

# Prevalence of autism traits and attention-deficit hyperactivity disorder symptoms in a clinical sample of children and adolescents with chronic pain

Camilla Wiwe Lipsker<sup>1,2</sup>

Sven Bölte<sup>3,4</sup>

Tatja Hirvikoski<sup>3-5</sup>

Mats Lekander<sup>2,6</sup>

Linda Holmström<sup>1,7</sup>

Rikard K Wicksell<sup>1,2</sup>

<sup>1</sup>Functional Area Medical Psychology/ Functional Unit Behavior Medicine, Karolinska University Hospital, Stockholm, Sweden; <sup>2</sup>Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden; <sup>3</sup>Center of Neurodevelopmental Disorders (KIND), Division of Neuropsychiatry, Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden; <sup>4</sup>Child and Adolescent Psychiatry, Center for Psychiatry Research, Stockholm County Council, Stockholm, Sweden; <sup>5</sup>Habilitation and Health, Stockholm County Council, Stockholm, Sweden; <sup>6</sup>Stress Research Institute, Stockholm University, Stockholm, Sweden; <sup>7</sup>Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden

**Purpose:** Recent research has suggested that autism spectrum disorder (ASD) and attention-deficit hyperactivity disorder (ADHD) may be comorbid to pediatric chronic pain, but the empirical support is yet scarce. Therefore, the current study aimed to investigate the occurrence of traits and symptoms consistent with clinically significant ASD and ADHD in a group of children and adolescents with chronic debilitating pain and examine potential differences in pain and demographic variables between children with and without clinically significant traits and symptoms of ASD and ADHD.

**Patients and methods:** This cross-sectional study included 146 parent-child dyads (102 girls, 111 mothers, children 8–17 years) consecutively referred to a tertiary pain clinic. Parents completed the Social Responsiveness Scale to assess autistic traits, and Conners-3 to measure symptoms of ADHD in their children. Children completed the Lübeck Pain Questionnaire to evaluate experienced pain.

**Results:** Among children, 20 (13.7%) received scores consistent with clinically significant ASD and 29 (19.9%) received scores consistent with clinically significant ADHD, with a combined prevalence of clinically significant ASD/ADHD traits and symptoms of 26% of the total sample. Only 4.8% of children were previously diagnosed with either disorder. Among children with clinically significant ASD traits, girls were more prevalent, parents reported lower health, and the pain was more likely triggered by being in school. Among children with clinically significant ADHD symptoms, there were no gender differences and pain was more likely triggered by the family situation and new situations. No differences regarding pain intensity, duration, or frequency were found between children with and without clinically significant ASD traits or ADHD symptoms.

**Conclusion:** Children with debilitating chronic pain, particularly girls, may present with an elevated risk of having a comorbid, possibly high-functioning, neurodevelopmental disorder. Results suggest that clinical assessment of pediatric chronic pain should include screening for neurodevelopmental disorders.

**Keywords:** attention-deficit hyperactivity disorder, autism spectrum disorder, executive function deficits, comorbidity, pediatric chronic pain, sensory over-responsivity

## Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder defined by alterations in social communication and interactions, and a range of restricted, repetitive behaviors and interests causing impairment.<sup>1</sup> Several studies have also reported an altered sensory perception in ASD,<sup>2,3</sup> and sensory abnormalities have recently been included in the diagnostic criteria for the disorder.<sup>4</sup> Of children in the general

Correspondence: Camilla Wiwe Lipsker  
Department of Clinical Neuroscience,  
Karolinska Institutet, Stockholm 171 77,  
Sweden  
Tel +46 76 225 6510  
Fax +46 85 248 3049  
Email camilla.wiwe.lipsker@ki.se

population, ASD has an estimated worldwide combined prevalence of 1.47%,<sup>5-8</sup> with an overall male:female ratio of 2.3:1.<sup>9</sup> Attention-deficit hyperactivity disorder (ADHD) is another neurodevelopmental disorder, characterized by overarching patterns of age-inappropriate inattention, hyperactivity, and impulsivity causing impairment.<sup>4</sup> ADHD has a worldwide combined prevalence of 5.29% in childhood<sup>10</sup> with an approximate overall male:female ratio of 2:1.<sup>11</sup> Research shows that ADHD and ASD frequently overlap,<sup>12</sup> and, despite differences in clinical manifestations, may in part depend on a shared neural dysfunction.<sup>13</sup> Both children with ADHD and children with ASD, eg, experience other challenges such as irregular sleep-wake rhythm, reduced motor coordination and balance,<sup>14-17</sup> and deficits in executive function, such as impairments in cognitive flexibility and planning.<sup>18</sup> Similar to children with ASD, children with ADHD may also display sensory over-responsivity, which has furthermore been associated with anxiety in both groups.<sup>19,20</sup> In children with ASD, sensory over-responsivity has also been linked to greater deficits in social and adaptive behavior.<sup>21</sup> In one study, when exposed to an aversive stimulus, children with ASD were not able to sustain the processing of social cues as the sensory stimulation disrupted the neural networks supporting this function.<sup>21,22</sup> In children with ADHD, sensory over-responsivity and impairments in the processing of stimuli, such as pain, have also been linked to maladaptive behavior.<sup>23</sup>

Medical comorbidities, particularly of immunological, neurological, and gastroenterological character, appear to be common in children with ADHD or ASD.<sup>24,25</sup> Research has also shown that children with chronic medical conditions inversely could present with an increased, but often unrecognized, risk of having a neurodevelopmental disorder,<sup>24,26,27</sup> and has recommended investigating the prevalence of ADHD and ASD, particularly when the etiology of the medical condition is unclear.

