Developmental trajectories of DSM-IV symptoms of attention-deficit/hyperactivity disorder: genetic effects, family risk and associated psychopathology

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**Background:** DSM-IV specifies three ADHD subtypes; the combined, the hyperactive-impulsive and the inattentive. Little is known about the developmental relationships underlying these subtypes. The objective of this study was to describe the development of parent-reported hyperactivity-impulsivity and inattention symptoms from childhood to adolescence and to study their associations with genetic factors, family risk, and later adjustment problems in early adulthood. **Method:** Data in this study comes from 1,450 twin pairs participating in a population-based, longitudinal twin study. Developmental trajectories were defined using parent-ratings of hyperactivity-impulsivity and inattention symptoms at age 8–9, 13–14, and 16–17. Twin methods were used to explore genetic influences on trajectories. Family risk measures included low socioeconomic status, large family size and divorce. Self-ratings of externalizing and internalizing problems in early adulthood were used to examine adjustment problems related to the different trajectory combinations. **Results:** We found two hyperactivity-impulsivity trajectories (low, high/decreasing) and two inattention trajectories (low, high/increasing). Twin modeling revealed a substantial genetic component underlying both the hyperactivity-impulsivity and the inattention trajectory. Joint trajectory analyses identified four groups of adolescents with distinct developmental patterns of hyperactivity-impulsivity and inattention: a low/low group, a primarily hyperactive, a primarily inattentive and a combined (high/high) trajectory type. These trajectory combinations showed discriminant relations to adjustment problems in early adulthood. The hyperactive, inattentive and combined trajectory subtypes were associated with higher rates of family risk environments compared to the low/low group. **Conclusion:** Study results showed that for those on a high trajectory, hyperactivity decreased whereas inattention increased. The combinations of these trajectories lend developmental insight into how children shift from (i) a combined to inattentive subtype, and (ii) a hyperactive-impulsive to a combined subtype. This study suggests that ADHD subtypes cannot be viewed as discrete and stable categories. **Keywords:** ADHD, twins, family factors, comorbidity, development.

The DSM-IV (American Psychiatric Association, 1994) conceptualizes attention-deficit/hyperactivity disorder (ADHD) based on two underlying symptom dimensions: a hyperactive-impulsive dimension including excessive activity and impulsive responding and an inattentive dimension including difficulties in sustaining attention, distractibility and disorganization. Using these two dimensions, DSM-IV specifies three ADHD subtypes: the combined, the hyperactive-impulsive and the inattentive. Follow-up studies of children with ADHD into adolescence and early adulthood show a substantial degree of continuity across time (Biederman et al., 1996; Hart, Lahey, Loeber, Applegate, & Frick, 1995), with around 65% of children with ADHD retaining the full syndrome or in partial remission by the age of 25 years (Faraone, Biederman, & Mick, 2006). However, uncertainty remains regarding the developmental progression of the DSM-IV subtypes. Studies explicitly exploring the joint development of hyperactivity-impulsivity and inattention are needed to understand the development of ADHD subtypes and to refine the DSM taxonomy into a more developmentally sensitive classification system.

Longitudinal studies suggest that symptoms of inattention tend to persist from childhood into adolescence to a greater extent than symptoms of hyperactivity-impulsivity (Biederman, Mick, & Faraone, 2000; Hart et al., 1995; Larsson, Lichtenstein, and Larsson, 2006). The limited developmental trajectory research also suggests only moderate stability in hyperactivity (Nagin & Tremblay, 1999; van Lier, van der Ende, Koot, & Verhulst, 2007). For instance, one study (Nagin & Tremblay, 1999), using teacher-rated hyperactivity from age 6 to 15, found that the majority of youths followed either a low or a moderate declining trajectory, whereas a small percentage of children (6% of the sample) followed a
chronic high hyperactivity trajectory. In addition, age-related changes in ADHD symptoms are also reflected in previously reported prevalence differences in ADHD subtypes across time (Graetz, Sawyer, Hazell, Arney, & Baghurst, 2001; Schaugheyney, McGee, Raja, Feehan, & Silva, 1994; Willcutt & Carlson, 2005); in younger age groups the primarily hyperactive-impulsive type is more frequently observed than the primarily inattentive type, whereas the opposite pattern has been found among adolescents. Age-of-onset studies (Applegate et al., 1997; Willoughby, Curran, Costello, & Angold, 2000) and one longitudinal study (Lahey, Pelham, Loney, Lee, & Willcutt, 2005) also suggest that some children demonstrate increased levels of inattention symptoms over the development. Together, these findings indicate that a subset of children may shift from the combined type to the inattentive type across time, whereas a number of those children who initially met criteria for the predominantly hyperactive-impulsive subtype may shift to a late-onset combined type. Unfortunately, none of the above-mentioned studies examined the joint development of hyperactivity-impulsivity and inattention; such an analytic strategy would allow for the identification of the developmental pathways underlying the combined type, and the predominantly inattentive and hyperactive-impulsive subtypes.

