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ORIGINAL RESEARCH

Frequent Pain is Common Among 10-11-Year-Old Children with Symptoms of Attention Deficit Hyperactivity Disorder

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Purpose: Adults with neurodevelopmental disorders have an increased risk for chronic pain. This study aimed to describe the prevalence of frequent and multisite pain among children with symptoms of attention deficit hyperactivity disorder (ADHD) and explore potential sex differences in pain prevalence.

Participants and Methods: Children born in 2008 included in the "Halland Health and Growth Study" were invited to a follow-up (n = 1186) in 2018–19. Parents received a digital screening questionnaire, the Swanson, Nolan and Pelham Rating Scale (SNAP-IV) for ADHD, and the children answered a pain questionnaire that included a pain mannequin. The main outcome was pain experience, and children with symptoms of ADHD were compared to children without these symptoms.

Results: In this general population of 10–11-year-old Swedish children, weekly pain was reported in 52.5% of children with symptoms of ADHD combined type, compared to 36.2% of children without these symptoms ($p < 0.05$). Hyperactivity and impulsivity were significant contributors to the increased risk for frequent pain (OR 2.33 95% CI 1.30 to 4.17, p = 0.004), but inattention was not a significant contributor (OR 1.17 95% CI 0.74 to 1.87, p = 0.497). Multisite pain was more common among girls with hyperactivity compared to boys with hyperactivity (51.4 vs 27.9%, p = 0.036). Weekly headache and/or abdominal pain was reported by a quarter of girls with symptoms of ADHD combined type, and up to a fifth of boys, compared to 11–13% of children without these symptoms.

Conclusion: Frequent pain was more common for children with symptoms of ADHD compared to children without symptoms of ADHD. Hyperactivity and impulsivity had a stronger association to pain than had inattention-related problems. Clinicians should be aware of the frequent occurrence and the association between pain and neurodevelopmental disorders among children, and that it could complicate both the clinical picture and the treatment.

Keywords: attention deficit hyperactivity disorder, ADHD, birth cohort, children, multisite pain, sex differences

Introduction

Adolescents and adults with attention deficit hyperactivity disorder (ADHD) have a higher prevalence of pain than the general population, but little is known about the age at which this increase emerges or if there are any sex differences.[1–4] Similarly, individuals with autism spectrum disorder (ASD) also tends to report more pain than the general population.[4–6] In International Classification of Diseases, 11th Revision (ICD-11), chronic primary pain is acknowledged as a health problem in itself, but no pediatric criteria exist[7] and studies on childhood pain differ in terms of definitions and durations. Moreover, neurodevelopmental disorders and pain are not evenly distributed among populations.[8–10] For example, pain is more common in children with obesity,[11] and among children in treatment for obesity neurodevelopmental disorders are also more common than in the general population.[12]

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In children, pain prevalence increases during adolescence and is more common among girls,[13–15] whereas neurodevelopmental disorders are more often diagnosed in boys.[16] Published prevalence numbers and definitions for pain in children differ, but up to 40% of children and adolescents report weekly pain[13,14,17] and, according to Gobina et al, 20.6% of adolescents reported multisite pain (>2 sites), while 11.3% of children reported headache on a weekly basis.[13]

It is likely that pain and neurodevelopmental disorders in children are intertwined.[1–4] The etiology of pain in association with neurodevelopmental disorders is unknown; however, in a review by Battison et al,[2] two different theories are proposed, together with neuroinflammation as an underlying factor in both conditions.[18] The first theory includes cognitive-affective problems with altered perception. The theory proposes that difficulties in emotional control or cognitive abilities make the individual interpretation of pain signals different from the neurotypical population.[2,18] Pain may also reduce attention,[1] which is why the combination of pain and symptoms of ADHD could have a mutually negative effect. Reduced attention span due to pain may increase the risk for an ADHD diagnosis for children with symptoms within this field. For children with ADHD in turn, pain may worsen problems with attention but also lower the tolerance for pain, thereby strengthening the association between the two conditions. Another theory is that difficulties in motor control and risky behavior increase the risk for physical injuries that could lead to pain, and that the hyperactivity itself, together with increased muscle tone may lead to more frequent pain, compared to the general population.[2,19,20] Kasahara et al[21] found that among adults with persistent chronic nonspecific lower back pain, a high percentage scored positive for ADHD, and that hyperactivity-impulsivity was associated to increased pain prevalence and pain intensity. They discussed that decreased dopaminergic function in both chronic pain patients and patients with ADHD could be the reason for this finding. Decreased dopaminergic function as a contributor to ADHD and fibromyalgia, a common chronic pain disorder, has also been proposed by Swanson et al[22] and Wood et al.[23] A study by Treister et al[24] showed that subjects with ADHD had lower tolerance to pain but when treated with methylphenidate their tolerance improved, indicating that ADHD and pain experience may be intertwined.

Independent of etiology, pain and ADHD often persist until adulthood[25,26] and both have major individual and societal consequences, due to economic costs and high medical dependence.[8,27–29] Pain and ADHD are both associated with co-morbidities, low quality of life and social problems, including a higher risk for substance abuse, economic problems and lower socioeconomic status.[13,25,30–37] Additionally, experiencing chronic pain during childhood may alter brain development.[38] For instance, Bhatt et al[39] showed that children with chronic pain have less grey matter and present with hyperconnectivity in the brain, compared to children without pain. If pain is addressed early, some cases of chronic pain might be prevented, and if unrecognized ADHD is diagnosed and treated, complications like substance abuse could possibly be prevented.[40,41] Therefore, pain and ADHD needs to be addressed early, before complications arise.