Chronic pain in children and adolescents, defined as pain lasting longer than 3 months,<sup>28</sup> has an estimated overall worldwide prevalence of 20%–35%,<sup>29-31</sup> and is more common in girls as shown in both community and clinical samples.<sup>29,30,32,33</sup> In many individuals, the etiology of pain remains unexplained,<sup>34</sup> and the assessment and treatment of children with persistent pain may therefore often be complex and multifaceted,<sup>35</sup> and should preferably also include parents and the child's social environment.<sup>36</sup> Although evidence-based multidisciplinary interventions exist, effect sizes are modest and the number of treatment responders is still unsatisfactory, especially at long-term follow up.<sup>37,38</sup> Understanding individual psychological attributes may be critical

to treatment outcome in pediatric chronic pain.<sup>39</sup> Recent research has shown that youths with chronic pain may show deficits in aspects of executive function and that some of these deficits, eg, difficulty with unexpected change, may, in fact, predate the onset of pain itself.<sup>40</sup> Moreover, psychiatric disorders, in particular, anxiety and depression, are common in pediatric chronic pain,<sup>41,42</sup> and have been associated with elevated levels of functional impairments.<sup>36,43-45</sup> A few clinical reports,<sup>46-49</sup> a number of studies on abdominal pain,<sup>20,50</sup> a study on migraine,<sup>51</sup> and a recent study on neuropsychological function in chronic pain<sup>40</sup> have suggested that ASD and ADHD may be comorbid to pediatric chronic pain and that such comorbid neurodevelopmental conditions may go undetected. Importantly, however, the prevalence of these disorders, including clinically significant traits, in pediatric patients with chronic pain is still unclear.<sup>40</sup>

Taken together, existing research suggests that children with chronic pain conditions may be at risk of having an undetected neurodevelopmental disorder, and due to such comorbidity display more functional impairments<sup>38,48</sup> and respond less well to treatment. Thus, there is an urgent need to scientifically evaluate the co-occurrence of ASD, ADHD, and pediatric chronic pain, and potential relations to pain and demographic factors.

Within a clinical sample of children and adolescents seeking tertiary care for chronic pain, we therefore aimed to examine: 1) the occurrence of clinically significant traits and symptoms of ASD and ADHD; 2) the proportion of children with a previous diagnosis of ASD or ADHD; and 3) possible differences in demographic- and pain-related variables between children with and without clinically significant traits and symptoms of ASD and ADHD.

## Materials and methods

### Participants and procedure

The study utilized a cross-sectional design and included 146 Swedish speaking children and adolescents (referred to as “children” unless specification is required) aged 8–17 years and their parents (one parent per child), consecutively referred to a tertiary pain clinic due to chronic pain. Data were collected from May 2013 to September 2016. At the child's first visit to the clinic, parent–child dyads were presented a study package including age-appropriate information about the study in writing, consent forms for both parent and child, and two sets of self-report questionnaires (parent and child). Participants were excluded if they were non-Swedish speakers and implicitly if the child was unable to answer the questionnaire by him- or herself. Data were then returned

in person from consenting participants prior to the clinical assessment. The regional ethical review board in Stockholm approved of the study (Dnr: 2013/231-31-4).

## Measures

### Demographic variables

Child demographic variables included gender, age (years, months), and chronic somatic disease other than pain. Parental demographic variables included gender, age (years), parental self-reported level of education (basic education/high school or university studies), parental self-reported health from 1 (poor) to 5 (excellent), and parental self-reported chronic pain (yes/no).

### Autistic traits

The Swedish version of the parent report form of the Social Responsiveness Scale (SRS) was used. The SRS measures autistic traits in children aged 4–18 years and comprises 65 items rated on a 4-point Likert scale ranging from 0 (never true) to 3 (almost always true), and its psychometric properties are well established.<sup>52–55</sup> General population norms are available from German, British, Dutch, and Finnish samples in Europe,<sup>54–57</sup> and for USA by the authors of the SRS.<sup>52</sup> As the cutoff scores in the original SRS manual have been higher than those in German, Dutch, Finnish and Japanese samples, the original norms were used to minimize false positives.<sup>54,56–58</sup> Upon completion of all items, raw total scores and total T-scores were calculated. Clinically significant ASD symptoms have been associated with T-scores  $\geq 60$ , and T-scores  $\geq 75$  are associated with an ASD diagnosis in the severe range.<sup>59</sup> Established thresholds reliably distinguish children with ASD from both non-affected children (sensitivity 0.75 and specificity 0.96) and those with other child psychiatric conditions (sensitivity 0.70 and specificity 0.90).<sup>52</sup> Completion time for the SRS was 15–20 minutes. Cronbach's alpha in the current sample was  $\alpha=0.94$ .

### Symptoms of ADHD

The Conners Rating Scales are widely used for assessing traits and problem behaviors associated with ADHD for diagnostic and research purposes.<sup>60,61</sup> The Conners-3 (C3) constitutes the latest edition of the Conners with a refined assessment of ADHD and updated norms.<sup>62</sup> For the current study, the Swedish version of the C3 parent report form was used and results were compared with Swedish norms.<sup>62,63</sup> The form comprises 110 items (of which 108 are numeric) that utilize a 4-point Likert-type scale (from 0= not true at all to 3= very much true) for each item. The C3 parent question-

naire also generates an ADHD Index that has been shown to accurately differentiate children with ADHD from those without a clinical diagnosis (pooled sensitivities of 0.75 and pooled specificities of 0.75).<sup>62,64</sup> Upon completion of all items, raw total scores and total T-scores for the ADHD Index were calculated. T-scores  $\geq 60$  indicate an elevated score and T-scores  $\geq 65$  are associated with clinically significant ADHD symptoms. Completion time for the C3 was 15–20 minutes. Cronbach's alpha in the current sample was  $\alpha=0.94$ .

### Pain variables

Children completed the Lübeck Pain Questionnaire (LPQ),<sup>65,66</sup> a structured self-report questionnaire that contains predefined single-item scales for the evaluation of pain duration and pain frequency during the preceding 3 months, and predefined multi-item scales for the evaluation of pain site/s, perceived trigger/s of pain, perceived reason/s for first pain onset (see Tables S1 and S2 for details on item content). The co-occurrence of other chronic somatic disease is assessed in the LPQ using an open question where the respondent writes the name of the disease. Single items have been shown to be valid and reliable measures of pain, including frequency, intensity, and duration,<sup>67</sup> and previous studies have shown that children and adolescents can report subjective pain experiences reliably.<sup>68,69</sup> The intensity of pain was assessed with a visual analog scale (VAS) included in the LPQ ranging from “hardly noticeable pain” (0 cm) to “strongest imaginable pain” (10 cm) and six faces ranging from laughter to crying. The LPQ was designed for epidemiological purposes and has been used in several European studies where it has shown satisfactory feasibility, content, and face validity.<sup>65–67,70</sup> The LPQ was translated from German into Swedish using international guidelines<sup>71</sup> and a pilot study was performed to ascertain that the questionnaire was easy to understand and could be completed within 10–15 minutes and required no further instructions.