To address this research gap, this study aimed to examine the joint development of parent-rated hyperactivity-impulsivity and inattention symptoms, and how these developmental trajectories interrelate over time. Given that the exact number of trajectories varies from data source to data source (e.g., Piquero, 2008), we expected at least two trajectories for hyperactivity-impulsivity, a high and a low/decreasing trajectory (Nagin & Tremblay, 1999; van Lier et al., 2007). We also expected at least two trajectories for inattention; that is, a persistent high and a persistent low inattention trajectory (Hart et al., 1995; Lahey et al., 2005; Larsson et al., 2006).

Guided by the DSM-IV taxonomy of ADHD, we expected hyperactivity-impulsivity and inattention to combine in the following manner: (i) the majority would be characterized as low in both; (ii) a subgroup would be primarily hyperactive-impulsive or primarily inattentive; (iii) a subgroup would be characterized as high in hyperactivity-impulsivity and high in inattention. Consistent with population-based prevalence studies of DSM-IV ADHD subtypes (Willcutt & Carlson, 2005), we expected the primarily inattentive trajectory combination to be most frequent, followed by the combined and the primarily hyperactive-impulsive groups.

To explore the etiology and external validity, we examined (a) the predictive value of family risk factors and (b) how the trajectory types relate to externalizing and internalizing problems in early adulthood. In addition to a strong genetic predisposition to ADHD, environmental influences are estimated to account for 10 to 40% of the variance in liability for the disorder (Faraone et al., 2005). The few available studies on family risk and ADHD (Banerjee, Middleton, & Faraone, 2007) suggest higher rates of psychosocial adversity (i.e., marital discord, low social class, large family size, paternal criminality, maternal mental disorder and foster placement) in children with ADHD compared to controls (Biederman et al., 1995; Biederman, Faraone, & Monuteaux, 2002). As prior studies suggest higher rates of psychosocial adversity in children with ADHD combined type than in children with ADHD predominantly inattentive type (Counts, Nigg, Stawicki, Rappley, & von Eye, 2005; Eiraldi, Power, & Nezu, 1997; Graetz et al., 2001), we expected adolescents in high trajectories of hyperactivity-impulsivity and inattention to show higher rates of family risk (low socioeconomic status homes, large family size and divorced parents) compared to other youths.

There is considerable agreement that externalizing problems occur most commonly in children with ADHD combined subtype, followed by the primarily hyperactive-impulsive and the primarily inattentive types (Faraone, Biederman, Weber, & Russell, 1998; Willcutt, Pennington, Chhabildas, Friedman, & Alexander, 1999). We therefore expected adolescents in high trajectories of hyperactivity-impulsivity and inattention to have higher levels of externalizing problems in early adulthood than youths in the primarily inattentive trajectory. In contrast, we expected adolescents in high trajectories of inattention to show elevated levels of internalizing problems in early adulthood compared to other youths (Eiraldi et al., 1997; Faraone et al., 1998; Willcutt et al., 1999).

The use of twin data also allowed us to explore the impact of genetic and environmental influences on hyperactivity-impulsivity and inattention. A strong genetic component was expected as prior family study findings suggest that persistent ADHD has a higher familial loading than remitting forms of the disorder (Faraone, Biederman, & Monuteaux, 2000). In addition, longitudinal twin studies have shown that the stability in ADHD symptoms is mainly due to genetic effects (Larsson et al., 2006).

Methods

Sample

This study is based on data from the Twin Study of Child and Adolescent Development (TCHAD; Lichtenstein, Tuvblad, Larsson, & Carlstrom, 2007). Twins were eligible for participation if they were alive and lived in Sweden, and were born between May 1985 and December 1986. The twins and their parents were contacted in four different waves: when the twins were 8–9, 13–14, 16–17 and 19–20 years old. In wave 1,
the parent questionnaire had a response rate of 75% \((n = 1,103)\). In wave 2, 73% of the parents \((n = 1,063)\) responded to the questionnaire. In wave 3, the parent questionnaire had a response rate of 76% \((n = 1,067)\). In wave 4, both parents were approached separately, giving 1,158 responses from at least one of the parents (mothers only: \(n = 1,061\), fathers only: \(n = 795\)), while self-reports had a response rate of 59% \((n = 1,705)\).

Each wave of data collection was separately approved by the Ethics Committee at Karolinska Institutet and all participants consented to the study.

