1   **ADHD symptoms and their neurodevelopmental correlates in children born very preterm**

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Abstract

This study investigated the association between attention-deficit/hyperactivity disorder (ADHD) symptomatology in preschool-aged children who were born very preterm (<32 weeks) and cognitive outcomes, clinical risk and socio-demographic characteristics. 119 very preterm children who participated in the Evaluation of Preterm Imaging Study at term-equivalent age were assessed at a mean age of 4.5 years. Parents completed the ADHD Rating Scale IV, a norm-referenced checklist that evaluates ADHD symptomatology according to diagnostic criteria, and the Behavior Rating Inventory of Executive Function-Preschool version. Children completed the Wechsler Preschool and Primary Scales of Intelligence and the Forward Digit Span task. Longitudinal data including perinatal clinical, qualitative MRI classification, socio-demographic variables and neurodevelopmental disabilities were investigated in relation to ADHD symptomatology. All results were corrected for multiple comparisons using false discovery rate. Results showed that although the proportion of very preterm children with clinically significant ADHD did not differ from normative data after excluding those with neurodevelopmental disabilities, 32.7% met criteria for subthreshold ADHD inattentive type and 33.6% for combined type, which was higher than the expected 20% in normative samples. Higher ADHD symptom scores (all) were associated with greater executive dysfunction (inhibitory self-control, flexibility, and emergent metacognition, corrected $p<0.001$ for all tests). Higher inattentive ADHD symptom scores were associated with lower IQ ($\rho=-0.241$, $p=0.036$) and higher perinatal clinical risk (more days on mechanical ventilation ($\rho=0.206$, $p=0.025$) and more days on parenteral nutrition ($\rho=0.223$, $p=0.015$)). Higher hyperactive ADHD symptom scores instead were associated with lower socio-economic status ($\rho=0.278$, $p=0.002$). These results highlight the importance of monitoring and supporting the development of very preterm children throughout the school years, as subthreshold ADHD symptoms represent risk factors for psychosocial problems and for receiving a future clinical diagnosis of ADHD.

46 **List of Abbreviations and Acronyms:**

47 ADHD (Attention-deficit/hyperactivity disorder)

48 MRI (magnetic resonance imaging)

49 NDD (Neurodevelopmental disability)

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Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental condition which affects 5-7% of children, depending on the source of information used to reach a diagnosis (1, 2). Children who were born very preterm (< 32 weeks of gestation) have a 2- to 3-fold increased risk of being diagnosed with ADHD compared to their term born peers (4-fold risk in those born at < 26 weeks) (3-7).

According to the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V), ADHD is characterized by two main symptom presentations, inattention and hyperactivity-impulsivity (8). Although symptoms often co-occur, their expression can be unbalanced, leading to a clinical subdivision of the disorder into inattentive, hyperactive-impulsive and combined types. In general population samples the most common form of ADHD presentation is the combined type, but among very preterm born children the inattentive subtype has higher prevalence (9, 10). There is further evidence that very preterm children display higher levels of subclinical inattentive symptomatology compared to controls, which falls below diagnostic thresholds (11, 12).

ADHD symptoms in very preterm children exhibit specific cognitive correlates that are not observed in term-born children with ADHD (3), and research has suggested that behavioural symptoms of inattention in very preterm children could be completely accounted for by slow responses and impairments in visuo-spatial working memory (13). Preterm children with ADHD do not show the typical pattern of higher prevalence in males compared to females (14, 15), and they tend not to have co-occurring conduct disorder (15, 16). Socio-demographic and environmental risks show a weaker association with ADHD in very preterm compared to term-born children, while, and perhaps not surprisingly, perinatal medical and neurological factors significantly contribute to their vulnerability to develop the disorder (17). These converging strands of evidence have led to the hypothesis of a possible 'purer' biological aetiology of ADHD following very preterm birth (3), supporting the idea of multiple pathways to ADHD (18).

85   The majority of studies to date in very preterm samples have focused on school age, when ADHD

86   is typically diagnosed. However, the importance of detecting early risk factors associated with ADHD is

87   well recognised (19). Attention problems identified during the pre-school years may mark the beginning

88   of escalating academic problems, school drop-out and psychopathology later in life (20); indeed attention

89   could be regarded as a building block for the development of many other cognitive functions and as a

90   prerequisite for learning (21).

