Assessing mental health in boys with Duchenne muscular dystrophy: Emotional, behavioural and neurodevelopmental profile in an Italian clinical sample

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Highlights

- Higher prevalence of Autism Spectrum Disorder (14.8%) in DMD boys.
- Higher prevalence of Intellectual Disability (36.2%) in DMD.
- Higher prevalence of CBCL Internalizing Problems (23.4%) in DMD.
- First study in DMD based on reliable psychopathological assessment.
- Assessment of impact of emotional/behaviour problems on everyday life.

Abstract

Objective

To evaluate through a comprehensive protocol, the psychopathological profile of DMD boys. The primary aim of this observational study was to describe the emotional and behavioural profile and

the neurodevelopmental problems of Italian boys with Duchenne Muscular Dystrophy (DMD); the secondary aim was to explore the relation between psychopathological profile and DMD genotype.

Method

47 DMD boys, aged 2–18, were included in the study and assessed through structured and validated tools including Wechsler scales or Griffiths for cognitive ability, Child Behavior Check List (CBCL), Youth Self Report (YSR) and Strengths and Difficulties Questionnaire (SDQ) for emotional and behavioural features. Patients “at risk” based on questionnaires scores were evaluated by a clinical structured interview using Development and Well Being Assessment (DAWBA) or Autism Diagnostic Observation Schedule (ADOS), as required.

Results

The 47 enrolled patients, defined with a Full Scale Intelligence Quotient (FSIQ) of 80.38 (one SD below average), and presenting a large and significant difference in FSIQ in relation to the site of mutation along the dystrophin gene (distal mutations associated with a more severe cognitive deficit), were showing Internalizing Problems (23.4%) and Autism Spectrum Disorders (14.8%).

Interestingly, an association of internalizing problems with distal deletion of the DMD gene is documented.

Conclusion

Even though preliminary, these data show that the use of validated clinical instruments, that focus on the impact of emotional/behaviour problems on everyday life, allows to carefully identify clinically significant psychopathology.

Keywords

- Developmental psychopathology;
- Duchenne muscular dystrophy (DMD);
- CBCL;
- DAWBA;
- ADOS;
- SDQ

1. Introduction

Duchenne muscular dystrophy (DMD) is an X-linked progressive muscular disorder affecting about 1:3000 boys caused by genetic mutations disrupting the protein dystrophin (DYS), which is normally present in many human tissues, especially in muscle. Lack of

DYS leads to progressive muscular weakness and death due to respiratory muscle insufficiency.1 DYS also plays an important role in the architectural organization of the central nervous system and has some functional consequences,2 i.e., disruption of normal synaptic terminal integrity, synaptic plasticity and regional cellular signal integration.3

Clinical literature consistently reports a higher rate of intellectual disabilities (ID; ranging from 20% to 50%) among DMD patients.4; 5; 6 ; 7 The cognitive impairment is neither progressive nor correlated with the severity of the muscle disease. A discrepancy between verbal intelligence quotient (VIQ) and performance IQ (PIQ) has often been found, with greater impairment of verbal components. Such findings hint at the possibility that the lack of dystrophin might have effects on the correct brain functioning, leading to cognitive impairments as well as neurobehavioral disorders.8

The occurrence of psychopathology in patients with DMD has been documented in several studies. In a recent multicenter study focused on neurodevelopmental, emotional and behavioural characteristics in DMD a high prevalence of autism spectrum disorder (ASD; 21%), hyperactivity (24%), inattention (44%), internalizing (24%) and externalizing problems (15%) has been found.9 These results are in line with previous studies on neurobehavioral functioning in DMD, which report a higher prevalence of attention deficit hyperactivity disorder (ADHD) and ASD than expected in the general population.

The prevalence rate of ADHD in patients with DMD reported in the literature varies from 11.7%10 to 33%,11 ; 12 whereas ASD prevalence rate ranges from 3.79% to 19%.10; 12; 13; 14; 15 ; 16 Variability in prevalence rate across different studies possibly reflects different methods used to assess the presence of the psychopathological diagnosis. The importance of detecting mental disorders in children and adolescents is widely accepted, and the accurate estimate of the prevalence of psychopathology for these age groups is essential, both in the general population and in children with a specific illness.