**Measures**

**ADHD.** At age 8–9, 13–14 and 16–17, parents provided ratings of ADHD symptoms in their children via a checklist of 14 DSM-IV-based items (American Psychiatric Association, 1994). The parents were asked to check symptoms persisting for at least six months. The symptoms were scored as 0 if the item was not true for the child and 1 if the item was true, and then summed to create two dimensional scales. Because of the changes in DSM during the follow-up period and because the twins in the sample were growing older, the full set of all 18 DSM-IV ADHD symptoms were not included on the three measurement occasions. Based on the 14 items that were present at all three time points, a hyperactivity-impulsivity scale was created from the sum of 8 symptoms of hyperactivity-impulsivity listed in DSM-IV and an inattention scale from the sum of 6 items related to inattention. For details see Larsson et al. (2006). Alpha reliabilities of the hyperactivity-impulsivity scale were .80, .83 and .81, and the inattentive scales were .68, .79 and .82.

At age 19–20, the twins themselves provided ratings of ADHD symptoms via a Likert-type scaled \(0 = \text{not true}; 1 = \text{sometimes true}; 2 = \text{often true}\) checklist of 18 DSM-IV-based items. The symptoms were summed to create two scales of hyperactivity-impulsivity and inattention. Alpha reliabilities of the hyperactivity-impulsivity and inattention scales were .79 and .76, respectively.

**Family risk factor.** Parents reported, in waves 1 and 2, on the number of siblings now living in the family. In line with one previous study of ADHD (Biederman et al., 1995), number of siblings was dichotomized \(0 = \text{fewer than 3 siblings and 1 = 3 or more siblings}\) to study the effects of large family size.

Parents reported, in waves 1 and 2, on marital status: (I) no partner, no cohabitation, (II) married/cohabiting, (III) widow/widower, (IV) divorced. Marital status was analyzed as a dichotomous variable to compare twins in divorced families (reported in wave 1 or wave 2) with those in groups I, II and III.

Socioeconomic status (SES) of the families was indicated by the occupational status of the parents: (I) unskilled and semi-skilled workers, (II) skilled workers/assistant non-manual employees, (III) intermediate non-manual collar workers, and (IV) employed and self-employed professionals, higher civil servants, and executives. SES was analyzed as a dichotomous variable to compare low SES families (class I) with those in classes II, II and IV.

**Externalizing and internalizing behavior in early adulthood.** At age 19–20 the twins and the parents (i.e., mothers and fathers gave separate reports) provided ratings of externalizing and internalizing problems via items from the Adult Behavior Checklist (ABCL) and the Adult Self Report (ASR) (Achenbach & Rescorla, 2003). The respondent was told to rate each item as ‘not true’, ‘somewhat or sometimes true’, or ‘very true or often true’, to describe the behavior within the past 6 months. Internalizing problems were assessed via items from the two empirical subscales of rule-breaking and aggressive behavior (Achenbach & Rescorla, 2003). Internal consistency, for the scales of externalizing and internalizing behavior, was good for all raters, with Cronbach’s alpha estimates between .85 and .90.

We combined all informants to obtain cross-informant (Achenbach & Rescorla, 2003) measures of the youth’s externalizing and internalizing problems. The cross-informant scales of externalizing and internalizing problems were created using items common to the different informants (Achenbach & Rescorla, 2003). Specifically, we first averaged the standardized scores from the mother-reports and father-reports of the twins’ externalizing and internalizing problems. To obtain a final measure of the twins’ externalizing and internalizing problems, we averaged the twins’ self-report and the parent-composite, allowing for one report to be missing.

**Statistical analyses**

The analyses proceeded in five steps. In step 1, models for the developmental trajectories were separately estimated for hyperactivity-impulsivity and inattention. We used growth mixture models (GMMs; Mutheén, 2004) to estimate the trajectories in Mplus Version 4.1 (Muthén & Mutheén, 2006). Robust standard errors were used to accommodate the non-independence of observations due to the twin design. GMMs are designed to identify clusters of individuals who follow unique patterns of growth, each of which may reflect distinct etiologies and/or outcomes. Missing data were handled through Full Information Maximum Likelihood.

A series of models was fitted, beginning with a 1-trajectory model and moving to a 5-trajectory model. Evaluation of the best-fitting models was accomplished using the Bayesian Information Criteria (BIC), the sample size adjusted BIC (aBIC), the Lo–Mendel–Rubin Likelihood Ratio Test (LMR-LRT), and entropy (McLachlan & Peel, 2000; Nyland, Asparouhov, & Muthén, 2007; Raftery, 1995). The BIC is a commonly used fit index where lower values indicate a more parsimonious model. LMR-LRT provides a \(k-1\) likelihood-ratio-based method for determining the ideal number of trajectories, a low \(p\)-value \((p < .05)\) indicating a better fit to the data. Entropy is a measure of classification accuracy, with values closer to 1 indexing greater precision \((\text{range } 0 \text{ to } 1)\).