91   Here we investigate ADHD symptoms, their cognitive and clinical correlates in preschool-aged

92   children who were born very preterm. We hypothesised that higher ADHD symptoms in very preterm

93   children would be associated with lower executive functions and intelligence, even in the absence of a

94   clinical diagnosis. We further hypothesised that inattentive ADHD symptoms would be associated with

95   perinatal clinical adversity rather than environmental risk.

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Methods

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Sample

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99 Study participants were 119 very preterm born children who were recruited at birth in 2010-2013 as part

100 of the Evaluation of Preterm Imaging Study (e-Prime Eudra: CT 2009-011602-42) from hospitals within

101 the North and Southwest London Perinatal Network (22). Infants were eligible if born before 33 weeks

102 gestational age and their mother was aged over 16 years and not a hospital inpatient; they were excluded

103 if they had major congenital malformation, prior Magnetic Resonance Imaging (MRI), metallic implants,

104 parents unable to speak English, or were subject to child protection proceedings. The original sample

105 recruited studied 511 of 1831 eligible infants and accurately reflected the population of preterm infants.

106 Full data on the trial are available (22). The current study was a convenience sample created by families

107 who accepted invitations to undergo further examination and testing at pre-school age (see Table 1 for a

108 description of children's perinatal, socio-demographic and cognitive characteristics). Current study

109   participants did not differ from those in the larger cohort in terms of gestational age (F = 3.42, p > 0.05)

110   and birth weight z score (F = 0.013, p > 0.05). Written informed consent was obtained from children's

111   carer(s) following procedures approved by the National Research Ethics Committee (14/LO/0677), in

112   accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki).

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Gestational age in weeks, median (range)	**30.00 (25.00 – 32.00)**
Birth weight in grams, median (range)	**1305 (600 – 2600)**
Males, No (%)	54 (45.4)
Days on mechanical ventilation, median (range)	0 (0 – 21)
Days on parenteral nutrition, median (range)	5 (0 – 54)
Intrauterine growth restriction, N (%)	17 (14.3)
Index of multiple deprivation quintile, N (%)	
1 (Least Deprived)	23 (19.3)
2	24 (20.2)
3	28 (23.5)
4	24 (20.2)
5 (Most Deprived)	20 (16.8)
Corrected age at assessment in months, mean (range)	53.78 (50.06 – 59.19)
Mother's age leaving full time education, at birth, N (%)*	
18 years or younger	33 (27.7)
19 years or older	82 (68.9)
Unknown	4 (3.4)
Qualitative MR rating*	
No perinatal brain lesions N (%)	35 (29.4)
Minor perinatal brain lesions N (%)	64 (53.8)
Major perinatal brain lesions N (%)	17 (14.3)
Full scale intelligence quotient, mean (range)	106 (50 -147)

114   Table 1. Study participants' perinatal, socio-demographic and cognitive characteristics.

115   **Three MRI datasets were corrupted and could not be evaluated

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Perinatal clinical and socio-demographic variables

118   Perinatal clinical and socio-demographic data were collected with permission from the

119 Standardized Electronic Neonatal Database and included gestational age at birth, sex, days of mechanical

120 ventilation, days of parenteral nutrition, intrauterine growth restriction (diagnosed by the obstetric team at

121 the hospital where antenatal care was provided), mother's age when leaving full time education and Index

122 of Multiple Deprivation (IMD) score, determined by parents' postcode at the time of infant's birth

123 (http://imd-by-postcode.opendatacommunities.org), which provide a proxy for socio-economic status.

124   Infants received MRI at term-equivalent age on a Philips 3 Tesla (Philips Medical Systems, Best,

125 The Netherlands) system sited on the neonatal intensive care unit using an eight-channel phased array

126 head coil. T2-weighted images were acquired (TR 8,670 ms; TE 160 ms; flip angle 90°; slice thickness 2

127 mm; in plane resolution 0.86 × 0.86 mm). An experienced neonatal radiologist qualitatively rated the

128 MRI scan of each infant and assigned an overall global score that described the clinical severity of brain

129 abnormalities. Scores ranged from 2-0; 2 = major lesion, defined as cystic periventricular leukomalacia,

130 >10 punctate white matter lesions, grade 3 or 4 germinal matrix haemorrhage; 1 = minor lesion, defined

131 as all any other lesions; 0 = no lesion.