The above-mentioned studies have used an assessment method based on clinical evaluations rather than structured interviews. However, structured or semi-structured interviews become necessary to accurately assess the prevalence of psychopathology in specific child populations as well as in general population. Structured interviews, besides collecting emotional and behavioural problems, provide specific questions about the onset, offset, frequency, intensity, quality, context of occurrence, and functional impairment, thus they are needed to determine clinical cases or to produce accurate diagnoses17 according to the main nosologic classifications (i.e., DSM-IV or V, ICD 10).

The main purpose of the current study is to describe the emotional and behavioural profile and the neurodevelopmental problems of boys with DMD, using structured clinical assessment based both on self-report questionnaires and clinical structured interviews or observational protocol, when needed. In addition, this study aims to explore the relation between psychopathological profile and DMD neurological phenotype.

2. Materials and methods

2.1. Procedure

To assess emotional and behavioural features, all parents completed the Child Behavior Checklist (CBCL) and the Strength and Difficulties Questionnaire (SDQ) parent-report form. In addition, patients up to 11 years old completed the Youth Self Report (YSR) and the SDQ self-report form. Patients with at least one CBCL/YSR syndrome scale or SDQ scale above the clinical cut-off were evaluated by a clinical structured interview using the Development and Well Being Assessment diagnostic interview (DAWBA). Patients with high scores on the Autism Spectrum Problems CBCL 1/5-5 scale and patients with a clinical diagnosis of ASD based on DSM-IV-TR criteria were further assessed with structured observation based on the Autism Diagnostic Observation Schedule (ADOS).

The study was approved by the Ethical Committee of the E. Medea Scientific Institute according to the Declaration of Helsinki. All parents signed a written informed consent form (Fig. 1).

2.2. Participants

A clinical population of 133 boys with DMD (aged from 2.8 to 32 years) attend each year the Neuromuscular Unit of IRCCS E. Medea for periodic clinical evaluation as indicated in international guidelines.1 Among these, 52 boys were responding to the inclusion criteria (see below) and were recruited during their attendance at the Institute as in patients or outpatients. Fifty patients and their families agreed to participate in the research and parents signed a written informed consent form, 47 completed the study.

Inclusion criteria were age between 2 and 18 years and diagnosis of DMD according to international standard criteria: progressive muscular weakness, increased muscle plasma enzymes, muscular biopsy and/or the presence of mutations in the dystrophin gene.1

Clinical conditions (including cardiac function, steroid treatment, and motor function) and demographic features (including age, family structure, and socioeconomic status) were collected.

We used parental employment as a measure of SES coded according to the Hollingshead 9-point scale for parental occupation.18

2.3. Measures

2.3.1. Cognitive assessment

Cognitive ability was assessed using the Wechsler Intelligence Scale (WISC-III or WIPPSI) or Griffiths scale as required based on the patient's age.

2.3.2. Psychiatric comorbidity based on self-reported questionnaires

Emotional and behavioural problems and their impact on patients' everyday life were assessed by Child Behavior Check List 6–18 (CBCL), Youth Self Report (YSR), and Strength and Difficulties Questionnaire (SDQ).

The CBCL 6–1819 is a questionnaire filled out by parents that is designed to assess social competence and behavioural problems in children and adolescents aged from 6 to 18 years. The CBCL consists of two parts: the first part explores the social competences of children and adolescents, and the second part investigates their behavioural and emotional problems, through 113 items rated on a 3-point: 0 = not true, 1 = somewhat or sometimes true and 2 = very true or often true. The CBCL includes 8 cross-informant syndrome scales (Anxious/Depressed, Withdrawn/Depressed, Somatic Complaints, Social Problems, Thought Problems, Attention Problems, Rule-Breaking Behaviour, and Aggressive Behaviour), two broadband scales (Internalizing, made up of Withdrawn, Somatic Complaints, and Anxious/Depressed scales, and Externalizing, made up of Rule-Breaking Behaviour and Aggressive Behaviour), and a Total Problem scale. YSR is a self-report version of the ASEBA questionnaire15 that is addressed to children and adolescents aged 11–18 years.

SDQ20 is a brief behavioural screening questionnaire addressed to 4–17-year-olds. It includes the following components: 25 items on psychological attributes, some positive and others negative that are divided among 5 scales with 5 items each (Emotional Symptoms, Conduct Problems, Hyperactivity/Inattention, and Peer Relationship Problems), a Total difficulties score and a Prosocial Behaviour scale. The impact supplement of the SDQ, enquires about chronicity, distress, social impairment, and burden to others of identified problems. The impact score ranges from 0 to 10 for the parent and self-report questionnaire.