In step 2, we used the starting values from the best-fitting trajectory models as the basis for estimating the joint trajectories of hyperactivity-impulsivity and inattention (i.e., the proportion of participants following
specific trajectory combinations). Participants were classified into the joint trajectory grouping they were most likely to follow, based on the posterior probabilities of joint group membership.

In step 3, we used logistic regression models to examine associations between family risk factors and joint trajectory membership. Odds ratios with 95% confidence intervals were estimated using generalized estimating equations in SAS version 9.2 (SAS Institute Inc., Cary, North Carolina), which allow us to account for the dependent nature of the twin observations.

In step 4, we examined mean differences in hyperactivity-impulsivity, inattention, internalizing and externalizing problems at ages 19–20 across the identified joint trajectories. We standardized these outcomes measures (i.e., Mean = 0 and SD = 1) to allow comparisons across trajectory groups. To account for the dependent nature of the twin observations, significance levels were adjusted using linear mixed-effect models in SAS version 9.2 (SAS Institute, Inc., Cary, North Carolina).

Auxiliary analysis. Using the probabilities of belonging to the different trajectories, we applied the classical twin design, using univariate liability threshold models (Rijndijk & Sham, 2002), to decompose the variance of the liability underlying hyperactivity-impulsivity and inattention into genetic factors (heritability), shared environmental factors (environmental influences that make twin siblings similar to each other), and nonshared environmental factors (environmental influences that make twin siblings different from each other). We used MX (Neale, Boker, Xie, & Maes, 2003), a structural equation modeling program, to perform maximum-likelihood model-fitting analyses with raw data.

Results

Descriptive statistics

Number of respondents, means, and standard deviations for the two symptom dimensions of ADHD, as well as the prevalence of having one or more and four or more parent-reported ADHD symptoms, are presented in Table 1. Mean symptom scores of hyperactivity-impulsivity decreased with age, whereas the mean symptom scores of inattention remained at the same level across time. The prevalence of hyperactivity-impulsivity symptoms declined from 42% at age 8–9 to 19% at age 16–17. In contrast, the observed prevalence for inattention symptoms remained stable across the three time points (Table 1). In line with these findings, we (Larsson et al., 2006) analyzed the developmental trend for the hyperactive-impulsive and the inattentive scales from childhood to adolescence. There was a highly significant negative trend in the hyperactive-impulsive scale from childhood to adolescence, whereas the inattentive scale showed no evidence of decline.

The correlations between hyperactivity-impulsivity at consecutive ages (8–9 to 16–17) varied between .37 and .49. The correlations between inattention at consecutive ages varied between .39 and .55. The correlations between hyperactivity-impulsivity and inattention were .52 at age 8–9, .53 at age 13–14 and .42 at age 16–17. All these correlations were statistically significant at \( p < .0001 \), but also underscore that the overlap between these two symptom dimensions is far from complete.

Selective attrition may bias estimates in longitudinal analyses. We therefore explored whether subjects lost to follow-up at wave 4 (i.e., at age 19–20) differed from responders on measures of ADHD symptoms at wave 3 (i.e., at age 16–17). Nonparticipants at wave 4 showed significantly higher mean symptom scores of inattention at wave 3 compared to participants (\( t(974) = 4.82, \ p < .001 \)).

Step 1: Trajectories of hyperactivity-impulsivity and inattention

For the two ADHD measures, a model with linear growth parameters was specified. We used a robust maximum likelihood estimator, which corrects standard errors, to account for non-normally distributed data. We also examined models using a censored adjustment to account for the inflated zero process, but the identified ‘censored’ trajectories showed poorer external validity compared to the model with only the robust estimator. As suggested by Bauer (2007), identifying the optimal number of trajectories was guided by: (1) the relative fit of the models (Table 2); (2) previous research; (3) taxometric theory (i.e., the DSM-IV classification system for ADHD subtypes); and (4) construct validation for the individual trajectories (Step 3 and 4).