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Behavioural outcomes

134 The ADHD Rating Scale-IV (ADHD-RS-IV) (23) was used to measure behaviours associated with

135 different ADHD presentations according to DSM-V diagnostic criteria (8). This 18-item norm-referenced

136 questionnaire provides scores from two separate subscales (Inattention and Hyperactivity/Impulsivity)

137 and a combined score. These scales have been shown to have strong psychometric properties in preschool

138 children (23). Raw scores were transformed into z scores using age- and sex-matched normative means

139 and standard deviations. Scores were defined as clinically significant when equal or greater than the 90th

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140   percentile of the sex-matched normative score distribution. The 80th percentile was also used to include

141   sub-threshold symptoms.

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Neuropsychological outcomes

144   General intellectual development was assessed with the Wechsler Preschool and Primary Scales of

145   Intelligence battery (WPPSI-IV) (24). Age corrected for prematurity was used to calculate scaled scores

146   (25, 26). Phonological short term memory was assessed using the digit span forward test, using an

147   adapted version of the Wechsler Intelligence Scale for Children IV digit span task (27). Inhibitory Self-

148   Control Index (Inhibition and Emotional Control scores), Flexibility Index (Shifting and Emotional

149   Control scores) and Emergent Metacognition Index (Working Memory and Planning/organisation scores)

150   were obtained from the Behavior Rating Inventory of Executive Function-Preschool version (BRIEF-P)

151   (28). Scores are reported as T-scores, with higher scores indicating greater executive dysfunction.

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Neurodevelopmental Disabilities

154   Motor impairment was determined on the basis of scores below 2 standard deviations on the Gross Motor

155   Scale of the Bayley Scales of Infant Development-III (29) obtained at 18-22 months of age. Neuromotor

156   development was further evaluated at current assessment by a trained researcher and reviewed by an

157   experienced paediatrician. The assessment consisted of a brief neurological examination to confirm the

158   presence or absence of cerebral palsy. Sensory deprivation, speech problems and psychiatric diagnoses

159   (or suspected clinical significance together with the child waiting for a specialist's opinion) were not

160   directly assessed and were based on parental reports. Psychiatric diagnoses included autism spectrum

161   disorder (ASD) and global developmental delay (GDD). In case of reported problems, the child's General

162   Practitioner was contacted, and medical notes were accessed after obtaining caregivers' consent.

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163   Children with at least one of the following were regarded as having a neurodevelopmental disability

164   (NDD): neuromotor impairment (assessed at 18-22 months and confirmed by subsequent diagnosis of

165   cerebral palsy), diagnosis of ASD and/or GDD, sensory or/and speech problems.

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Data analysis

168   SPSS version 22.0 (SPSS Inc, Chicago, IL) and Matlab (MathWorks Inc, Natick, MA, U.S.A) were used

169   for analyses. Binomial tests were used to compare the proportion of very preterm children with clinically

170   significant (and subclinical) levels of behavioural problems against age-matched UK population norms.

171   Analyses were run before and after exclusion of children with NDD.

172   To assess the prevalence of inattention and hyperactivity/impulsivity, a data-driven clustering procedure

173   was also used on the ADHD-RS-IV scores to fractionate the sample into groups, defined by the imbalance

174   between their inattentive and hyperactive/impulsive symptoms, similar to (30). An Expectation-

175   Maximisation (EM) algorithm fitting a Gaussian mixture model was used to identify relatively

176   homogeneous groups of cases. Coordinates for centroids were initialized by running k-means clustering,

177   for which centroid coordinates were initialised at random.

178   The associations between ADHD symptoms, IQ and neurocognitive skills (phonological short-term

179   memory, inhibitory self-control, flexibility and emergent metacognition) were investigated using non-

180   parametric Spearman's rank-order correlation. Analyses were run after exclusion of children with NDD

181   and p values were always corrected for multiple comparisons using a false discovery rate (FDR) approach

182   controlling alpha error to 5% (31). Spearman's correlations were used to investigate the relationship

183   between ADHD symptoms and perinatal clinical variables and socio-economic status. Sex differences in

184   ADHD scores were investigated using the Mann-Whitney U test. After testing for the presence of

185   significant outliers (calculated using an interquartile range), variance homogeneity among groups

186   (Levene's test of Equality of Error Variances), and approximately normal distribution in the different

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187 groups, Kruskal-Wallis tests were used to test the association between severity of neonatal brain

188 abnormalities and ADHD symptoms.