2.3.3. Prevalence of psychiatric disorders based on a structured clinical interview or protocol observation

The clinical assessment was conducted using the Development and Well Being Assessment diagnostic interview (DAWBA)21 or the Autism Diagnostic Observation Schedule (ADOS).22

The DAWBA combines a structured part and a semi-structured part, and it is designed to generate present-state psychiatric diagnoses based on the DSM-IV and ICD 10 criteria for children and adolescents. The structured sections explore the following psychopathological areas: separation anxiety, simple phobia, social phobia, panic disorder with/without agoraphobia, post-traumatic stress disorder (PTSD), obsessive-compulsive disorder, generalized anxiety disorder, major depression, attention deficit and hyperactivity disorder,

behavioural disorder, and less common disorders. The semi-structured part of the interview elicits a verbatim account of any reported problems. The DAWBA has satisfactory validity and inter-rater reliability. 21 ; 23 The answers to the structured questions from the interviews and questionnaires were fed into a computerized diagnostic algorithm. This algorithm provided six levels of prediction of the probability of a disorder, ranging from very unlikely to probable, the “DAWBA Bands.” The individual is assigned to one of six probability bands corresponding to the approximate prevalence in an epidemiological sample24 ranging from less than .1% likely to more than 70% likely (the other thresholds are .5%, 3%, 15%, and 50%). The interviews were administered by a trained interviewer.

The ADOS22 is a standardized, semi-structured observational assessment used to assess communication, reciprocal social interaction, imagination/creativity, and stereotyped behaviours and restricted interests to inform the diagnosis of ASD. The ADOS is organized into four modules based on the individual's chronological age and expressive language level, ranging from preverbal to verbally fluent. All ADOS assessments were administered and scored by a licensed clinical child psychiatrist.

2.4. Data analysis

Descriptive statistics were generated for demographic and clinical variables and are reported as mean and SD values for continuous variables and frequencies/rates for categorical variables.

To detect the prevalence of psychopathology in the DMD sample group, frequencies/rates of clinical syndrome and broadband scales were calculated. According to ASEBA Multicultural Manual, we considered clinical range scores corresponding to $T > 69$ for the syndrome scales, and $T > 63$ for the Internalizing, Externalizing, and Total Problems Scales.

The level of agreement between the parent report and self-report for each scale was assessed by the Pearson correlation coefficient. The correlation between SDQ and CBCL was assessed by the Pearson correlation test.

The association between emotional disorders and genetic profile was assessed by X2 test.

To evaluate possible association of emotional behavioural problems with different clinical features of the sample (motor function, steroid treatment, site of mutation, FSIQ, and age), a series of t tests was performed on continuous CBCL and YSR t-scale scores. The level of significance was set at $P < .05$.

Data analysis was performed using SPSS for Windows (version 17.0).

3. Results

3.1. Patients and family characteristics

The clinical and demographic features (including age, family status, and socioeconomic status) of the 47 patients completing the study are reported in Table 1. Genetic profile (available for 46 boys), wheelchair use, steroid therapy, and presence of cardiomyopathy are also reported in Table 1. The mean age of DMD participants was 10.96 years (SD: 3.85, range 2–18 y), the mean age of diagnosis was 3.2 (SD: 1.5) all the boys with DMD were Caucasian. Families of enrolled patients were mainly biparental (91.5%), and they had a medium socioeconomic status.

At the time of the assessment, 28 out of 47 patients were under current steroid therapy (currently treated with deflazacort; 59.57%), 10 out of 47 (21.28%) stopped treatment more than 1 year before the beginning of the study, 9 boys were steroid naïve (19.15%). 32 boys (68.09%) were wheelchair bound, and 31.9% had a cardiomyopathy.

The site of mutation along the DMD gene was “proximal” (upstream to exon 44) in 54.35% of the whole sample and “distal” (down-stream to exon 44) in 45.65%.