Table 1 Number of respondents (n), means, standard deviations (SD), and prevalence for hyperactive-impulsive and inattentive symptoms

<table>
<thead>
<tr>
<th>Measure</th>
<th>n</th>
<th>Mean</th>
<th>SD</th>
<th>Prevalence 1 symptom</th>
<th>Prevalence 2 symptom</th>
<th>Prevalence 3 symptom</th>
<th>Prevalence 4 symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperactive/impulsive, age 8–9</td>
<td>2,019</td>
<td>1.04</td>
<td>1.60</td>
<td>850</td>
<td>42%</td>
<td>185</td>
<td>9%</td>
</tr>
<tr>
<td>Hyperactive/impulsive, age 13–14</td>
<td>1,998</td>
<td>.50</td>
<td>1.17</td>
<td>469</td>
<td>23%</td>
<td>81</td>
<td>4%</td>
</tr>
<tr>
<td>Hyperactive/impulsive, age 16–17</td>
<td>2,007</td>
<td>.36</td>
<td>.97</td>
<td>378</td>
<td>19%</td>
<td>46</td>
<td>2%</td>
</tr>
<tr>
<td>Inattentive, age 8–9</td>
<td>2,025</td>
<td>.69</td>
<td>1.09</td>
<td>791</td>
<td>39%</td>
<td>46</td>
<td>3%</td>
</tr>
<tr>
<td>Inattentive, age 13–14</td>
<td>1,996</td>
<td>.61</td>
<td>1.05</td>
<td>699</td>
<td>35%</td>
<td>85</td>
<td>3%</td>
</tr>
<tr>
<td>Inattentive, age 16–17</td>
<td>2,001</td>
<td>.72</td>
<td>1.20</td>
<td>721</td>
<td>36%</td>
<td>110</td>
<td>5%</td>
</tr>
</tbody>
</table>
The obtained fit statistics (Table 2) are bivalent in support for two hyperactivity-impulsivity trajectories and two inattention trajectories. That is, LMR-LRT and Entropy favor two trajectory groups for both measures, whereas BIC favors additional groups. We chose the two trajectory group models as the best heuristic models for four main reasons: (i) the additional trajectories mainly split the low groups into additional low groups that were limited in heuristic value; (ii) the joint combinations of models with 3 or more trajectories (i.e., 9 or more joint hyperactivity-impulsivity and inattention trajectory groupings) resulted in cells with zero participants, and had convergence difficulties; (iii) these additional combinations of groups were not validated or differentiated based on the predictors and outcomes in this study; and (iv) sole reliance on the BIC can very well result in a model that over-fits the number of trajectories (Muthén, 2004; Nagin, 2005).

Hyperactivity-impulsivity. For the two hyperactivity-impulsivity trajectories (Figure 1, A), 91% (n = 2,186) of the adolescents followed a low trajectory and 9% (n = 219) followed a high trajectory. Boys and girls were equally represented in the low trajectory (51% girls), whereas more boys (58%) than girls followed the high hyperactivity-impulsivity trajectory.

Inattention. For the two inattention trajectories (Figure 1, B), 86% (n = 2,067) of the adolescents followed a low trajectory and 14% (n = 338) followed a high/increasing trajectory. Boys and girls were equally represented in the low trajectory (52% girls), whereas more boys (62%) than girls followed the high inattention trajectory.

Table 2  Fit indices for GMMs of hyperactivity-impulsivity and inattention

<table>
<thead>
<tr>
<th>Hyperactive-impulsive dimension</th>
<th>BIC</th>
<th>aBIC</th>
<th>LMR-LRT</th>
<th>Entropy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-trajectory model 19,538.99 19,523.11 - -</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-trajectory model 17,276.79 17,251.38 .000 .961</td>
<td></td>
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</tr>
<tr>
<td>3-trajectory model 16,259.40 16,224.45 1.000 .960</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>4-trajectory model 15,295.53 15,251.05 1.000 .946</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-trajectory model Ncs - - -</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Inattentive dimension</th>
<th>BIC</th>
<th>aBIC</th>
<th>LMR-LRT</th>
<th>Entropy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-trajectory model 18,415.48 18,399.59 - -</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-trajectory model 16,474.22 16,448.80 .002 .902</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-trajectory model 15,814.83 15,779.89 1.000 .906</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4-trajectory model 15,330.47 15,285.99 1.000 .888</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>5-trajectory model 15,040.68 14,986.66 1.000 .898</td>
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</tbody>
</table>

Abbreviations: BIC, Bayesian information criteria; aBIC, sample size adjusted BIC; LMR-LRT, Lo–Mendel–Rubin Likelihood Ratio Test; ncs, non-convergent solution.

Step 2: Joint trajectories of hyperactivity-impulsivity and inattention

The joint trajectory analyses identified four groups of adolescents with distinct co-developmental patterns of hyperactivity-impulsivity and inattention. Table 3 shows the proportion of adolescents in each group. Group 1, the low hyperactivity-impulsivity and low inattention (low/low) group, represents 83% of the sample (n = 2,004; 52% girls). Group 2, the high hyperactivity-impulsivity and low inattention (primarily hyperactive) group, consists of 3% of the sample (n = 63; 47% girls). Group 3, the high inattention and low hyperactivity-impulsivity (primarily inattentive) group, comprises 8% of the sample (n = 182; 36% girls). Group 4, the high hyperactivity-impulsivity and high inattention (combined subtype) group, represent 6% of the sample (n = 156; 40% girls). Boys were more strongly represented than girls in all of the groups except in the low/low group.