189   Comorbidities between NDD and behavioural problems were defined by having NDD plus ADHD

190 symptoms above the 90th centile of the sex-matched normative score distribution.

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Results

ADHD Symptomatology

194 The proportion of very preterm children with clinically significant inattentive (20.2%),

195 hyperactive/impulsive (16.0%) and combined symptoms (16.8%) was higher than the expected 10% in

196 normative samples of predominantly term-born individuals (after FDR correction; see Table 2). However,

197 after exclusion of children with NDD, who represented 10.1% of the sample, the proportion of very

198 preterm children with clinically significant ADHD symptoms did not differ from the population norm. In

199 fact, comorbidity between NDD and clinically significant ADHD symptoms was high: 66.7% of children

200 with NDD had inattention symptoms above the 90th centile cut-off, 25.0% had hyperactivity/impulsivity

201 and 58.3% had combined symptoms. When using the 80rd percentile cut-off and excluding children with

202 NDD, 32.7% of very preterm children had inattentive symptoms and 33.6% had combined symptoms,

203 which was higher than the expected 20% in normative samples.

204

205 Table 2. Rates of clinical (>90th centile cut-off) and subthreshold (>80th centile cut-off) ADHD

206 symptoms in very preterm children before and after exclusion of those with NDD.

	Norms	Very Preterm		Adj p	Very preterm no NDD		Adj p
	%	N	%		N	%	
ADHD-RS-IV I >90th	10	24	20.2	**.003**	16	15.0	.100
ADHD-RS-IV H/I >90th	10	19	16.0	**.021**	16	15.0	.100
ADHD-RS-IV C >90th	10	20	16.8	**.028**	13	12.1	.271

ADHD-RS-IV I >80th	20	44	37.0	**.000**	35	32.7	**.002**
ADHD-RS-IV H/I >80th	20	34	28.6	**.016**	27	25.2	**.109**
ADHD-RS-IV C >80th	20	44	37.0	**.000**	36	33.6	**.000**

207 I = Inattention; H/I = Hyperactivity/Impulsivity; C = Combined; p= probability of binomial tests

208 uncorrected; Adj *p* = probability values of binomial tests after FDR correction.

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210

211 K-means clustering identified four ADHD groups: 13 children with predominantly inattentive symptoms

212 (10.9%), 12 with high levels of both inattentive and hyperactive/impulsive symptoms (10.1%), 44 with

213 medium levels of both symptoms (37%), 50 with low levels of both symptoms (42%) and no child with

214 mainly hyperactive/impulsive symptoms.

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216 **Figure 1.** Visual representation of inattentive and hyperactive symptoms in all study participants after

217 exclusion of children with NDD.

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Sex differences in ADHD symptomatology

221 Mann-Whitney tests showed no sex differences in inattentive (U = 1.429; *p* = 0.082),

222 hyperactive/impulsive (U = 1.656; *p* = 0.598) and combined ADHD symptom scores (U = 1.536; *p* =

223 0.243), even after exclusion of children with NDD.

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Associations between ADHD symptomatology and cognitive variables

226 After excluding children with NDD, higher inattentive ADHD symptom scores were associated with

227 lower full-scale IQ (ρ = -0.245, *p* = 0.011) but not with hyperactive and combined ADHD symptom

228 scores (ρ = -0.135, *p* = 0.168 and ρ = -0.190, *p* = 0.050, respectively). Higher ADHD symptom scores

229 (all) were associated with poorer inhibitory self-control, flexibility and emergent metacognition scores, as

230 shown in Table 3.

231

232 Table 3. Associations between ADHD-RS-IV symptom subtype scores and cognitive outcomes after

233 exclusion of children with NDD (n=107).