ADHD is one of the most common neurodevelopmental disorders and adolescents and adults with ADHD have been shown to report a higher prevalence of pain than the general population,[1–4] but it is not known whether this correlations is evident already at age ten to eleven, nor if there are any sex differences at this age. Moreover, most studies report increased pain prevalence in patients with ADHD but given the possible common etiology, it is not known whether this increased pain prevalence is seen even among people with just symptoms of ADHD that do not reach the threshold for diagnosis. Therefore, the aim of this study was to present prevalence numbers for children with both frequent pain and symptoms of ADHD and/or symptoms of ASD and to compare those to children without these symptoms, and to identify possible sex differences between groups. Furthermore, we wanted to advance the knowledge further, by studying pain with regard to hyperactivity-impulsivity on the one hand, and inattention on the other and to investigate whether the cut-off level for ADHD screening was associated to increased pain prevalence.

Materials and Methods

Study Design, Population and Data Collection

This study formed part of the larger Halland Health and Growth Study (H^2GS),[42] an ongoing population-based birth cohort of 2666 children born in Halland, southwest Sweden, between October 1, 2007 and December 31, 2008. There were no exclusion criteria, but parents had to understand Swedish well enough to provide informed consent and to understand the questionnaires in Swedish. In 2018, a large follow-up was rolled out for these children. However, for

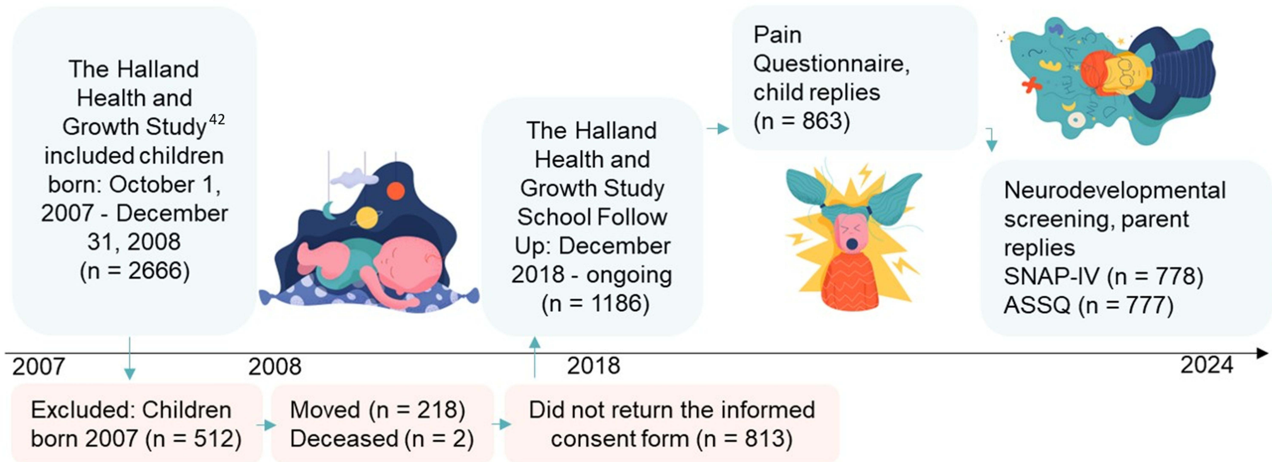

Figure 1 Flowchart of the study population. This study was part of the follow up for the Halland Health and Growth Study,[42] a longitudinal, population-based, birth cohort study that recruited children born between October 1, 2007, and December 31, 2008. Total births in the county (n = 3680) October 1, 2007 to December 31, 2008.

practical reasons, we wanted children born in the same year, and found that 1999 children were born in 2008 and still living in Halland. These children and their parents were asked to continue participation in the follow-up H^{2}GS Goes to School Study (Figure 1). In total, 1186 (59.3%) returned the informed consent form and were thereby included in the school follow-up.

For this study, the Swanson, Nolan and Pelham Rating Scale (SNAP-IV)[43] and the Autism Spectrum Screening Questionnaire (ASSQ)[44] were chosen and emailed to the parents in December 2018. A pain questionnaire was addressed to the child and emailed to the parents in May 2019. Three reminders were sent out. All children who answered the pain questionnaire from May to July 2019 (n = 863) were included in the current study. The response rate was 72.8%, representing 27.2% of all children born in Halland 2008 (n = 3167). All children had turned 10 years of age at the time of completing the questionnaires, and about half had turned 11.

Measures

SNAP-IV

The SNAP-IV questionnaire was chosen for its high sensitivity, simplicity and adequate screening abilities.[45] The SNAP-IV questionnaire, with 26 items, corresponds to the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, American Psychiatric Associations (DSM-IV) criterion for ADHD and Oppositional Defiant Disorder. Only the first 18 questions were used for this study, including nine questions about inattention and nine for hyperactivity-impulsivity.[43] The parents rated their child's behavior by answering the questionnaire using a 4-point Likert scale from 0, "not at all" to 3, "very much". To find children with less profound symptoms of ADHD rather than being likely to fulfill criteria for a diagnosis, we chose to lower the cut-off to ≥9p for inattention and ≥9p for hyperactivity-impulsivity, or ≥9p + ≥9p for combined difficulties. We used the same cut-off for boys and girls, aware that girls generally score lower than boys.[46] Thereafter, we performed a sensitivity analysis using the mean cut-offs stated by the instrument for parent rating (1.78 for ADHD-Inattention, 1.44 for ADHD-Hyperactivity-Impulsivity and 1.67 for ADHD-Combined).[47]

ASSQ

The ASSQ, a screening instrument for ASD,[48] contains 27 questions to which the parent has to report a graded reply: 0 "do not agree", 1 "partly agree" and 2 "strongly agree". The cut-off was set to 15p, meaning that children with a score ≥15 had symptoms of ASD.