### Data analysis

Assessments were included when data were available from both parent and child in the dyad. Analyses of missing items were performed for all measures. All continuous variables were tested for assumptions of normality.<sup>72</sup> Descriptive statistics were used to assess and describe ASD and ADHD traits (T-score means, SD, and cases in percent of T-scores above stated cutoffs for clinically significant symptoms), child and parent demographic and pain variables, and the proportion of children already diagnosed with ASD, ADHD, or both. Differences in child and parental pain and demographic variables

between individuals with and without clinically significant symptoms of ASD and/or ADHD (below or above T-score cutoffs) were assessed with independent *t*-tests for continuous data (or Mann–Whitney *U* tests for skewed continuous data). For dichotomous variables, equality of proportions by group status was assessed with  $\chi^2$ -tests and confirmed/disconfirmed with Fisher’s exact tests when the observed proportion of positive cases in the sample was <5. *P*-value was set at <0.05. The effect size for  $\chi^2$ -tests and Mann–Whitney’s *U* tests were transformed to Cohen’s *d* according to the formulas by Fritz et al.<sup>73</sup> Effect sizes were considered small (*d*=0.3), medium (*d*=0.5) and large (*d*=0.8).<sup>74</sup> All analyses were computed using SPSS version 25.<sup>75</sup>

### Power analysis

Power analyses were calculated based on the primary research question, ie, the occurrence of clinically significant traits and symptoms of ASD and ADHD. For  $\beta$ =0.2 (power 80%) and  $\alpha$ =0.05, calculations indicated minimum *n*=61 for a descriptive study of a continuous variable (calculations based on SRS and C3 with SD=10). However, for the subgroup analyses of differences between individuals with and without symptoms of ASD and/or ADHD ( $\chi^2$ -test) calculations indicated a minimum *n*=143 to detect a small effect size (*d*=0.3) with a maximum of 5 degrees of freedom (*df*). Likewise, for independent sample *t*-test and Mann–Whitney’s *U* tests with an unequal allocation of participants into each group (20 minimum in one group), the achieved power was  $\beta$ =0.2 (power 80%) using  $\alpha$ =0.05, effect size (*d*=0.7), and two tails.<sup>76</sup> Overall the current study had sufficient power to detect statistically significant differences.

## Results

### Sample characteristics

A total of 223 potential participants were approached and 190 parent–child dyads agreed to participate and provided consent. Sixteen parent–child dyads were excluded for not completing any measures, and a further 28 dyads were excluded for returning incomplete forms (only child or only

parent ratings). Data from 146 parent–child dyads (102 girls and 111 mothers) were finally included in the analyses. For SRS and C3, less than 0.5% of values were missing on either instrument, and missing data were imputed according to scoring instructions in the respective manual.<sup>52,62</sup> Across all items in the LPQ, 3.9% of data were missing. Missing data from single item/categorical scales were not imputed. All missing data were found to be missing completely at random (Little’s MCAR=ns.).<sup>77</sup>

### Demographic variables

Detailed demographic information is presented in [Table S1](#). Mean age in years was 14.6 (children) and 45.7 (parents). Of children, 34.5% reported comorbid chronic diseases, mainly allergies and asthma (30.1%). Among parents, 32.8% reported own chronic pain condition/s, and a mean parental self-rated health of 3.6, ie, between “Good” and “Very good.” A majority of parents (58.6%) were educated at the university level.

### Pain variables (LPQ)

Data on pain variables are presented in [Table S2](#). In short, 93.8% of children reported a pain duration of more than 6 months and the remaining 6.2% of at least 3 months. Furthermore, 69.2% reported being in pain every day and an additional 24% several times a week, 74% had pain from three or more body sites with a headache being the most common pain type (79.5%), followed by back pain (61%), stomach pain (59.6%), and leg pain (48.6%). A total of 61.7% of children reported not knowing of any diagnosis for their pain condition. Reported pain triggers included physical exercise (35.5%), being at school (22%), and worry (22%), but 41.1% were not able to identify any specific triggers. Illness (22.9%), injury (16%), and physical exercise (13.9%) were the most frequently perceived reasons for initial pain onset, and 35.4% reported not knowing of any reason.

### Autistic traits (SRS)

Results are presented in [Table 1](#). SRS T-scores were calculated for all 146 children in the sample. In total, 20

**Table 1** Summary of SRS T-scores and cases within significant clinical range by gender and in total

| Variable                                 | Girls (n=102)  | Boys (n=44) | Total sample (n=146) |
|--|----------------|-------------|----------------------|
| T-score mean (SD)                        | 49.13 (11.375) | 45.52 (7.2) | 48.04 (10.404)       |
| Skewness                                 | 1.535          | 0.861       | 1.627                |
| Kurtosis                                 | 3.127          | 0.552       | 3.872                |
| Cases above T-score cutoff $\geq 60$     | 18 (17.6%)     | 2 (4.5%)    | 20 (13.7%)           |
| Cases with indicated prior ASD diagnosis | 3 (2.9%)       | 0 (0%)      | 3 (2%)               |

**Abbreviations:** ASD, autism spectrum disorder; SRS, Social Responsiveness Scale.

Journal of Pain Research downloaded from <https://www.dovepress.com/> by 165.215.209.15 on 11-Jun-2019  
For personal use only.

children (13.7% of the total sample) including 18 girls (17.6% of girls) and two boys (4.5% of boys) received scores within the range consistent with clinically significant ASD (T-score  $\geq 60$ ). Three girls (2% of the total sample) had a prior diagnosis of ASD, including one that was also diagnosed with ADHD, and all these children had T-scores above the cutoff (100; 75; 73). Although the mean value for girls (49.13) was slightly below the norm average mean of 50, the sample of autistic traits for girls was not normally distributed, with a larger number of cases at both the lower and the higher end as compared to the normal distribution. For boys, the sample mean value (45.52) was below the norm average mean.

### Symptoms of ADHD (C3)

Results are presented in Table 2. T-scores for the ADHD Index in C3 were calculated for all 146 children in the sample. In total, 29 children (19.9% of the total sample) including 20 girls (19.6% of girls) and nine boys (20.5% of boys) received scores within the range consistent with clinically significant ADHD (T-score  $\geq 65$ ). Five children (three girls and two boys; 3.4% of the total sample) had a prior diagnosis of ADHD, including the girl with a diagnosis of ASD (see above), and all these children had T-scores above the cutoff (90; 89; 89; 88; 73). The current sample mean value was higher for both girls (55.80) and boys (54.55) than the norm average mean of 50.