	Digit Span		Inhibitory Self-Control		Flexibility		Emergent Metacognition	
	ρ	*p*	ρ	*p*	ρ	*p*	P	*p*
Inattentive	-0.064	0.516	0.542	<0.001*	0.481	<0.001*	0.735	<0.001*
Hyperactive	-0.140	0.150	0.554	<0.001*	0.459	<0.001*	0.582	<0.001*
Combined	-0.101	0.299	0.586	<0.001*	0.505	<0.001*	0.718	<0.001*

234 Spearman correlation; ρ=Rho; *p* = probability values; * significant after FDR correction.

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Associations between ADHD symptomatology, perinatal clinical risk and socio-demographic variables

238 Higher inattentive ADHD symptom scores were associated with more days on mechanical ventilation

239 (ρ(119) = 0.196, *p* = 0.032) and more days on parenteral nutrition (ρ(119) = 0.222, *p* = 0.015). All results

240 survived FDR correction. There was no evidence of differences in ADHD symptom scores according to

241 severity of perinatal brain lesions (inattentive, *H* = 3.038, p = 0.219; hyperactive, *H* = 1.646, p = 0.439;

242 combined, *H* = 1.858; p = 0.395).

243   Hyperactive/impulsive and combined ADHD symptom scores were correlated with higher IMD

244 scores which reflect lower socio-economic status (ρ(119) = 0.259, *p* = 0.004 and ρ(119) = 0.198, *p* =

245 0.031, respectively). Children belonging to the 5th IMD quintile, reflecting the most deprived socio-

246 economic group, had a z score of 0.438, while those children belonging to the 1st IMD quintile, reflecting

247 the least deprived socio-economic group, had a z score of -0.433. After FDR correction, these

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248 associations remained unaltered. Similar findings persisted when children with NDD were excluded from

249 each analysis.

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Discussion

252 Although the proportion of very preterm children with clinically significant ADHD did not differ

253 from normative data after excluding those with neurodevelopmental disabilities, 32.7% met criteria

254 for subthreshold ADHD inattentive type and 33.6% for combined type, which was higher than the

255 expected 20% in normative samples. These results highlight the importance of monitoring and supporting

256 the development of very preterm children throughout the school years, as subthreshold ADHD symptoms

257 have been associated with an increasing risk of psychosocial problems and of receiving a future diagnosis

258 of the clinical disorder (32-34).

259 In addition to the high subthreshold ADHD inattentive symptom prevalence, our results showed

260 that inattention was a core deficit in this sample of very preterm children. K-means clustering identified a

261 group of very preterm children with predominantly inattentive or combined symptoms, but did not

262 identify a subgroup of children with predominantly hyperactive/impulsive ADHD symptoms. This is in

263 contrast with what described by Sanefuji and colleagues (2016) who similarly used k-means clustering in

264 a sample of 165 children diagnosed with ADHD and were able to parse children based on the three

265 typical ADHD clinical presentations (30).

266 Psychiatric risk in extremely preterm children has been found to be higher in those with coexisting

267 neurodevelopmental disabilities (35), although neurodevelopmental disabilities have been also associated

268 with psychopathology irrespective of very preterm birth (36). In this study, up to two thirds of children

269 with clinically significant ADHD-inattentive symptoms had comorbid neurodevelopmental disabilities, as

270 did one quarter of those with clinically significant ADHD-hyperactive/impulsive symptoms. In atypically

271 developing children a complex relationship exists between cognitive outcome, biological and

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272   environmental factors (37), and here we attempted to elucidate the association between ADHD

273   symptomatology, cognitive and environmental outcomes, cerebral injury and perinatal clinical risk.

274   Inattentive ADHD symptoms were associated with lower IQ, which has been studied as a

275   longitudinal predictor of educational outcomes (20). There is a strong phenotypic association between

276   ADHD and lower IQ which has been attributed to shared genes (38) and previous research suggested that

277   this association may be particularly strong for inattentiveness (39). It is therefore possible that preterm

278   birth may share common genetic influences with IQ and academic achievement (40).

279   Previous findings in older preterm children suggested that a core executive difficulty underlined

280   their inattentive problems (13, 41, 42), while the current study reported an association between higher

281   ADHD symptoms (all types) and executive scores. These included inhibitory self-control, flexibility and

282   emergent metacognition, which refers to the process of active control over one's own cognition,

283   encompassing processes involved in self-appraisal and self-management (43) and have been studied as

284   core features of ADHD (44, 45). The lack of ADHD symptom specificity in relation to executive

285   functions observed here could be explained by methodological issues associated with modelling executive

286   function early in development (46). More studies are therefore required to further investigate these

287   associations.