The mean FSIQ in DMD patients was more than one SD below the mean (80.38), with a greater impairment of verbal components (VIQ: 82.88) than of performance components (PIQ: 85.83); a large and significant difference in FSIQ between the two types of mutations was found (proximal deletion FSIQ: 86.88 vs distal deletion FSIQ: 74.62; $t = -2.170$; $p = .035$). FSIQ < 70 was seen in 36.2% of the total sample.

3.2. Prevalence of psychopathology based on self-report questionnaires and structured interviews

The CBCL syndromic and broadband scales t scores (mean and SD) are reported in Fig. 2 ; Fig. 3. In addition, in order to ensure that behavioural outcome data were “clinically relevant,” t scores were split into t values above the border cut-off (t value ranging from 65 to 68 for syndrome scales; t value ranging from 60 to 62 for broadband scales) and t values above clinical cut-off (t value up to 69 and 63, respectively). For each scale, the prevalence and rate of border and clinical cases were reported.

As shown in Fig. 2, parent reports t scores were higher than self-reports for each scale. However, a large correlation among parent ratings and self-rating was found, according to Cohen's criteria. 25 Significant r values were detected for Withdrawn/Depressed ($r = .63$; $p < .01$), Social Problems ($r = .45$; $p < .05$), Thought Problems ($r = .59$; $p < .01$), Aggressive Behavior ($r = .70$; $p < .01$), Internalizing Problems ($r = .60$; $p < .01$), Externalizing Problems ($r = .51$; $p < .05$), and Total Problems ($r = .62$; $p < .01$).

The Internalizing Problems scale together with the Depressed Problems, Anxious/Depressed Problems, and Somatic Compliant subscales showed a higher mean score.

Data from the SDQ Questionnaires showed significant positive correlations with all of the CBCL syndrome and broadband subscales (ranging from r = .465, Internalizing Problems,

to r = .696, Attention Problems). SDQ Hyperactivity scale showed a significant high correlation with the Attention Problems CBCL scale (r = .775). In our sample, the SDQ Impact Score ranged from 0 to 4 (mean: .26; SD: .759).

Being in clinical range of CBCL/YSR scales was not associated with the site of mutation ($\chi 2$ = .877; p = .645). Assessment with the clinical structured interview DAWBA was performed on 11 (23.40%) patients (only the parent or both parents and self as required). The computerized diagnostic algorithm of DAWBA assessment identified only one patient with more than a 70% probability for Social Phobia disorder. In all other cases, although some emotional symptoms were confirmed, we found at most the level 2 DAWBA band for each psychopathological investigated area, corresponding to a 3% probability of having a diagnosis. Indeed, assessed boys did not meet the diagnostic criteria for any specific psychopathological disorder according to the DSM-IV.

Based on protocol criteria, 7 DMD boys (14.89%) were assessed by ADOS; all the boys met the criteria for ASD, and 4 of them presented proximal deletion, whereas the other 3 presented distal deletion on the DMD gene ($\chi 2$ = .205; p = .902). The FSIQ was significantly lower than in the whole sample (t = 2.462; p = .018), as shown in Table 2.

3.3. Association of emotional behaviour problems with type of mutation, wheelchair, steroid, FSIQ and age

Data analysis showed that only the CBCL Anxious/Depressed subscale scores were significantly higher in patients with distal than proximal deletion (58.20 vs 54.04; t = 2.12; p = .04). The same difference was detected on the YSR: boys with distal deletion scored significantly higher (46.60 vs 36.60; t = 2.70; p = .015) on the Internalizing Problem Scale.

Significantly higher Withdrawn/Depressed scores were reported in patients using a wheelchair vs not using wheelchair (60.86 vs 55.88; t = 2.10; p = .04). All patients who completed the YSR were in a wheelchair, therefore it was not possible to perform this comparison on YSR data.

Boys with ID showed significantly higher Withdrawn/Depressed scores (62.87 vs 57.03; t = −2.07, p = .04) and Internalizing Problems scores (59.07 vs 52.57; t = −2.08; p = .04), but only on the CBCL questionnaire.

No significant association of either ongoing steroid therapy or age with any CBCL and YSR t score scales was found.