Pain

Pain was evaluated by a digital pain mannequin, showing the ventral and dorsal part of the body, covering 20 body sites marked with letters. Next, to the mannequin was a table that specified in text which body site the letter belonged to[10] and pain frequency (never / rarely / monthly / weekly / more than once a week / almost daily) were asked for, for each body site separately. Children who reported between weekly and almost daily pain in at least one body region were categorized as having “frequent pain”, while children reporting between never and monthly pain were categorized as not having frequent pain. Multisite pain was defined as reporting pain in at least three different body sites and reporting pain on a weekly basis. More precisely, this could either be children reporting pain from ≥4 regions on a monthly basis, or reporting pain in at least one area on a weekly basis together with pain in two other body regions at least monthly. Headache and abdominal pain were included in the 20 body regions; they were both assessed separately and were considered to be part of frequent and/or multisite pain. Overall pain intensity during the last week was assessed by a numeric rating scale (NRS), ranging from 1 to 10, with 1 representing no pain and 10 the worst imaginable pain. NRS was categorized into no pain-mild pain (1–3p), moderate pain (4–6p), and severe pain (7–10p).

Body Mass Index

BMI was calculated based on height and weight measurements made by the child’s school nurse between 9.7 and 11.8 years of age. Children were dichotomized as having a normal weight or overweight/obesity in accordance with the International Obesity Task Force (IOTF).[49]

Statistical Methods

Descriptive data are reported as numbers and percentages or as mean and standard deviations (SD). Comparisons of means between boys and girls were analyzed with Independent samples *t*-test and frequencies of categorial data compared with the Chi-square test or Fisher’s Exact test, when appropriate. Groups were formed based on the SNAP-IV and differences in pain experience were analyzed with the chi-square test between these groups and the rest of the children in this study. A child could therefore be included in one group, for instance having symptoms of hyperactivity-impulsivity but for the analyses on ADHD combined-type the same child would not fulfill the criteria for inattention and therefore be part of the comparison group for children without symptoms of ADHD combined type. Logistic regression analyses were performed to study associations between the dependent variable (frequent pain) and the independent variables (SNAP-IV screening, BMI and sex). Results were presented as odds ratios (OR) with 95% confidence intervals (CI). The statistical analyses were performed using SPSS statistics for Windows, version 29.0 (IBM Corp, New York, USA) and the significance level was set at $p < 0.05$.

Ethics

The research was carried out in accordance with the ethical guidelines presented in the Declaration of Helsinki.[50] The study was approved by the Regional Ethical Review Board in Lund, Sweden (No. 299/2007) and the Swedish Ethical Review Authority (2018/141). Written informed consent was obtained from the parents. Participation was voluntary and participants could withdraw at any time without giving a reason. This study adhered to the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines.[51]

Results

A total of 863 children out of 1186 eligible replied to the pain questionnaire and formed the base for this study. Of these 863 children, 857 children (421 boys and 436 girls) replied to the pain mannequin, and 853 replied to the question about pain intensity. These children were not completely overlapping. For the 857 children who replied to the pain mannequin, frequent pain was reported by 36.5% (35.4% of the boys and 37.6% of the girls, $p = 0.523$) and 29.8% reported multisite pain (27.6% of the boys and 31.9% of the girls, $p = 0.179$). Headache was reported by 15.5% of girls and 10.8% of boys ($p = 0.043$) and abdominal pain was reported by 14.5% of girls and 9.1% of boys ($p = 0.015$). For these 857 children, parents of 778 children replied to the SNAP-IV screening questionnaire and 777 parents to the ASSQ screening questionnaires, height and weight measurements were available for 731 children. One of the 778 parents, only responded to the hyperactivity-impulsivity domain of SNAP-IV, and two parents replied to either SNAP-IV or ASSQ, meaning that the 777 are not completely overlapping. Using our adjusted cut offs (see method section) on SNAP-IV, 20.0% (n = 155) of children presented with symptoms of ADHD. Separating the domains, 136 children scored ≥9p on the inattention domain, with 77 presenting with no symptoms of hyperactivity-impulsivity (<9p). Likewise, 78 children scored ≥9p on the hyperactivity - impulsivity domain, whereof 19 children with no symptoms of inattention, 59 children had symptoms of ADHD combined type.

Of the 777 replies to the ASSQ, 22 children (2.8%), 13 boys and 9 girls, had symptoms of ASD, of whom 16 were also positive for ADHD combined type, and another child had symptoms of inattention but not hyperactivity-impulsivity.

Frequent Pain and Symptoms of ADHD

Frequent pain was reported by 52.5% of children with symptoms of ADHD combined type as compared to 36.2% (p = 0.012) of children with no symptoms of ADHD combined type, Table 1. There were no sex differences between children reporting frequent pain based on SNAP-IV screening (Table 1).

Of the 78 children with symptoms of hyperactivity-impulsivity 52.6% reported frequent pain compared to 35.7% (p = 0.004) for the rest of the children in this study. For those with symptoms of inattention (n = 136), 46.3% reported frequent pain, but when removing the 59 children with cooccurring symptoms of hyperactivity-impulsivity 41.6% reported frequent pain, with no difference compared to children without symptoms of inattention (Table 1 and Figure 2). Logistic regression modelling showed that hyperactivity was a significant contributor in frequent pain, while inattention was not (Table 2). The difference did not change when adjusted for sex and BMI, Table 2.

For children reporting frequent pain, 25.1% had symptoms of any of the three ADHD subtypes as compared to 16.8% for children with infrequent pain (Frequent pain n = 291, Infrequent pain n = 487, p = 0.005).