### ASD traits and ADHD symptoms combined

In total, 38 children (26% of the total sample) scored within the significant clinical range of either ASD or ADHD, including 11 children (8% of the total sample) that scored above the cutoff for both disorders. A total of seven children (4.8% of the total sample) had a prior diagnosis of ASD or ADHD, including one child (0.7% of the total sample) with a prior diagnosis of both disorders.

## Comparing children below and above cutoff for clinically significant autistic traits

### Demographic variables

Detailed results are presented in Table S3. A  $\chi^2$ -test examining child gender showed that children in the above cutoff group for clinically significant autistic traits were more likely to be girls,  $\chi^2(1, n=146)=4.463, P<0.035, d=0.36$ . Child age, comorbid chronic illness, parental gender, parental age, parental education, and parental chronic pain did not differ between the below and the above cutoff groups for clinically significant autistic traits. A Mann–Whitney's *U* test on parental health showed that the health among parents of children with scores below the clinical cutoff for autistic traits (Mdn =4) was significantly better than the health among parents of children with scores above cutoff (Mdn =3),  $U=787.500, P=0.020, d=0.46$ .

### Pain variables

Results are presented in Table S4. In short, pain intensity, pain duration, pain frequency, and pain sites did not differ between children with and without clinically significant autistic traits.  $\chi^2$ -tests performed on perceived pain triggers showed that among children with clinically significant autistic traits, the pain was more likely to be reported as triggered by being in school,  $\chi^2(1, n=141)=7.197, P<0.007, d=0.46$ . Finally, a  $\chi^2$ -test examining differences in the perceived reasons for initial pain onset showed that children with clinically significant autistic traits were more likely to not know of any reason for pain onset,  $\chi^2(1, n=144)=8.887, P<0.003, d=0.52$ .

## Comparing children below and above cutoff for clinically significant ADHD symptoms

### Demographic variables

Results are presented in Table S5. Child age, child gender, comorbid chronic illness, parental gender, parental age,

**Table 2** Summary of C3 ADHD Index T-scores and cases within significant clinical range by gender and in total

| Variable                                  | Girls (n=102)  | Boys (n=44)    | Total sample (146) |
|---|----------------|----------------|--------------------|
| ADHD Index T-score, mean (SD)             | 55.80 (12.981) | 54.55 (12.539) | 55.42 (12.819)     |
| Skewness                                  | 1.595          | 1.430          | 1.536              |
| Kurtosis                                  | 1.284          | 0.900          | 1.141              |
| Cases above T-score cutoff $\geq 65$      | 20 (19.6%)     | 9 (20.5%)      | 29 (19.9%)         |
| Cases with indicated prior ADHD diagnosis | 3 (2.9%)       | 2 (4.5%)       | 5 (3.4%)           |

**Abbreviations:** C3, The Conners-3; ADHD, attention-deficit hyperactivity disorder.

parental health, and parental chronic pain did not differ between children with and without clinically significant traits of ADHD. However, a  $\chi^2$ -test examining the relationship between parental education and cutoff group status showed that parents of children with clinically significant traits of ADHD were less likely to be educated at the university level,  $\chi^2 (1, n=133)=4.479, P<0.034, d=0.37$ .

### Pain variables

Results are presented in [Table S6](#). Pain intensity, pain duration, pain frequency, pain sites, and perceived reasons for pain debut did not differ between children with and without clinically significant traits of ADHD.  $\chi^2$ -tests performed on all included pain trigger variables showed that the pain of children with clinically significant traits of ADHD was more likely to be triggered by “New situations,”  $\chi^2 (1, n=141)=7.466, P<0.006, d=0.47$  and by the “Family situation,”  $\chi^2 (1, n=141)=6.955, P<0.008, d=0.46$ .

## Discussion

The aim of the present study was to investigate the occurrence of diagnoses as well as clinically significant traits and symptoms of ASD and ADHD in children with chronic pain referred to a tertiary pain clinic, and to evaluate differences in demographic- and pain-related variables between children with and without clinically significant traits and symptoms of ASD and ADHD. It was found that 20 children (13.7%) scored within the significant clinical range of ASD and 29 children (19.9%) scored within the significant clinical range of ADHD, with a combined 26% of all children displaying clinically significant traits and symptoms of either or both conditions. As comparison, a large, population-based longitudinal case-control study using the parental SRS found 6.5% of control participants (mixed gender) to be within the clinical ASD range,<sup>78</sup> while a recent, although comparatively small, study on youth with chronic pain in intensive interdisciplinary pain treatment found ASD in 8% and ADHD in 18% of participants.<sup>40</sup> Furthermore, the scores for the C3 in the current sample were clearly elevated compared to the norm average mean.

Although tentative due to the use of screening instruments rather than a complete diagnostic assessment, the results from the current study possibly illustrate an elevated prevalence of ASD and ADHD in the present sample compared to the general population,<sup>5,6,9</sup> suggesting that children with chronic pain may be at risk for having a comorbid neurodevelopmental disorder. Notably, only 4.8% of the children in the sample were already diagnosed with ASD or ADHD, supporting the

notion that neurodevelopmental disorders may go unrecognized in many children with chronic pain.<sup>24</sup>

Interestingly, no significant differences regarding pain intensity, duration, frequency, or pain sites were found between children with and without clinically significant ASD traits or ADHD symptoms. It is possible that the current study did not include children with more severe neurodevelopmental deficits for whom other medical problems or functional limitations may have been prioritized over presenting to a tertiary pain clinic. Therefore, the group of children with clinically significant ASD traits or ADHD symptoms in the current study could constitute an overall more high-functioning group within the neurodevelopmental spectrum, with a pain profile more similar to other children with chronic pain.