Step 3: Predicting joint trajectory membership with family risk factors

Figure 2 shows that the prevalence rates of family risk measures were highest in the hyperactive and
combined trajectory subtypes. Results show that the combined trajectory group differed significantly from the low/low on all family risk factors (Table 4). The hyperactive group differed significantly from the low/low group on large family size and low SES, whereas low SES was the only childhood environmental risk measure that significantly differentiated the inattentive group from the low/low group.

Step 4: Predicting outcomes in early adulthood with joint trajectories

Figure 3 reports summary statistics on ADHD symptoms, externalizing and internalizing problems at age 19–20 for each of the four joint trajectories. Sex was included as a covariate in all linear mixed-effects models presented below.

ADHD symptoms at age 19–20. The hyperactive, the inattentive and the combined trajectory subtypes had significantly higher levels of self-reported hyperactivity-impulsivity in early adulthood compared to youths in the low/low group (Table 4). The combined subtype also had higher levels of hyperactivity-impulsivity compared to youths in the primarily inattentive group (see eTable 1). This was expected, given that the primarily inattentive subtype was represented by youths with low levels of hyperactivity-impulsivity from childhood to adolescence.

The inattentive and the combined trajectory subtypes had significantly higher levels of self-reported inattention in early adulthood compared to youths in the low/low group (Table 4), whereas no significant differences were observed between the hyperactive type and low/low group. The inattentive (p = .08) and the combined (p < .05) trajectory groups also had higher levels of inattention symptoms compared to youths in the hyperactive group (eTable 1), which was expected given that these youths were characterized by low levels of inattention from childhood to adolescence.

Adjustment problems at age 19–20. The hyperactive, the inattentive and the combined trajectory subtypes had significantly higher levels of externalizing problems in early adulthood compared to youths

![Figure 2 Differences in prevalence rates of family risk factors across the four joint trajectory groups](image_url)

<table>
<thead>
<tr>
<th>Family risk</th>
<th>Primarily hyperactive vs. low/low</th>
<th>Primarily inattentive vs. low/low</th>
<th>Combined group vs. low/low</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Large family size</td>
<td>2.48 (1.31–4.71)</td>
<td>1.46 (.94–2.26)</td>
<td>1.79 (1.11–2.87)</td>
</tr>
<tr>
<td>Divorce</td>
<td>1.91 (.98–3.73)</td>
<td>1.29 (.83–2.02)</td>
<td>2.29 (1.47–3.57)</td>
</tr>
<tr>
<td>Low SES</td>
<td>1.94 (1.05–3.59)</td>
<td>1.57 (1.05–2.36)</td>
<td>1.91 (1.23–2.98)</td>
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</table>

<table>
<thead>
<tr>
<th>ADHD symptoms at age 19–20</th>
<th>Effect size*</th>
<th>Effect size*</th>
<th>Effect size*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperactivity-impulsivity</td>
<td>.61 (Moderate)</td>
<td>.37 (Moderate)</td>
<td>.75 (Moderate)</td>
</tr>
<tr>
<td>Inattention</td>
<td>.23 (Small)</td>
<td>.55 (Moderate)</td>
<td>.63 (Moderate)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Adjustment problems at age 19–20</th>
<th>Effect size*</th>
<th>Effect size*</th>
<th>Effect size*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Externalizing</td>
<td>.52 (Moderate)</td>
<td>.46 (Moderate)</td>
<td>.74 (Moderate)</td>
</tr>
<tr>
<td>Internalizing</td>
<td>.03 (N.S.)</td>
<td>.39 (Moderate)</td>
<td>.33 (Small)</td>
</tr>
</tbody>
</table>

Table 4. Joint trajectory group comparisons with regard to family risk factors, ADHD symptoms and adjustment problems

Abbreviations: CI, Confidence interval; OR, odds ratio; N.S., non-significant. *Effect sizes were considered small at .35 or less, moderate at greater than .35 to .80, and large at greater than .80.
in the low/low group (Table 4). The combined subtype also had higher levels of externalizing problems compared to youths in the inattentive group (eTable1).

The inattentive and the combined trajectory subtypes had significantly higher levels of internalizing problems in early adulthood compared to youths following the hyperactive and low/low trajectory groups (Table 4). No significant differences in internalizing problems were observed between the hyperactive and low/low group.