In a sensitivity analysis using the widespread mean cut-offs intended to find the top 5% with the most symptoms, 3.8% of the population were likely to have ADHD combined type (n=30) and 7.6% (n = 59) were positive for any ADHD type using the widespread mean cut offs. For children screening positive for ADHD combined type using the mean cut offs, 50.0% (n = 15) reported frequent pain, as compared to 36.9% (276 of 747) of children screening negative for ADHD combined type. For children with hyperactivity-impulsivity, 50.0% (23 of 46 children) reported frequent pain, as compared to 36.6% of children screening negative for hyperactivity-impulsivity, differences being non-significant but similar to the prevalences found using the lower cut offs in this study. From the perspective of weekly pain, 9.6% (28 of 291 children) as compared to 6.4% (31 of 487 children) were positive for any ADHD subtype using the mean cut offs, non-significant difference (p = 0.097).

For the 22 children with symptoms of ASD, one girl (11.1%) reported frequent pain, compared to seven (53.8%) of the boys, see Table 1. Of these seven boys, six also had symptoms of ADHD combined type.

Multisite Pain and Symptoms of ADHD

Overall, multisite pain was reported by 30.5% of children with no symptoms of ADHD combined type and by 33.9% of children with symptoms of ADHD screening combined type (p = 0.582), Table 1. While boys with symptoms of hyperactivity-impulsivity reported about the same prevalence of multisite pain as the rest of the study population (27.9% vs 28.3%), girls with hyperactivity-impulsivity reported a higher prevalence of multisite pain compared to the remaining population (51.4% vs 31.3%, p = 0.016), Table 1. The difference between boys and girls was statistically significant (p = 0.034), Table 1. Boys with symptoms of inattention tended to report more multisite pain than girls (41.7% vs 34.5%, p = 0.010), Table 1.

For children with symptoms of ASD, one of the nine girls and three of 13 boys reported multisite pain, being so few this group was veritably too small for statistical analyses, Table 1.

Headache, Abdominal Pain and Symptoms of ADHD

Weekly headache was reported by 13.3% of the study population without symptoms of ADHD combined type, while 22.8% (p = 0.046) with symptoms of ADHD combined type reported weekly headache, with similar numbers for boys and girls, Table 3. For children with symptoms of hyperactivity-impulsivity, 23.7% (18 of 76 children) reported weekly headache, a significant difference compared with the rest of the study population. No difference was seen for weekly headache between children with symptoms of inattention compared to the rest of the study population (p = 0.355), Table 3.

Table 1 Data Showing the Number and Percentage of Children Reporting Frequent or Multisite Pain, Stratified by Sex and Neurodevelopmental Screening Outcome

	Child Experiences Pain in at Least One Body Region on a Weekly Basis									Sex p[e]
	Both Sexes			Boys			Girls			
	n	Pain n (%)	p*	n	Pain n (%)	p*	n	Pain n (%)	p*	
Symptoms of ADHD combined type[a]	59	31 (52.5)	**0.012**	33	18 (54.5)	**0.026**	26	13 (50.0)	0.196	0.225
No symptoms of ADHD combined type[a]	719	260 (36.2)		346	121 (35.0)		373	139 (37.3)		
Symptoms of inattentention[b]	136	63 (46.3)	**0.019**	81	39 (48.1)	**0.017**	55	24 (43.6)	0.362	0.605
No symptoms of inattention[b]	641	228 (35.6)		297	100 (33.7)		344	128 (37.2)		
Symptoms of inattention but not hyperactivity[b]	77	32 (41.6)	0.433	48	21 (43.8)	0.283	29	11 (37.9)	0.985	0.221
No symptoms of inattention[b]	700	259 (37.0)		330	118 (35.8)		370	141 (38.1)		
Symptoms of hyperactivity[c]	78	41 (52.6)	**0.004**	43	23 (53.5)	**0.015**	35	18 (51.4)	0.089	0.856
No symptoms of hyperactivity[c]	700	250 (35.7)		336	116 (34.5)		364	134 (36.8)		
Symptoms of hyperactivity, but not inattention[c]	19	10 (52.6)	0.165	10	5 (50.0)	0.376	9	5 (55.6)	0.275	0.886
No symptoms of hyperactivity[c]	759	281 (37.0)		369	134 (36.3)		390	147 (37.7)		
Symptoms of ASD[d]	22	8 (36.4)	0.925	13	7 (53.8)	0.186	9	1 (11.1)	0.092	**0.040**
No symptoms of ASD[d]	755	282 (37.4)		365	131 (35.9)		390	151 (38.7)		
	Child Experiences Pain in Three or More Body Regions, With Pain Experience on a Weekly Basis									**Sex p[e]**
	Both sexes			**Boys**			**Girls**			
	n	**Pain n (%)**	**p***	**n**	**Pain n (%)**	**p***	**n**	**Pain n (%)**	**p***	
Symptoms of ADHD combined type[a]	59	20 (33.9)	0.582	33	8 (24.2)	0.594	26	12 (46.2)	0.143	0.654
No symptoms of ADHD combined type[a]	719	219 (30.5)		346	99 (28.6)		373	120 (32.2)		
Symptoms of inattentention[b]	136	50 (36.8)	0.095	81	28 (34.6)	0.158	55	22 (40.0)	0.240	0.519
No symptoms of inattention[b]	641	189 (29.5)		297	79 (26.6)		344	110 (32.0)		
Symptoms of inattention but not hyperactivity[b]	77	30 (39.0)	0.100	48	20 (41.7)	**0.028**	29	10 (34.5)	0.868	**0.010**
No symptoms of inattention[b]	700	209 (29.9)		330	87 (26.4)		370	122 (33.0)		
Symptoms of hyperactivity[c]	78	30 (38.5)	0.118	43	12 (27.9)	0.960	35	18 (51.4)	**0.016**	**0.034**
No symptoms of hyperactivity[c]	700	209 (29.9)		336	95 (28.3)		364	114 (31.3)		
Symptoms of hyperactivity, but not inattention[c]	19	10 (52.6)	**0.036**	10	4 (40.0)	0.402	9	6 (66.7)	0.065	0.370
No symptoms of hyperactivity[c]	759	229 (30.2)		369	103 (27.9)		390	126 (32.3)		
Symptoms of ASD[d]	22	4 (18.2)	0.199	13	3 (23.1)	0.685	9	1 (11.1)	0.156	0.474
No symptoms of ASD[d]	755	234 (31.0)		365	103 (28.3)		390	131 (33.6)		