Overall, the present study sample displayed similar demographic and pain-related characteristics to other clinical samples in pediatric chronic pain research, eg, included a majority of girls.<sup>29,32,40</sup> Clinically significant ASD traits were also more prevalent among girls than boys in the current sample, with 17.6% of girls presenting scores in the clinical range (as tentative comparison, the prevalence of ASD among girls in the general population is 0.53% as reported by the Centers for Disease Control and Prevention)<sup>8</sup>, as compared to 4.5% of the boys. This result is also interesting in the light of the ASD male:female ratio of 2.3:1 in the general population.<sup>9</sup> Previous research has suggested that girls with ASD traits in general populations may be harder to detect than boys,<sup>79</sup> possibly due to the existence of an atypical female autistic phenotype, which may be missed in clinical practice. For example, it has been indicated that girls with ASD may have behavioral abilities more similar to typically developing children,<sup>80</sup> that they may be able to develop social “compensatory or camouflaging techniques,” and therefore be more likely to appear in other areas of the health care system than in psychiatric care due to their difficulties.<sup>81</sup>

For children with clinically significant ADHD symptoms, there were no differences in the gender proportions in the respective symptom cutoff groups, where 19.6% of girls and 20.5% of boys received scores above the clinical cutoff. As a comparison (although again tentative), the overall prevalence of ADHD among girls in the general population has been estimated to ~3.2%,<sup>82</sup> and among boys between 5.3%–7.1%, depending on inclusion criteria.<sup>83</sup> Among girls with ADHD, research has also found the disorder to be more likely to be disregarded, even by health care professionals, and girls are overall less likely to be referred for ADHD diagnosis and treatment.<sup>82</sup> This may also indicate that girls

with ADHD are more likely to seek health care outside of psychiatric care.

Parents of children with clinically significant ASD traits reported lower self-rated health than parents of children without, which is in line with previous research that found parents of children with autism to suffer from more stress and negative health outcomes than parents of children with other disabilities.<sup>84</sup>

In children with clinically significant ASD traits, the pain was more likely to be reported as triggered by being in school compared to children without clinically significant traits. Previous research has indicated that children with ASD frequently experience difficulties with academic performance, due to, eg, deficits in executive functions.<sup>85</sup> The school environment also creates social challenges, which may be difficult for these children.<sup>86</sup> Among the children with clinically significant ADHD symptoms, the pain was more likely to be reported as triggered by new situations and the family situation compared to those without clinically significant traits. This finding is in line with research showing that the environments in families of children with ADHD tend to be more stressful and conflict-ridden compared to families with children without ADHD.<sup>87</sup> Moreover, ADHD has also been linked to dysfunction in, eg, social situations, including a lower ability to handle common social demands, as well as to deficits in executive function.<sup>88</sup>

As earlier noted, ADHD and ASD may in part depend on an overlapping neural dysfunction,<sup>13</sup> and both children with ASD and ADHD have in previous studies been shown to display sensory over-responsivity associated with non-adaptive behavior.<sup>22,23</sup> Future studies should explore if such altered sensory processing in combination with deficits in managing competing stimuli, eg, pain, may influence the development of chronic debilitating pain conditions. Moreover, deficits in executive function rendering social interaction and academic performance more burdensome may function as a chronic stressor for these children, which may further increase the risk for problems with health and functioning.<sup>40</sup> Future studies may also explore if pain may share etiological mechanisms with neurodevelopmental disorders, particularly in individuals with altered sensory processing.

A number of limitations should be considered when interpreting the findings from this study. First, participation was voluntary, which implies potential data bias. Notably, however, the current sample characteristics were similar to other research studies in pediatric chronic pain. Second, it should be noted that participants did not receive the extensive

clinical assessment, including neuropsychological tests and developmental history that are required for a full diagnosis of ASD or ADHD, which makes any comparisons to prevalences based on full diagnoses tentative. Still, the sensitivity and specificity reported for the instruments used indicate that they can accurately differentiate between children with and without ASD or ADHD.<sup>52,62,64</sup> Third, although the study was adequately powered, larger sample size would have benefitted sub-group analyses further. Finally, given the cross-sectional nature of data, it is not possible to analyze any trajectories or temporal relations between variables.

The current study contributes to the growing knowledge about concomitant ASD or ADHD traits in chronic pediatric pain. The findings from this study have clinical implications for screening procedures, including assessment of neurodevelopmental disorders, and tailored treatments to match the specific needs of children with these difficulties. Data also indicate that parental interventions may be essential, as both parental health and the family situation were factors associated with the level of neurodevelopmental symptoms, which is in line with new research on both pediatric chronic pain and neurodevelopmental disorders, suggesting the importance of parental factors.<sup>38,89</sup> Future research may benefit from studies focused on understanding the pathophysiology behind the co-occurrence of pain and neurodevelopmental disorders, including the relation between the relation between sensory over-responsivity, executive alterations, and social functioning. The investigation of functional disability associated with clinically significant ASD and ADHD traits in children with chronic pain is also warranted, given that these children may be at risk for more functional impairments than other children with chronic pain. Finally, it appears important to examine whether neurodevelopmental comorbidity moderates treatment outcome in, eg, cognitive behavioral treatments for pediatric chronic pain.

## Conclusion

In a sample of 146 pediatric chronic pain patients, 13.7% and 19.9% scored within the significant clinical range of ASD and ADHD respectively, with a combined 26% of children displaying clinically significant traits and symptoms of either or both conditions. Only a small subset of these children had already been diagnosed with either diagnosis. Data suggest that children with debilitating chronic pain, particularly girls, may present with an elevated risk of having a comorbid, possibly high functioning, neurodevelopmental disorder. Clinical assessment of pediatric chronic pain should include screening for neurodevelopmental disorders.

## Acknowledgments

This work was supported by KID funding at Karolinska Institutet, the research fund at the Functional Area Medical Psychology at Karolinska University Hospital, Jerringfonden, and the regional agreement on medical training and clinical research (ALF) between Stockholm City Council and Karolinska Institutet. The funding sponsors did not have a role in the design of the study, in the collection, analyses, or interpretation of data, in the writing of the manuscript, or in the decision to publish the results.

## Disclosure

S Bölte discloses that he has in the last 5 years acted as an author, consultant, or lecturer for Shire, Medice, Roche, Eli Lilly, Prima Psychiatry, Gerson Lehrman Group, System Analytic, Ability Partner, Kompetent, Expo Medica, and Prophase and that he receives royalties for textbooks and diagnostic tools from Huber/Hogrefe, Kohlhammer, and Uni-Taschenbuecher. The authors report no other conflicts of interest in this work.