288   The current finding of a positive correlation between inattentive ADHD symptoms and perinatal

289   medical complications suggests that preterm-born pre-schoolers display a phenotypic profile that differs

290   from that observed in the general population, with aetiological underpinnings in the clinical risk

291   associated with preterm birth. This was assessed using markers of general infant health: number of days

292   of parenteral nutrition (reflecting gut failure) and number of days spent on invasive ventilation via

293   an endotracheal tube (reflecting respiratory failure). In a larger sample of infants the current study

294   participants were drawn from, these two risk factors were independently associated with lower fractional

295   anisotropy values throughout the white matter at term equivalent age, reflecting alterations in brain

296   development (47). These results suggest that although in this study ADHD symptomatology did not differ

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297 according to qualitatively-rated severity of perinatal brain lesions (unlike previous findings in 11 years

298 old children who were born extremely preterm (5)), future studies should include measures of brain

299 structure and function to further characterise the association between clinical risk and brain development

300 in order to better understand possible causative pathways leading to inattention in preterm children.

301   The idea that perinatal events can be implicated in the aetiology of psychiatric disorders has long

302 since been proposed (48) and several studies have supported this hypothesis by showing that preterm birth

303 may act as independent predictor of later psychopathology (49). The causal pathway to later psychiatric

304 disorder could be interpreted in the context of the neurodevelopmental sequelae of preterm birth (50),

305 although little is known about the neurobiological mechanisms leading to different ADHD subtypes. In

306 children with ADHD a double dissociation has been shown between resting state functional connectivity

307 in specific networks associated with inattentiveness and hyperactivity-impulsivity, indicating that

308 different brain alterations may characterise ADHD subtypes (30).

309   The early identification of a preterm profile characterised by inattentive ADHD symptomatology

310 associated with lower IQ and perinatal clinical risk suggests the need for early screening and educational

311 interventions aimed at improving specific attention problems in very preterm children, many of whom

312 exhibit academic difficulties at school age and are three times more likely to have special educational

313 needs than their term-born peers (51). Attention is a crucial requirement in school settings as it allows the

314 child to engage with classroom education activities. A strong relation between attention problems and

315 academic achievement has been shown in previous studies (even after accounting for IQ) (20) and

316 attention is considered one of the major areas of competence, which contribute to determine a successful

317 transition to school ("school readiness") (52). The use of easy and quick screening questionnaires, such as

318 the ADHD-RS-IV, could help to identify potential targets for the prevention of the escalation of academic

319 problems that have been associated with inattentiveness (53). This is especially important, given that

320 attention problems tend to be more persistent in time and more difficult to be detected in the school

321 setting compared to hyperactive/impulsive behaviours (10, 20). Moreover, preschool-age inattention is

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322 associated with other areas of difficulty, including communication and socio-emotional skills (52).

323 Therefore, the allocation of additional support for very preterm children before school entry could enable

324 them to enter school on a more equal footing with their peers.

325 Environmental variables including socio-economic status have been studied as risk factors for

326 ADHD (54), although the majority of published studies have not differentiated between ADHD

327 symptoms subtypes. Our results showed that children from socially disadvantaged families had increased

328 hyperactive/impulsive but not inattentive ADHD symptoms. These findings and are in line with others,

329 showing selective associations between hyperactivity/impulsivity and environmental variables, i.e. an

330 unsupportive home environment (55). The relationship between socioeconomic disadvantage and ADHD

331 is likely to be intricate and may be mediated by other factors that are associated with lower socio-

332 economic status, such as lower parental education and a less stimulating home environment (56).

333 Limitation of this study include the lack of a locally matched control group. This could have

334 influenced the results, possibly underestimating the level of problems experienced by very preterm

335 children (57). Strengths of this study include the use of a wide battery of tests and of a questionnaire

336 aimed at exploring ADHD subtypes, the use of a strict statistical procedure to correct for multiple testing,

337 the inclusion of children with NDD in the analysis, the use of data driven together with theory driven

338 approaches, the use of longitudinal information together with cross-sectional data.