Notes: [a] Symptoms of ADHD combined type = Scoring ≥ 9p on the inattention domain + ≥ 9p on the hyperactivity-impulsivity domain on SNAP-IV (Q: 1–18) and no symptoms of ADHD combined type scoring ≤ 8p+ ≤ 8p. [b] Symptoms of inattention = scoring ≥ 9p on the SNAP-IV ADHD-Inattention domain (Q: 1–9) and no symptoms of inattention scoring ≤ 8p. Symptoms of inattention but not hyperactivity = scoring ≥ 9p on the SNAP-IV ADHD-Inattention section (Q: 1–9) but less than 9 on the hyperactivity domain. [c] Symptoms of hyperactivity = scoring ≥ 9p on SNAP-IV ADHD-Hyperactivity-Impulsivity section (Q: 10–18) and no symptoms of hyperactivity scoring ≤ 8p. Symptoms of hyperactivity not inattention meaning scoring ≥ 9p on SNAP-IV ADHD-Hyperactivity-Impulsivity section (Q: 10–18) but less than 9 on the inattention-domain. [d] Symptoms of ASD = scoring ≥15p on ASSQ (45 items), no symptoms of ASD scoring ≤ 14p. *p < 0.05 was regarded statistically significant and marked in bold type. Comparison between children based on neurodevelopmental screening was performed by Chi-Square-test. [e] Comparison between boys and girls was performed by Chi-Square-test or Fisher's Exact test, two-sided when appropriate.

Abbreviations: ADHD, attention deficit hyperactivity disorder; ASD, autism spectrum disorder; SNAP-IV, the Swanson, Nolan and Pelham Rating Scale; ASSQ, autism spectrum screening questionnaire.

Abdominal pain was reported by 19.0% of children with symptoms of ADHD combined type, compared to 11.5% for the rest of the population (p = 0.091). Numbers were similar, independent of hyperactivity or inattention, with only inattention being statistically significant (p = 0.045), Table 3. Girls tended to report more abdominal pain independent of neurodevelopmental screening, but for girls with symptoms of inattention, abdominal pain was more prevalent than for girls without symptoms of inattention (p = 0.014), Table 3.

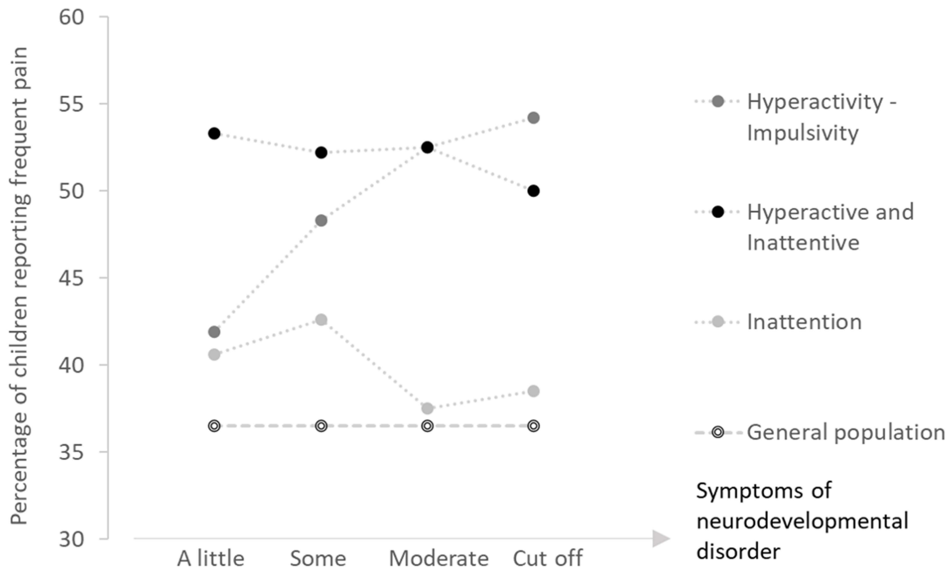

Figure 2 Diagram showing the varying percentages of children reporting frequent pain based on reported symptoms of hyperactivity-impulsivity and inattention on SNAP-IV respectively. For hyperactivity-impulsivity, dark grey dots, "A little" is equivalent to 7p on the hyperactivity-impulsivity domain, "Some" to 8p, "Moderate" to 9p and the Cut-off is the mean of 1.44 on the same domain. For Inattention, light grey dots, "A little", "Some", and "Moderate" were defined as, respectively, 9p, 11p, and 13p, while the cut-off was the recommended mean of 1.78 on the inattention domain. For Hyperactive and Inattentive, black dots, 7p, 8p, 9p on the hyperactivity-impulsivity domain were used together with a cut-off of 9p on the inattention domain, while the Cut-off was set at the recommended 1.67 mean for both domains together. Ring-shaped dots indicate general population.