## References

- Tanguay PE. Autism Spectrum Disorder. *J Clin Psychiatry*. 2015;76(6):e841–841.
- Leekam SR, Nieto C, Libby SJ, Wing L, Gould J. Describing the sensory abnormalities of children and adults with autism. *J Autism Dev Disord*. 2007;37(5):894–910.
- Klintwall L, Holm A, Eriksson M, et al. Sensory abnormalities in autism. A brief report. *Res Dev Disabil*. 2011;32(2):795–800.
- Doernberg E, Hollander E. Neurodevelopmental Disorders (ASD and ADHD): DSM-5, ICD-10, and ICD-11. *CNS Spectr*. 2016;21(4):295–299.
- Baxter AJ, Brugha TS, Erskine HE, Scheurer RW, Vos T, Scott JG. The epidemiology and global burden of autism spectrum disorders. *Psychol Med*. 2015;45(3):601–613.
- Fombonne E. Epidemiology of pervasive developmental disorders. *Pediatr Res*. 2009;65(6):591–598.
- Christensen DL, Bilder DA, Zahorodny W, et al. Prevalence and characteristics of autism spectrum disorder among 4-year-old children in the autism and developmental disabilities monitoring network. *J Dev Behav Pediatr*. 2016;37(1):1–8.
- Christensen DL, Baio J, Van Naarden Braun K, et al. Prevalence and Characteristics of Autism Spectrum Disorder Among Children Aged 8 Years – Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2012. *MMWR Surveill Summ*. 2016;65(3):1–23.
- Idring S, Lundberg M, Sturm H, et al. Changes in prevalence of autism spectrum disorders in 2001–2011: findings from the Stockholm youth cohort. *J Autism Dev Disord*. 2015;45(6):1766–1773.
- Polanczyk G, de Lima MS, Horta BL, Biederman J, Rohde LA. The worldwide prevalence of ADHD: a systematic review and meta-regression analysis. *Am J Psychiatry*. 2007;164(6):942–948.
- Bahmanyar S, Sundström A, Kaijser M, von Knorring AL, Kieler H. Pharmacological treatment and demographic characteristics of pediatric patients with Attention Deficit Hyperactivity Disorder, Sweden. *Eur Neuropsychopharmacol*. 2013;23(12):1732–1738.
- Ghirardi L, Brikell I, Kuja-Halkola R, et al. The familial co-aggregation of ASD and ADHD: a register-based cohort study. *Mol Psychiatry*. 2018;23(2):257–262.
- Kernbach JM, Satterthwaite TD, Bassett DS, et al. Shared endo-phenotypes of default mode dysfunction in attention deficit/hyperactivity disorder and autism spectrum disorder. *Transl Psychiatry*. 2018;8(1):133.
- Piek JP, Dyck MJ. Sensory-motor deficits in children with developmental coordination disorder, attention deficit hyperactivity disorder and autistic disorder. *Hum Mov Sci*. 2004;23(3-4):475–488.
- Stray LL, Kristensen Ø, Lomeland M, Skorstad M, Stray T, Tønnesen FE. Motor regulation problems and pain in adults diagnosed with ADHD. *Behav Brain Funct*. 2013;9:18.
- Fournier KA, Hass CJ, Naik SK, Lodha N, Cauraugh JH. Motor coordination in autism spectrum disorders: a synthesis and meta-analysis. *J Autism Dev Disord*. 2010;40(10):1227–1240.
- Couturier JL, Speechley KN, Steele M, Norman R, Stringer B, Nicolson R. Parental perception of sleep problems in children of normal intelligence with pervasive developmental disorders: prevalence, severity, and pattern. *J Am Acad Child Adolesc Psychiatry*. 2005;44(8):815–822.
- Craig F, Margari F, Legrottaglie AR, Palumbi R, de Giambattista C, Margari L. A review of executive function deficits in autism spectrum disorder and attention-deficit/hyperactivity disorder. *Neuropsychiatr Dis Treat*. 2016;12:1191–1202.
- Reynolds S, Lane SJ. Sensory overresponsivity and anxiety in children with ADHD. *Am J Occup Ther*. 2009;63(4):433–440.
- Mazurek MO, Vasa RA, Kalb LG, et al. Anxiety, Sensory Over-Responsivity, and Gastrointestinal Problems in Children with Autism Spectrum Disorders. *J Abnorm Child Psychol*. 2013;41(1):165–176.
- Mazurek MO, Petroski GF. Sleep problems in children with autism spectrum disorder: examining the contributions of sensory over-responsivity and anxiety. *Sleep Med*. 2015;16(2):270–279.
- Green SA, Hernandez LM, Bowman HC, Bookheimer SY, Dapretto M. Sensory over-responsivity and social cognition in ASD: Effects of aversive sensory stimuli and attentional modulation on neural responses to social cues. *Dev Cogn Neurosci*. 2018;29:127–139.
- Shimizu VT, Bueno OF, Miranda MC. Sensory processing abilities of children with ADHD. *Braz J Phys Ther*. 2014;18(4):343–352.
- Muskens JB, Velders FP, Staal WG. Medical comorbidities in children and adolescents with autism spectrum disorders and attention deficit hyperactivity disorders: a systematic review. *Eur Child Adolesc Psychiatry*. 2017;26(9):1093–1103.
- Holingue C, Newill C, Lee LC, Pasricha PJ, Daniele Fallin M. Gastrointestinal symptoms in autism spectrum disorder: A review of the literature on ascertainment and prevalence. *Autism Res*. 2018;11(1):24–36.
- Merikangas KR, Calkins ME, Burstein M, et al. Comorbidity of physical and mental disorders in the neurodevelopmental genomics cohort study. *Pediatrics*. 2015;135(4):e927–e938.
- Van Tongerloo MA, Bor HH, Lagro-Janssen AL. Detecting autism spectrum disorders in the general practitioner's practice. *J Autism Dev Disord*. 2012;42(8):1531–1538.
- Treede R-D, Rief W, Barke A, et al. A classification of chronic pain for ICD-11. *Pain*. 2015;156(6):1–1007.
- King S, Chambers CT, Huguet A, et al. The epidemiology of chronic pain in children and adolescents revisited: a systematic review. *Pain*. 2011;152(12):2729–2738.
- Huguet A, Miró J. The severity of chronic pediatric pain: an epidemiological study. *J Pain*. 2008;9(3):226–236.
- Palermo T, Eccleston C, Goldschneider K, et al. *Assessment and management of children with chronic pain: a position statement from the American Pain Society*. 2012. Available from: <http://americanpainsociety.org/uploads/get-involved/pediatric-chronic-pain-statement.pdf>. Accessed October 21, 2018.
- Holmström L, Kemani MK, Kanstrup M, Wicksell RK. Evaluating the Statistical Properties of the Pain Interference Index in Children and Adolescents with Chronic Pain. *J Dev Behav Pediatr*. 2015;36(6):450–454.
- Konijnenberg AY, Uiterwaal CS, Kimpfen JL, van der Hoeven J, Buitelaar JK, de Graeff-Meeder ER. Children with unexplained chronic pain: substantial impairment in everyday life. *Arch Dis Child*. 2005;90(7):680–686.