**Auxiliary analysis: Genetic influences on trajectories of hyperactivity-impulsivity and inattention**

Owing to the low cell counts in the joint solution, we could not assess the genetic and environmental influences underlying the different hyperactivity-impulsivity and inattention trajectory combinations. eTable 2 shows twin correlations for the trajectories of hyperactivity-impulsivity and inattention, respectively. Monozygotic twin correlations were substantially higher than dizygotic twin correlations, suggesting strong genetic influences on both trajectories. Monozygotic twin correlations were less than 1, suggesting nonshared environmental influences.

The results from fitting two separate univariate liability threshold models suggest that the variance in liability of the hyperactivity-impulsivity trajectory was explained by genetic (80%; 95% CI: .62–.90) and nonshared environmental (20%; .10–.34) influences. The variance in liability underlying the inattention trajectory was due to genetic (72%; .56–.84) and nonshared environmental (28%; .10–.34) influences.

**Discussion**

To our knowledge, this study is the first to explore the joint development of hyperactivity-impulsivity and inattention from childhood to adolescence. On the basis of empirical fit indices and correspondence with a priori expectations derived from previous empirical studies, we identified two hyperactivity-impulsivity trajectories (low, high/decreasing) and two inattention trajectories (low, high/increasing) (e.g., Larsson et al., 2006; Nagin & Tremblay, 1999; van Lier et al., 2007). The combinations of these trajectories lend developmental insight into how children shift from (i) a combined to inattentive subtype, and (ii) a hyperactive-impulsive to a combined subtype. Thus, in line with prior suggestions (Lahey et al., 2005; Willoughby, 2003), the present study clearly shows that the ADHD subtypes cannot be viewed as discrete and stable categories; individual variation in the development course must be considered. Importantly, finding developmental shifts such as these does not necessarily invalidate the distinction between the DSM-IV subtypes of ADHD, but they may suggest modifications of current diagnostic criteria. In particular, the DSM-IV age-at-onset criterion may be too stringent, especially for the inattentive dimension of ADHD. Last, in a twin analysis, we revealed a strong genetic component underlying the developmental trajectories of both hyperactivity-impulsivity and inattention – a result that extends prior findings from family-based studies of persistent ADHD (Faraone et al., 2000).

Our results confirm findings of a general decline in hyperactivity-impulsivity symptoms across the development (Biederman et al., 2000; Hart et al., 1995; Nagin & Tremblay, 1999; van Lier et al., 2007), and a general increase in inattentive symptoms, which might explain why a subset of children with combined diagnosis shifts to an inattentive type over time (Lahey et al., 2005). Interestingly, this finding confirms DSM-IV ADHD-based prevalence studies (Graetz et al., 2001; Schauhency et al., 1994), age-of-onset studies (Applegate et al., 1997; Willoughby et al., 2000), and one longitudinal study (Lahey et al., 2005), all of which showed a late-onset pattern (or increasing levels) for the inattentive symptom dimension of ADHD. Although necessarily speculative, increases of inattention symptoms may be linked to a delay in cortical maturation (Shaw et al., 2007). Such a cortical maturational delay may interact with a stressful environment, such as transitioning to different school environments (e.g., more complex academic tasks or different teachers) or...
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negative peer relationships, to contribute the late-starting inattention pathway.

Consistent with most prior community-based studies reporting on the prevalence of the three DSM-IV subtypes (Willcutt & Carlson, 2005), the results of the joint trajectory analysis of the present study indicated the primarily inattentive group to be the most common trajectory combination (8%), followed by the combined trajectory group (6%) and the primarily hyperactive-impulsive group (3%). Nevertheless, the rate of children on high trajectories of hyperactivity-impulsivity and/or inattention (17%) is higher than the recently reported worldwide prevalence of ADHD (5.29%; Polanczyk, de Lima, Horta, Biederman, & Rohde, 2007), which indicate that the use of trajectory models, based on frequencies of symptoms, to represent change over time may capture subclinical as well as clinical cases. Nevertheless, these results provide further support for the developmental stability of ADHD symptoms into young adulthood.

Although all three trajectory combinations showed some signs of psychosocial adversity compared to the low/low group, this link was most evident in adolescents following the combined trajectory subtype, who were disadvantaged on all three family risk variables. Similar observations have been reported in previous research (Counts et al., 2005; Eiraldi et al., 1997; Graetz et al., 2001). Nevertheless, we failed to identify environmental risk indicators that discriminated between the three trajectory combinations (i.e., all confidence intervals for the risk associations were overlapping). These results may indicate that our indicators of psychosocial adversity have subtype-general (Lee et al., 2008) rather than subtype-specific effects (Counts et al., 2005). Clearly, future studies need to include additional risk measures to identify the environmental factors characterized by pronounced subtype-specific effects. Neurocognitive measures of spatial working memory and response variability (Castellanos, Sonuga-Barke, Milham, & Tannock, 2006) are other etiological influences that may differentiate between the three DSM-IV ADHD subtypes.