Mean Score for Pain Intensity and Symptoms of ADHD

For the question about pain intensity there were 853 replies, these were however not completely overlapping with the 857 children who replied to the pain mannequin. For the pain intensity question, 776 had parental replies to the SNAP-IV, of these 137 children had symptoms of inattention, 78 for hyperactivity–impulsivity and 59 for ADHD combined type. The numeric rating scale (NRS) showed a mean score for pain intensity of 2.54 during the last week for those without symptoms of ADHD combined type (n = 717), while children with symptoms of ADHD combined type (n = 59) had a mean score for pain intensity of 3.20 (p = 0.026). For children without symptoms of ADHD combined type 23.7% (n = 170) reported ≥4, equivalent to moderate pain during the last week, while 35.6% (n = 21, p = 0.042) of children with a positive screening for ADHD combined type reported ≥4.

Severe pain, NRS ≥7 was reported by 8.5% (n = 5 of 59, p = 0.078) of children with symptoms of ADHD combined type screening, compared to 3.6% (26 of 717) of children without these symptoms.

Similar numbers were seen for children with symptoms of inattention with or without hyperactivity (n = 137), with a mean of 3.0 vs 2.5 (p = 0.004) for children without these difficulties. For children with symptoms of hyperactivity-impulsivity (n = 78), the NRS was 3.01 vs 2.55 for the rest of the population (p = 0.012). However, for children with

Table 2 Regression Model of Frequent Pain in Relation to SNAP-IV Screening Outcome and for Sex and BMI (n = 731)

	B	S.E	OR	p	95% CI for OR
(Frequent pain)	−0.766	0.359	0.465	0.033	
Hyperactivity-Impulsivity*	0.845	0.297	2.328	**0.004**	1.300 to 4.167
Inattention*	0.160	0.236	1.174	0.497	0.739 to 1.865
Sex	0.062	0.155	1.064	0.692	0.785 to 1.442
Child BMI	0.049	0.230	1.051	0.830	0.670 to 1.648

Notes: *Hyperactivity-impulsivity meaning that children scored ≥ 9p on SNAP-IV ADHD-Hyperactivity-Impulsivity section (Q: 10–18), Inattention meaning that children scored ≥ 9p on the SNAP-IV ADHD-Inattention domain (Q: 1–9), bold type indicates significance level <0.05.
Abbreviations: BMI, Body mass index; B, Unstandardized coefficient; S. E, Standard Error; OR, Odds ratio; p, p value; CI, Confidence Interval.

Table 3 Children Experiencing Headache or Abdominal Pain Every Week, Based on Neurodevelopmental Screening Outcome

	Child Reports Headache on a Weekly Basis								
	Both sexes			Boys			Girls		
	n	Pain n (%)	p*	n	Pain n (%)	p*	n	Pain n (%)	p*
Symptoms of ADHD combined type[a]	57	13 (22.8)	**0.046**	33	7 (21.1)	0.081	24	6 (25.0)	0.256
No symptoms of ADHD combined type[a]	715	95 (13.3)		344	36 (10.5)		371	59 (15.9)	
Symptoms of inattention[b]	133	22 (16.5)	0.355	80	14 (17.5)	0.055	53	8 (15.1)	0.774
No symptoms of inattention[b]	638	86 (13.5)		296	29 (9.8)		342	57 (16.7)	
Symptoms of hyperactivity[c]	76	18 (23.7)	**0.010**	43	10 (23.3)	**0.009**	33	8 (24.2)	0.208
No symptoms of hyperactivity[c]	696	90 (12.9)		334	33 (9.9)		362	57 (15.7)	
Symptoms of ASD[d]	21	3 (14.3)	0.970	13	3 (23.1)	0.177	8	0 (0)	0.363
No symptoms of ASD[d]	750	105 (14.0)		363	40 (11.0)		387	65 (16.8)	
	Child Reports Abdominal Pain on a Weekly Basis								
	Both sexes			**Boys**			**Girls**		
	n	**Pain n (%)**	**p***	**n**	**Pain n (%)**	**p***	**n**	**Pain n (%)**	**p***
Symptoms of ADHD combined type[a]	58	11 (19.0)	0.091	32	5 (15.6)	0.201	26	6 (23.1)	0.245
No symptoms of ADHD combined type[a]	716	82 (11.5)		345	30 (8.7)		371	52 (14.0)	
Symptoms of Inattention[b]	134	23 (17.2)	**0.045**	79	9 (11.4)	0.473	55	14 (25.5)	**0.014**
No symptoms of inattention[b]	639	70 (11.0)		297	26 (8.8)		342	44 (12.9)	
Symptoms of hyperactivity[c]	77	13 (16.9)	0.166	42	6 (14.3)	0.256	35	7 (20.0)	0.344
No symptoms of hyperactivity[c]	697	80 (11.5)		335	29 (8.7)		362	51 (14.1)	
Symptoms of ASD[d]	21	3 (14.3)	0.747	12	2 (16.7)	0.309	9	1 (11.1)	1.0
No symptoms of ASD[d]	752	90 (12.0)		664	33 (9.1)		388	57 (14.7)	

Notes: [a] Symptoms of ADHD combined type = Scoring ≥ 9 on the inattention domain + ≥ 9p on the hyperactivity-impulsivity domain on tSNAP-IV (Q: 1–18) and no symptoms of ADHD combined type scoring ≤ 8 + ≤ 8p. [b] Symptoms of inattention = scoring ≥ 9p on the SNAP-IV ADHD-Inattention domain (Q: 1–9) and no symptoms of inattention scoring ≤ 8p. [c] Symptoms of hyperactivity = scoring ≥ 9p on SNAP-IV ADHD-Hyperactivity-Impulsivity section (Q: 10–18) and no symptoms of hyperactivity scoring ≤ 8p. [d] Symptoms of ASD = scoring ≥15p on ASSQ (45 items), No symptoms of ASD scoring ≤ 14p. *p < 0.05 was regarded statistically significant and marked in bold type. Comparison between children based on neurodevelopmental screening was performed by Chi-Square-test or Fisher's Exact test, two-sided when appropriate.