34. Konijnenberg AY, de Graeff-Meeder ER, Kimpen JL, et al. Children with unexplained chronic pain: do pediatricians agree regarding the diagnostic approach and presumed primary cause? *Pediatrics*. 2004;114(5):1220–1226.
35. Yazdani S, Zeltzer L. Treatment of chronic pain in children and adolescents. *Pain Manag*. 2013;3(4):303–314.
36. Sinclair CM, Meredith P, Strong J, Feeney R. Personal and contextual factors affecting the functional ability of children and adolescents with chronic pain: A systematic review. *J Dev Behav Pediatr*. 2016;37(4):327–342.
37. Fisher E, Heathcote L, Palermo TM, de C Williams AC, Lau J, Eccleston C. Systematic review and meta-analysis of psychological therapies for children with chronic pain. *J Pediatr Psychol*. 2014;39(8):763–782.
38. Hechler T, Kanstrup M, Holley AL, et al. Systematic Review on Intensive Interdisciplinary Pain Treatment of Children With Chronic Pain. *Pediatrics*. 2015;136(1):115–127.
39. Morley S, Williams A, Eccleston C. Examining the evidence about psychological treatments for chronic pain: time for a paradigm shift? *Pain*. 2013;154(10):1929–1931.
40. Low Kapalu CM, Hall JJ, Wallace DP. Neuropsychological Functioning of Youth Receiving Intensive Interdisciplinary Pain Treatment. *J Pediatr Psychol*. 2018;43(8):870–881.
41. Tegethoff M, Belardi A, Stalujanis E, Meinschmidt G. Comorbidity of Mental Disorders and Chronic Pain: Chronology of Onset in Adolescents of a National Representative Cohort. *J Pain*. 2015;16(10):1054–1064.
42. Konijnenberg AY, de Graeff-Meeder ER, van der Hoeven J, et al. Psychiatric morbidity in children with medically unexplained chronic pain: diagnosis from the pediatrician's perspective. *Pediatrics*. 2006;117(3):889–897.
43. Caes L, Fisher E, Clinch J, Tobias JH, Eccleston C. The role of pain-related anxiety in adolescents' disability and social impairment: ALSPAC data. *Eur J Pain*. 2015;19(6):842–851.
44. Khan KA, Tran ST, Jastrowski Mano KE, Simpson PM, Cao Y, Hainsworth KR. Predicting Multiple Facets of School Functioning in Pediatric Chronic Pain: Examining the Direct Impact of Anxiety. *Clin J Pain*. 2015;31(10):867–875.
45. Hoftun GB, Romundstad PR, Zwart JA, Rygg M. Chronic idiopathic pain in adolescence—high prevalence and disability: the young HUNT Study 2008. *Pain*. 2011;152(10):2259–2266.
46. Bursch B, Ingman K, Vitti L, Hyman P, Zeltzer LK. Chronic pain in individuals with previously undiagnosed autistic spectrum disorders. *J Pain*. 2004;5(5):290–295.
47. Clarke C. Autism spectrum disorder and amplified pain. *Case Rep Psychiatry*. 2015;2015:930874.
48. Wiwe Lipsker C, von Heijne M, Bölte S, Wicksell RK. A case report and literature review of autism and attention deficit hyperactivity disorder in paediatric chronic pain. *Acta Paediatr*. 2018;107(5):753–758.
49. Loades ME. Evidence-Based Practice in the Face of Complexity and Comorbidity: A Case Study of an Adolescent With Asperger's Syndrome, Anxiety, Depression, and Chronic Pain. *J Child Adolesc Psychiatr Nurs*. 2015;28(2):73–83.
50. Mazurek MO, Keefer A, Shui A, Vasa RA. One-year course and predictors of abdominal pain in children with autism spectrum disorders: The role of anxiety and sensory over-responsivity. *Res Autism Spectr Disord*. 2014;8(11):1508–1515.
51. Arruda MA, Arruda R, Guidetti V, Bigal ME. ADHD Is Comorbid to Migraine in Childhood: A Population-Based Study. *J Atten Disord*. 2017;1087054717710767.
52. Constantino JN, Gruber CP. *Social Responsiveness Scale (SRS) Manual*. Los Angeles, CA: Western Psychological Services; 2005.
53. Constantino JN, Todd RD. Autistic traits in the general population: a twin study. *Arch Gen Psychiatry*. 2003;60(5):524–530.
54. Bölte S, Poustka F, Constantino JN. Assessing autistic traits: cross-cultural validation of the Social Responsiveness Scale (SRS). *Autism Res*. 2008;1(6):354–363.
55. Wigham S, McConachie H, Tandos J, Le Couteur AS. The reliability and validity of the Social Responsiveness Scale in a UK general child population. *Research in Developmental Disabilities*. 2012;33(3):944–950.
56. Roeyers H, Thys M, Druart C, de Schryver M, Schittekatte M. SRS Screeningslijst voor autismespectrumstoornissen [SRS screening list for autism spectrum disorders]. Amsterdam: Hogrefe; 2011. Dutch.
57. Jussila K, Kuusikko-Gauffin S, Mattila M-L, et al. Cross-cultural differences in the Parent Rated Social Responsiveness Scale (SRS)? Evaluation of the Finnish version among high-functioning school aged males with and without autism spectrum disorder. *Res Autism Spectr Disord*. 2015;9(Supplement C):38–44.
58. Kamio Y, Inada N, Moriwaki A, et al. Quantitative autistic traits ascertained in a national survey of 22 529 Japanese schoolchildren. *Acta Psychiatr Scand*. 2013;128(1):45–53.
59. Constantino JN, Davis SA, Todd RD, et al. Validation of a brief quantitative measure of autistic traits: comparison of the social responsiveness scale with the autism diagnostic interview-revised. *J Autism Dev Disord*. 2003;33(4):427–433.
60. Sparrow EP. *Essentials of Conners Behavior Assessments*. Vol 67. Hoboken: John Wiley & Sons, Inc.; 2010.
61. Schmidt M, Reh V, Hirsch O, Rief W, Christiansen H. Assessment of ADHD Symptoms and the Issue of Cultural Variation: Are Conners 3 Rating Scales Applicable to Children and Parents With Migration Background? *J Atten Disord*. 2017;21(7):587–599.
62. Conners CK. *Conners 3 [Swedish version: Thorell L, Hammar M, Berggren S, Zander E, Bölte S]. Manual*. Hogrefe: Stockholm; 2015.
63. Thorell LB, Christiansen H, Hammar M, Berggren S, Zander E, Bölte S. Standardization and cross-cultural comparisons of the Swedish Conners 3® rating scales. *Nord J Psychiatry*. Epub 2018 Sep 29.
64. Chang LY, Wang MY, Tsai PS. Diagnostic Accuracy of Rating Scales for Attention-Deficit/Hyperactivity Disorder: A Meta-analysis. *Pediatrics*. 2016;137(3):e20152749.
65. Roth-Isigkeit A, Thyen U, Stöven H, Schwarzenberger J, Schmucker P. Pain among children and adolescents: restrictions in daily living and triggering factors. *Pediatrics*. 2005;115(2):e152–e162.
66. Roth-Isigkeit A, Thyen U, Raspe HH, Stöven H, Schmucker P. Reports of pain among German children and adolescents: an epidemiological study. *Acta Paediatrica*. 2004;93(2):258–263.
67. Haraldstad K, Sørum R, Eide H, Natvig GK, Helseth S. Pain in children and adolescents: prevalence, impact on daily life, and parents' perception, a school survey. *Scand J Caring Sci*. 2011;25(1):27–36.
68. Haugland S, Wold B. Subjective health complaints in adolescence – reliability and validity of survey methods. *J Adolesc*. 2001;24(5):611–624.
69. Petanidou D, Giannakopoulos G, Tzavara C, Dimitrakaki C, Kolaitis G, Tountas Y. Adolescents' multiple, recurrent subjective health complaints: investigating associations with emotional/behavioural difficulties in a cross-sectional, school-based study. *Child Adolesc Psychiatry Ment Health*. 2014;8(1):3–3.
70. Haraldstad K, Christophersen KA, Helseth S. Health-related quality of life and pain in children and adolescents: a school survey. *BMC Pediatr*. 2017;17(1):174.
71. Beaton DE, Bombardier C, Guillemin F, Ferraz MB. Guidelines for the process of cross-cultural adaptation of self-report measures. *Spine*. 2000;25(24):3186–3191.
72. Gravetter FJ, Wallnau LB. *Statistics for the Behavioral Sciences*. Singapore: Cengage Learning; 2016.
73. Fritz CO, Morris PE, Richler JJ. Effect size estimates: current use, calculations, and interpretation. *J Exp Psychol Gen*. 2012;141(1):2–18.
74. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. Mahwah, NJ: Lawrence Erlbaum Associates; 1988.
75. Petanidou D, Giannakopoulos G, Tzavara C, Dimitrakaki C, Kolaitis G, Tountas Y. Adolescents' multiple, recurrent subjective health complaints: investigating associations with emotional/behavioural difficulties in a cross-sectional, school-based study. *Child and Adolescent Psychiatry and Mental Health*. 2014;8:3.