In line with previous studies that have compared comorbidity patterns across the three DSM-IV ADHD subtypes (Faraone et al., 1998; Willcutt et al., 1999), we observed the highest levels of externalizing problems in the ADHD combined subtype, followed by the primarily hyperactive-impulsive and primarily inattentive trajectory types. In contrast, the primarily inattentive and combined trajectories were characterized by higher levels of internalizing problems than the primarily hyperactive-impulsive type, which is consistent with prior research (Eiraldi et al., 1997; Faraone et al., 1998; Willcutt et al., 1999). It should, however, be noted that our finding of elevated levels of externalizing problems in the ADHD combined trajectory type may, in part, be driven by higher rates of conduct problems in childhood. Nevertheless, the differential results from the present study provide support for discriminant validity of the identified trajectory combinations and subtypes of DSM-IV ADHD.

We also extend previous research by showing a strong genetic component underlying the high/decreasing trajectory of hyperactivity-impulsivity and the high/increasing trajectory of inattention. Thus, the familial component found to underlie persistent ADHD (Faraone et al., 2000) may be genetic in origin. These results are also broadly consistent with results from a recent publication from our group (Larsson et al., 2006), showing that the stability in ADHD symptoms from childhood to adolescence is primarily influenced by genetic factors. However, we note here that the high heritability in ADHD symptoms does not imply that vulnerability to ADHD is deterministically set for life or that it is non-mutable. More specifically, the heritability of a certain trait only reflects a population average and is not related to individual changes over time in the expression of the trait. In addition, environmental factors can impact the expression of highly heritable traits. However, like many other twin studies, we have not modeled for gene–environmental interactions; the presence of these – with regard to ADHD – has been suggested (Ficks & Waldman, 2009). Thus, the heritability estimates observed here may also capture influences of gene–environmental interplay.

This study has limitations that should be taken into account. First, we used a longitudinal population-based sample of twins. In addition, we did not have information regarding impairment caused by inattention or hyperactivity-impulsivity symptoms in different settings, such as social or occupational environments. Moreover, information regarding age of onset of ADHD was not available. Hence, our results may not be extrapolated to clinical settings. However, since the observed pattern of findings is in general accord with prior clinic or outpatient-based research on the developmental course of ADHD (Biederman et al., 2000; Lahey et al., 2005), generalizability may not necessarily be limited. Second, a significant association between symptoms of inattention at age 16–17 and willingness to participate at wave 4 suggests selective attrition. Third, although we used comprehensive cross-informant data (i.e., self-, mother- and father-report) to assess externalizing and internalizing behavior, we relied on a single type of informant (i.e., parent-reports) to assess ADHD symptoms. Nevertheless, meaningful divergent associations with hyperactivity-impulsivity, inattention, externalizing and internalizing problems provide support for construct validity of the identified developmental trajectories. Fourth, the developmental trajectories of hyperactivity-impulsivity and inattention were limited to the period between the ages of 8 and 17 years. Given that hyperactivity emerges early in life (Shaw, Lacourse, & Nagin, 2005) and that inattention tends to persist into adulthood (Hart et al., 1995),
longitudinal studies of hyperactivity-impulsivity and inattention from early childhood to early adulthood will give a better understanding of how developmental changes in the two symptom dimensions influence instability of the DSM-IV subtypes of ADHD. Fifth, although comorbidity is a distinct clinical feature of ADHD, we did not examine the mediating/moderating role of associated behavior symptoms (e.g., conduct problems, depressive symptoms) on ADHD symptom trajectories. Such an avenue of investigation is an important area for future research.

Supporting information

Additional Supporting Information may be found in the online version of this article:

**eTable S1.** Standardized means and standard error for self-reports of hyperactivity-impulsivity, inattention and externalizing, internalizing at age 19–20, by joint trajectory group membership.

**eTable S2.** Intra-class correlations (MZ and DZ) and model-fitting estimates (heritability and nonshared environment) for hyperactivity-impulsivity and inattention trajectories (Word document)

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**Author note**

Henrik Larsson had full access to all the data and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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**Key points**

- Little is known about the developmental relationships underlying three ADHD subtypes.
- We found two hyperactivity-impulsivity trajectories (low, high/decreasing) and two inattention trajectories (low, high/increasing) for which twin analyses revealed a strong genetic component.
- For those on a high trajectory, hyperactivity decreased whereas inattention increased.
- The combinations of these trajectories lend developmental insight into how children shift from (i) a combined to inattentive subtype, and (ii) a hyperactive-impulsive to a combined subtype.
- This study suggests that ADHD subtypes cannot be viewed as discrete and stable categories.

**References**


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