Abbreviations: ADHD, attention deficit hyperactivity disorder; ASD, autism spectrum disorder; ASSQ, autism spectrum screening questionnaire; SNAP-IV, the Swanson, Nolan and Pelham Rating Scale.

symptoms of inattention without hyperactivity - impulsivity (n = 78), the NRS was 2.90 vs 2.56 (p = 0.105) for the rest of the population.

For children with symptoms of ADHD combined type two of 59 children had NRS=10 as compared to no child without these symptoms (n= 717, p = 0.006).

Discussion

The main finding of this study was that one in two children with symptoms of ADHD combined type reported pain on a weekly basis, which may be compared to one in three among children without symptoms of ADHD combined type. Our study shows that increased pain experience is mainly associated with symptoms of hyperactivity-impulsivity. For children with symptoms of inattention but not hyperactivity-impulsivity, weekly pain prevalence was not higher, compared to the rest of the study population. The reason for this is unknown, but having problems with hyperactivity and impulsivity predisposes a child to more injuries,[2,19] and hyperactivity may also be secondary to pain or stiffness[20,21] and a lowered attention span might increase the risk for injuries even more. Injuries in turn may lead to secondary pain. The etiology of pain in ADHD is unknown, but the findings that hyperactivity and impulsivity correlated to more frequent pain is in line with the findings of Battinson et al,[2] Kerekes et al[18] and Kasahara et al.[21] Furthermore, a lowered attention span may impact the ability to filter out pain signals increasing pain perception.[2,24] But not only, did children with symptoms of ADHD of combined type report more frequent pain they also rated a higher mean score for pain intensity compared to the rest of the population, and a higher percentage of children reported moderate pain and extreme pain. In other words, children with high symptom scorings on SNAP-IV report more frequent pain and higher intensity of pain. This is in line with an adult study on ADHD symptoms and pain that showed that ADHD symptoms were associated with extreme pain,[52] and with a study by Fuller-Thomsen et al,[53] who found a markedly higher prevalence of activity-restricting pain among adult women with self-reported ADHD. The reason for this association between pain and ADHD is likely multifactorial and beside theories of increased injuries, altered perception, increased muscle tone, decreased dopaminergic function and an underlying neuroinflammation might be part of this.[20–23,54,55]

In this study, we chose to lower the cut offs to find more children with symptoms of ADHD and not only the five to seven percentages with the most severe symptoms likely to fulfil criteria for an ADHD diagnosis.[56] Still, the same high pain prevalence was seen for children when we used these less strict cut offs as when we used the recommended mean cut offs for ADHD screening, this indicating, that in our study, it was not the severity of symptoms but having symptoms that increased the likelihood for frequent pain. This finding, that not only pronounced ADHD symptoms but also to have just some symptoms of ADHD, increased the likelihood for pain, strengthens the theory of a common etiology.

Discussing these lower cut offs used, our study showed that for children with frequent pain it was significantly more common to have symptoms of ADHD compared to children with infrequent pain, but it was not significantly more common to have a positive screening for any of the ADHD subtypes using the mean cut offs. This may be compared to the study by Lipsker et al[4] who showed that children with a positive screening for ADHD or ASD were overrepresented among children with chronic pain at a tertiary pain clinic in Sweden. These children with a positive ADHD or ASD screening did however not report higher intensity, increased frequency or prolonged duration of pain, compared to children with a negative screening. However, when comparing our results the setting is important. In the study by Lipsker et al,[4] they studied children seeking medical care for chronic pain while our study was a non-clinical study population and children were expected to have less frequent and lower intensity pain, compared to children in clinical studies. Contrary to Lipsker et al[4] and Kindgren et al[57] that proposes screening for ADHD for children with Ehlers Danlos syndrome, we do not propose screening for all children seeking medical advice for pain, but it is important that clinicians keep neurodevelopmental disorders in mind, both when it comes to possible referral and also when treatment for pain does not meet expectations. Early referral for children with pain could help to identify children who are in need of support for their ADHD, which is important, given that adults with symptoms of ADHD report worse sleep, early adversities, and mental and physical health problems.[53]

When it comes to potential sex differences, there were no significant differences between boys and girls in the experience of frequent pain for this age group. Likewise, about the same magnitude of boys and girls reported multisite pain in this study population, albeit girls reported more headache and abdominal pain. This is worth pointing out, given that other studies have shown that multisite pain is more common among girls and women, compared to boys and men in the general population.[13–15] One reason for this conflicting finding might be that the potential difference between the sexes is smaller for prepubertal children as shown in the study by Malmborg et al.[17] Still, some tendencies for increased pain were seen for girls with symptoms of hyperactivity-impulsivity when it came to the experience of multisite pain, headache and abdominal pain which were reported by quarter of girls and about a fifth of boys with symptoms of ADHD combined type as compared to one in eight to ten of the rest of the population. So, even though our numbers indicate that somewhat more girls compared to boys report pain in some respects, girls and boys with symptoms of ADHD are likely to report more frequent pain, headache and abdominal pain than the general population.