4. Discussion

In the present study, 47 Italian boys with DMD were assessed for emotional and behavioural problems and neurobehavioral disorders. Our assessment method was relying on screening questionnaires in the first step and subsequent assessment with clinical structured interviews (DAWBA) or observational protocol (ADOS), in order to enhance diagnostic accuracy. Several studies found a high level of psychopathological comorbidity in DMD9; 10; 11; 12; 13; 14; 15 ; 16: these studies frequently did not use recommended assessment methods, such as structured or semi-structured interviews that include specific questions about the onset, offset, frequency, intensity, quality, context of occurrence, and functional impairment, which are necessary elements to determine clinical caseness or to assign a diagnosis.17 In fact, most of former studies that investigate psychopathology among DMD patients have used an assessment method based on parent-reported questionnaires9; 10; 11; 13; 14 ; 15 or clinical evaluations.11; 13 ; 14 Less frequently we found studies including both standardized questionnaires and structured clinical assessments across a broad range of psychopathological problems (such as ADOS for ASD and DAWBA), as the present study does.

Our data indicate that young children with DMD exhibit higher prevalence of ASD and ID (neurodevelopmental disorders as defined in the DSM-5) than expected in the general population. In detail, 14.89% of the boys with DMD had a diagnosis of ASD, performed using a standardized protocol (ADOS).

ID was found in 36.2% of the assessed boys (FSIQ < 70), and the FSIQ average level was 80.38, more than 1 SD below the general population average, with a greater impairment of verbal than performance components (VIQ: 82.88; PIQ: 85.83). These findings are consistent with previous studies focused on cognitive and neurobehavioral profile of DMD conducted over the past 20 years, suggesting that the non-progressive, cognitive impairment does not correlate with the severity of muscle disease, and primarily involves verbal rather than nonverbal intelligence.8; 26; 27; 28 ; 29 A significant difference in FSIQ between the two sites of mutation was found (proximal FSIQ: 86.88 vs distal FSIQ: 74.62; $p = .035$). This result replicates findings of previously published studies, which show an association between distal DMD mutations and a more severe cognitive deficit. 9; 16; 27; 28; 29 ; 30 Mutations in the distal portion of the DMD gene are associated with loss of cerebral dystrophin isoforms, which might explain the reduced intellectual functioning found among our DMD children with distal deletion. Dystrophin isoforms of the central nervous system (CNS) are in fact more expressed in the cerebellum and limbic system and play a role in glutaminergic synapses and in synaptic maturation and function. 31 ; 32 Support to the hypothesis of an association between lack of brain dystrophin and cognitive impairment is provided both by clinical and animal-model studies.33 Focussing on cerebellum, DMD patients have been reported to have cerebellar hypo-metabolism through positron emission tomography.34 Both neuroimaging and neuropsychological investigations provided evidence of the possible implication of the cerebellum in a wide range of cognitive functions,35 and although with fewer data, this could be true for DMD patients as well. Lack of dystrophin in the cerebellum may thus be the neurobiological explanation for the neurodevelopmental disorders observed in our group of patients, and further support to this

hypothesis comes from a range of behavioural observations and neuroimaging investigations which have found evidence of a cerebellar role in two neurodevelopmental conditions: ASD and ADHD. Interestingly, literature provides evidence of a cerebellar contribution even to aspects of social emotional and regulatory behaviour, which are frequently impaired in ASD and ADHD. 35 ; 36

Although the prevalence of neurodevelopmental disorders (ASD and ID) is evident, in the present study a broad range of emotional and behavioural problems (internalizing and externalizing) were also assessed: we found a remarkable number of boys who exceeded the clinical cut-off for CBCL Internalizing Problems (N = 11), which constitutes a high rate (23.4%) when compared to Italian normative data. 37 This is an interesting finding, as this rate is very consistent with that recently reported by Ricotti and colleagues using the same screening questionnaire (24% of males scored above the clinical threshold).

In contrast to aforementioned studies, in our DMD sample no ADHD comorbidity was found. Some of the questions on the CBCL, SDQ, and DAWBA that address ADHD symptoms are not as useful, as children with DMD cannot display the same type of hyperactivity symptoms, such as fidgetiness, due to their motor problems, and measures regarding physical movement (e.g., being restless, being fidgety, running around at dinner time) may not be rated high if the child has limited mobility. Although these instruments represented a gold standard of screening and detecting psychopathology in children and adolescents, it is possible that they are not the best way to detect specific psychopathological problems in boys with DMD, given the physical limitations of such patients, which could result in false negatives.

