the majority, these symptoms appear to alleviate by midlife.

Previous longitudinal studies have found hyperactive symptoms to decrease with age more than inattentive symptoms (Biederman et al., 2000). Differing from these results, the cADHD group reported more hyperactive symptoms than the Non-cAP group. Hyperactivity may have declined with age in our cohort, but we were unable to estimate this as the same measure was not used in childhood. The ASRS screener contains only two questions on hyperactivity and might thus not capture all symptoms of hyperactivity. Nonetheless, group-level differences suggest that hyperactivity, or the feeling of restlessness, continues to identify those with childhood ADHD in midlife. In a study of ADHD symptom trajectories in adulthood, it was more common for hyperactivity to increase over time than impulsivity or inattention (Karam et al., 2017). These results signal the importance of assessing hyperactivity in adults, despite the general trend of these symptoms decreasing with age (Biederman et al., 2000).

Childhood ADHD was associated with greater self-reported

executive dysfunction in adulthood. Executive functioning is linked to adult ADHD and suggested to be a better predictor of the disorder than symptoms in diagnostic criteria only (Adler et al., 2017; Barkley et al., 2008; Kessler et al., 2011). Behavioral regulation, particularly inhibitory control and monitoring one's behavior in social situations, was poorer in the cADHD group than in the remaining cohort and controls. Deficits in these skills could result in risky and impulsive behavior, as well as difficulties in maintaining social relationships due to lack of understanding how one's behavior affects others. The capacity to maintain and hold information in mind, and the ability to plan and organize future events were also affected, which are skills highly needed in educational and work settings. In another longitudinal study, Biederman and colleagues (Biederman et al., 2012) found similar results: Scores on most BRIEF-A scales were impaired in men who had ADHD as boys compared to controls. Our results add to the evidence of executive dysfunction being a key element in ADHD, and highlight the importance of evaluating executive functions if adult ADHD is suspected (Adler et al., 2017; Barkley et al., 2008).

As expected on the basis of literature and previous studies of our cohort (Barkley et al., 2008; Klein et al., 2012; Michelsson and Lindahl, 1987; Tervo et al., 2017), educational underachievement was prominent in the cADHD group; one third had completed only basic education by the age of 40. Educational underachievement was accompanied with poor academic performance as the cADHD group reported the lowest grade average among the groups. Our results indicate that those with childhood ADHD do not continue their studies at a later age, but permanently remain on a low educational track.

We found no differences in the employment status or psychiatric symptoms across the study groups, but life-time use of drugs was higher in the cADHD group. This result supports previous evidence of an association between childhood ADHD and later substance use (Caye et al., 2016; Klein et al., 2012). As for employment status, it is only a snapshot of the situation at one given time. When we asked the participants to estimate their future work ability, the cADHD group estimated their ability as worse than the controls. This is in line with other studies indicating occupational impairment among children with ADHD followed to adulthood (Barkley and Fischer, 2011; Klein et al., 2012). Lack of significant differences between the groups on other outcome measures may partly be explained by attrition bias. Our study group likely represents high functioning individuals as participating in the follow-up required commitment (Launes et al., 2014).

Overall, our results suggest that varied perinatal risks per se are not associated with negative life outcomes, executive problems, or ADHD symptoms in midlife as individuals in the perinatal risk group without childhood ADHD did not differ from controls. However, we cannot exclude the mediating effect of childhood ADHD associated with perinatal risk as we did not have a group with childhood ADHD without perinatal risks. Previous research has showed certain pre- and perinatal risk factors to be associated with adult ADHD (Halmøy et al., 2012). Investigating perinatal risks separately might reveal differences in associated ADHD symptom trajectories but could not be done in our study due to small numbers in risk groups.

In the present cohort, subthreshold ADHD symptoms were not associated with high rates of ADHD symptoms or negative outcomes in midlife. Similar to our findings, a longitudinal study found subthreshold ADHD not to predict the full syndrome over the course of 15 years (Shankman et al., 2009). Also, in a cross-sectional study individuals with subthreshold ADHD were less impaired and had fewer psychiatric disorders than those with a full disorder (Faraone et al., 2006b).

However, in a recent meta-analysis subthreshold ADHD was associated with functional impairment similar to that of the full disorder (Kirova et al., 2019). Even though the subthreshold group in this study did not differ from the other groups on negative outcomes, there was a trend for the cAP group to exhibit higher rates of smoking and psychiatric symptoms and lower rates of employment and tertiary education. Because the subthreshold group was small and we compared three

groups and performed multiple analyses, statistical analyses might not have reached significance even if group-level differences were present. Also, most evidence for negative outcomes in subthreshold ADHD come from children and young adults (Biederman et al., 2018; Kirova et al., 2019). Our subthreshold group might have had more problems at a younger age but do not manifest these negative outcomes at a group level later in adulthood, possibly due to catching up with peers later in development. Supporting this view, subthreshold ADHD did not to develop into the full syndrome in any participants in a longitudinal study over 15 years with several follow-ups in adulthood, implying that the core symptoms of ADHD do not tend to increase after adolescence (Shankman et al., 2009).

Childhood subthreshold symptoms have been proposed to underlie adult ADHD without known history of childhood ADHD (Asherson et al., 2016; Faraone and Biederman, 2016; Moffitt et al., 2015), but based on the current findings alternative hypotheses should be considered. Half of those exceeding the screener cutoff for ADHD did not have ADHD or subthreshold symptoms in childhood. As these individuals did not exhibit ADHD symptoms in several assessment situations or informant-reports in childhood, the cause for significant ADHD-like symptoms at age 40 is unlikely to be childhood ADHD. It is more likely that scoring high on the ADHD screener is due to other factors, namely psychiatric symptoms, causing attentional problems (Sibley et al., 2018). This seems to be the case in our cohort, as self-reported psychiatric symptoms were a significant predictor for exceeding the cutoff. Also, five out of 14 participants without childhood ADHD/ AP exceeding the cutoff had concomitant conditions that could explain the high screener score. However, psychiatric disorders have a high degree of genetic correlation, implying that having a psychiatric disorder does not exclude having ADHD as well (The Brainstorm Consortium, 2018). Thus, the possibility of few individuals presenting an onset of ADHD later in childhood or during adolescence or adulthood cannot be ruled out.

The greatest strengths of the study are the long prospective follow-up period and similarity in early environmental and perinatal risk factors between the study groups. Comparisons between childhood ADHD symptom groups and controls enables better evaluation of the impact of childhood ADHD and subthreshold symptoms on outcomes in adulthood. Another strength is that the life-time medical history of the subjects is known in detail. One of the limitations of the study may be that ADHD was not a diagnostic disorder at the time of childhood follow-up. Therefore, the classification had to be performed retrospectively. However, the diagnosis is based on extensive data from investigators and informants collected especially for recognizing behavioral symptoms. The ADHD screener measure of this study is widely used (Kessler et al., 2007), but consists of only 6 questions and does not cover all features of ADHD symptoms listed in DSM-IV diagnostic criteria (American Psychiatric Association, 2000). However, the six-question screener has been shown to outperform the full 18-question scale (Kessler et al., 2005), and the scoring method used in the present study has a good predictive value for clinical diagnosis (Kessler et al., 2007). In a longitudinal study, attrition bias cannot be avoided. While the cADHD group was similarly represented in participants and non-participants, fewer members of the cAP group, and fewer men, participated in the follow-up than in the childhood assessments. Despite these limitations, our results suggest that childhood ADHD, but not subthreshold levels of ADHD symptoms, are associated with evident ADHD symptoms and poor educational outcome at age 40 in a perinatal risk population.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.psychres.2019.112574.

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