A limitation of this study, was the lack of power for all statistics on ASD, due to small groups we could not show any differences in pain experience between children with or without symptoms of ASD. Therefore, all data presented in the tables for ASD should be interpreted with great caution. Still, it is interesting that girls with symptoms of ASD reported pain to a lower or the same extent than the rest of the study population. It has been shown that children with high-functioning autism can self-report pain.[6] Still, we cannot exclude that the verbal difficulties often associated with ASD, or that a different concept of pain, might have impacted our results.[5] Additionally, both ASD and ADHD are coexisting neurodevelopmental disorders, shown in our study population by the 22 children with symptoms of ASD of whom 16 also had symptoms of ADHD combined type and another one with symptoms of inattention, which makes interpretation challenging.

Furthermore, the longitudinal design, and relatively rare condition of having symptoms of pain and ADHD, made our study population somewhat small for firm conclusions in some respects even for children with symptoms of ADHD. For instance, fewer girls than boys are diagnosed with ADHD,[58] and using SNAP-IV girls generally score lower compared to boys.[46] Still, using our lower cut offs the ratio between boys and girls where somewhat more even compared to what was expected using the mean cut offs. Another potential limitation is that according to ICD-11 for adults, chronic primary pain is pain lasting for more than three months. One may consider it a limitation that we did not restrict the period to three months. However, given that children might experience time and pain differently than adults[7,59] and that chronic widespread pain is considered to develop after years with frequent or multisite pain,[60] we wanted to detect pain at earlier stages. Therefore, all children in this study were younger than the mean age for an ADHD diagnosis in Sweden, which is 13.5 years for males and 16.0 years for females.[16] This was one of the reasons why we did not address diagnoses at all in this study, another being the intention of studying symptoms rather than diagnoses. The aim to study symptoms rather than diagnoses was also why we chose to lower the cut-offs, ≥9p for inattention and ≥9p for hyperactivity-impulsivity. With this lower cut of, 20.5% of children had symptoms for any of the ADHD types or 7.6% for ADHD combined type. Some but not all of these children would likely fulfill criteria for an ADHD diagnosis. According to Willcutt et al,[56] worldwide, about 5.9–7.1% of children are expected to have ADHD, and a previous publication on our study population showed that 7.6% of all children included at birth had an ADHD diagnosis at 12 years of age[16] This is the same percentage of children that were positive for any of the ADHD subtypes in our sensitivity analysis using the widespread mean cut offs.[47] However, these cut offs have been questioned since the estimates were not based on a group of children that may be considered representative to Swedish norms. No validation on these cut offs have been made in a Swedish setting and the use of these cut offs is thereby uncertain and validation is recommended.

A strength of this study, was that it covered a quarter of the population in the region, which makes our numbers a good estimate of the overall prevalence of pain and neurodevelopmental traits. The generalizability of this cohort has been evaluated before,[61] and even so participants had somewhat older and more highly educated parents, child characteristics did not differ between participants and drop outs. Another strength of this study was that we could adjust the regression model for BMI, since BMI has been proposed to be associated to both pain[62] and ADHD.[63] This adjustment did not change our results, implying a different mechanism than overweight or obesity for the association between pain and ADHD.

The aim of this study was to present prevalence numbers for children with both frequent pain and symptoms of ADHD and to identify possible sex differences between groups. From a school perspective, pain may lower attention and overall function, which may exacerbate difficulties experienced by children with ADHD.[1] Further studies are needed to increase the understanding of the mechanisms related to this association and it is important to combine this research with clinical tools to help affected children. Few studies have shown beneficial effects on pain with stimulant treatment for adults[24,64] and for girls with ADHD.[1] What if stimulant treatment could lower pain with beneficial effects on grades, quality of life and a lower lifetime-risk for substance abuse? With the high prevalence of pain among children with symptoms of ADHD found in this study, we propose the need for long-term studies on pain, ADHD and medical treatment. In addition, other treatments such as an educational program (eg pain-school) could be offered at the pediatric clinic for all children with symptoms of ADHD. This could help children learn to understand what pain is, how to interpret various pain signals and what the child can do to reduce the feeling of pain. If shown effective and this was offered before pain emerged or worsened, or allodynia or chronicity have appeared, this could have major effects on these children's future health. Another practical suggestion from the results of this study could be screening opportunities for ADHD at clinics treating childhood pain and early referral to other clinics when appropriate to hinder future negative complications and substance abuse.

Conclusion

Children with symptoms of ADHD report more frequent pain and higher pain intensity, compared to children without these symptoms already at the age of ten to eleven. This increased pain experience was seen, not just for children with a positive screening for ADHD, but already at lower level of ADHD symptoms, pronounced symptoms did not seem to increase this likelihood for more pain any further. For children with symptoms of hyperactivity-impulsivity, pain was reported more often than for children with only inattention, but inattention strengthened the association. Girls with symptoms of hyperactivity reported more multisite pain, compared to boys with symptoms of hyperactivity. We lacked the power to evaluate in detail the influence of ASD. Practical implications of this study include screening opportunities in the clinic with early referral and educational opportunities when there is a probable coexistence of neurodevelopmental disorders and pain.

Data Sharing Statement

The datasets generated and analysed during this study are not publicly available for ethical reasons and in line with Swedish legislation. Requests to make data available to reproduce the findings in the study should be made to the board of the Halland Health and Growth Study, represented by Maria V Andersson (maria.v.andersson@regionhalland.se) and Josefine Roswall (josefine.roswall@regionhalland.se).

Ethics Approval and Consent to Participate

The research was carried out in accordance with the ethical guidelines presented in the Declaration of Helsinki.[50] The Halland Health and Growth Study was approved by the Regional Ethical Review Board in Lund, Sweden (No. 299/2007) and the Swedish Ethical Review Authority (2018/141). Written informed consent was obtained from the parents. Participation was voluntary and participants could withdraw at any time without giving a reason. This study adhered to the STROBE guidelines.[51]

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Disclosure

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