76. Faul F, Erdfelder E, Lang AG, Buchner A. G\*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav Res Methods*. 2007;39(2):175–191.
77. Little RJA. A test of missing completely at random for multivariate data with missing values. *J Am Stat Assoc*. 1988;83(404):1198–1202.
78. Lyall K, Constantino JN, Weisskopf MG, Roberts AL, Ascherio A, Santangelo SL. Parental social responsiveness and risk of autism spectrum disorder in offspring. *JAMA Psychiatry*. 2014;71(8):936–942.
79. Kothari R, Skuse D, Wakefield J, Micali N. Gender differences in the relationship between social communication and emotion recognition. *J Am Acad Child Adolesc Psychiatry*. 2013;52(11):1148–1157.
80. Hull L, Mandy W, Petrides KV. Behavioural and cognitive sex/gender differences in autism spectrum condition and typically developing males and females. *Autism*. 2017;21(6):706–727.
81. Lehnhardt FG, Falter CM, Gawronski A, et al. Sex-Related Cognitive Profile in Autism Spectrum Disorders Diagnosed Late in Life: Implications for the Female Autistic Phenotype. *J Autism Dev Disord*. 2016;46(1):139–154.
82. Quinn PO, Madhoo M. A review of attention-deficit/hyperactivity disorder in women and girls: uncovering this hidden diagnosis. *Prim Care Companion CNS Disord*. 2014;16(3):PCC.13r01596.
83. Thomas R, Sanders S, Doust J, Beller E, Glasziou P. Prevalence of attention-deficit/hyperactivity disorder: a systematic review and meta-analysis. *Pediatrics*. 2015;135(4):e994–e1001.
84. Dunn ME, Burbine T, Bowers CA, Tantleff-Dunn S. Moderators of stress in parents of children with autism. *Community Ment Health J*. 2001;37(1):39–52.
85. Whitby PJS, Mancil GR. Academic Achievement Profiles of Children with High Functioning Autism and Asperger Syndrome: A Review of the Literature. *Education and Training in Developmental Disabilities*. 2009;44(4):551–560.
86. Groden J, Diller A, Bausman M, Velicer W, Norman G, Cautela J. The development of a stress survey schedule for persons with autism and other developmental disabilities. *J Autism Dev Disord*. 2001;31(2):207–217.
87. Pressman LJ, Loo SK, Carpenter EM, et al. Relationship of family environment and parental psychiatric diagnosis to impairment in ADHD. *J Am Acad Child Adolesc Psychiatry*. 2006;45(3):346–354.
88. Roizen NJ, Blondis TA, Irwin M, Stein M. Adaptive functioning in children with attention-deficit hyperactivity disorder. *Arch Pediatr Adolesc Med*. 1994;148(11):1137–1142.
89. Dykens EM. Family adjustment and interventions in neurodevelopmental disorders. *Curr Opin Psychiatry*. 2015;28(2):1–126.

## Journal of Pain Research

### Publish your work in this journal

The Journal of Pain Research is an international, peer reviewed, open access, online journal that welcomes laboratory and clinical findings in the fields of pain research and the prevention and management of pain. Original research, reviews, symposium reports, hypothesis formation and commentaries are all considered for publication.

Submit your manuscript here: <https://www.dovepress.com/journal-of-pain-research-journal>

Dovepress

The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

© 2018. This work is licensed under

<https://creativecommons.org/licenses/by-nc/3.0/> (the “License”).

Notwithstanding the ProQuest Terms and Conditions, you may use this content  
in accordance with the terms of the License.