This result is both unusual and challenging: it opens interesting issues about not only methodology, but perhaps on the phenomenology of ADHD in the Duchenne clinical population. Indeed, it is important to note that, because of muscle weakness and physical limitations, symptoms of hyperactivity may be less obvious in DMD boys. It is likewise important to know that some of the cognitive patterns observed in Duchenne (such as language or discrete short-term memory deficits) can lead to a child being misidentified as having ADHD.

To our knowledge, the assessment protocol applied in our study, providing information not only about emotional and behavioural problems but also on the impairment due to these emotional and behavioural problems, could have given useful information to define clinical caseness.

Specifically, the Strength and Difficulties Questionnaire impact supplement was used to assess associated distress together with social, educational, and family life impairment.38 For children with emotional/behavioural difficulties, parents and adolescents were asked to respond to one item about level of child distress and up to four items about interference of the child's emotional/behavioural problems with family life, leisure activities (both items for parents only), friendships, and classroom learning (all scored 0–2). Impact scores ranged

from 0 to 10 for parents and adolescents. Goodman suggests that impact scores are better than symptom scores at discriminating between the community and clinic samples.20

As outlined above, results obtained for our Institute study group replicate many findings from previously published studies on both cognitive deficits, association of mutation site with IQ, ASD prevalence and internalizing problems, using a strong and extended assessment protocol.

Yet, even though rates of emotional problems (Internalizing Problems and Anxious/Depressed Problems) among children with DMD are higher than in the general population (as expected with any chronic illness), the majority of children affected do not have behavioural problems. Additionally, it is noteworthy that self-perception among many children and adolescents with DMD is more positive than what their caregivers imagine.

Although all the children enrolled in this study live with a chronic, progressive, and eventually fatal neuromuscular disorder, a remarkable 67% were not found to be psychopathologically “at risk” by a standard child behaviour measure. A possible explanation, as already noted, could be the lack of assessment tools for this special clinical population. However, this result led to the hypothesis that these patients and their families may use specific coping strategies that have a positive influence on dealing with illness and stressful situations, and thus emotional and behavioural difficulties may become milder. In future research it would be interesting to investigate coping strategies in families with neuromuscular diseases and to develop specific emotional and behavioural measures for this clinical population.

Limitations

These results should be regarded as preliminary and with some limitations in mind.

Firstly, we did not have a control group, whereas other studies have compared DMD patients with their siblings or with patients who have other neuromuscular diseases. This limitation will be addressed in future studies, as this observational clinical study is proposed to be the first step of a larger study.

Secondly, even though this sample is appropriate for a monocentric study, the sample size is relatively low for the range of age and clinical phenomenology. Nevertheless, the use of standardized questionnaires, with a psychometric validation and normalized scores for gender and age (age range 6–18), should provide consistent data. Validity and reliability studies have shown that the CBCL 6–18 is an effective instrument for assessing emotional and behavioural problems in children and adolescents.17 Moreover, in this preliminary observational study we use validated clinical instruments that focus also on the impact of emotional/behavior problems on everyday life, even in the first screening (SDQ).

Finally, additional structured interviews (i.e. ADOS and DAWBA) were administered only in a subsample of 18 patients (38.3% of the total sample), according to our assessment procedure (see Fig. 1): this may lead to an underestimation of the true rate of psychopathology in this special clinical population. Nevertheless, the utility of behavioural screening instruments for risk stratification was largely demonstrated.17 ; 39 Sheldrick et al. (2015) reported that children who screened positive – at CBCL 6–18 and SDQ – were approximately 2–5 times more likely than children who screened negative to qualify for a psychiatric diagnosis.

6. Conclusions

In the present study, 47 Italian boys with DMD were assessed for emotional and behavioural problems and neurobehavioral disorders. Our data indicate that young children with DMD exhibit higher prevalence of ASD (14.89%) and ID (36.2%) and a higher rate of CBCL Internalizing Problems (23.4%) than expected in the general population Yet, even though rates of emotional problems (Internalizing Problems and Anxious/Depressed Problems) among children with DMD are higher (as expected with any chronic illness), the majority of children affected do not have behavioural problems. Additionally, it is noteworthy that self-perception among many children and adolescents with DMD is more positive than what their caregivers imagine. Even though preliminary, these data show that use of validated clinical instruments, that focus on the impact of emotional/behaviour problems on everyday life, allows to carefully identify clinically significant psychopathology.

Conflict of interest

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

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