339 In summary, this study shows that already during preschool age very preterm children are at

340 increased risk of sub-threshold ADHD symptoms, especially the inattentive type. Inattentive ADHD

341 symptoms were associated with intellectual functioning at time of assessment, and with perinatal clinical

342 risk, supporting the hypothesis of a possible neurobiological origin of ADHD. In light of these findings,

343 further investigation of early inattentive symptoms may support the development of effective

344 interventions and provide new models for understanding the neurofunctional trajectories leading to

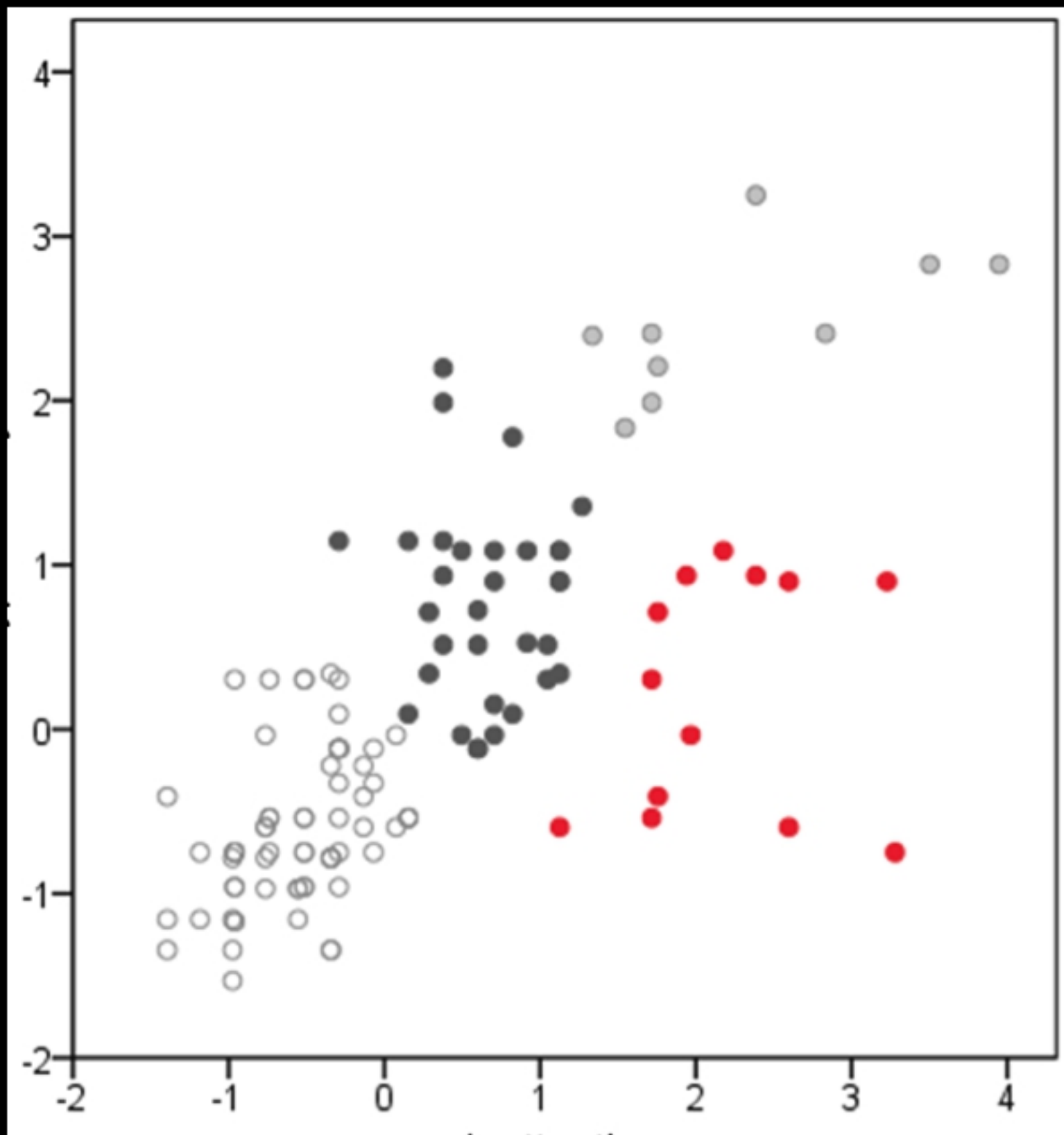345 ADHD in children born very preterm.

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