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Delusional and Psychotic Disorders in Juvenile Myotonic Dystrophy Type-1

Delphine Jacobs,[1]* Diane Willekens,[1] Christine de Die-Smulders,[2] Jean-Pierre Frijns,[1] and Jean Steyaert[1]

[1]Centre for Human Genetics, University of Leuven, Leuven, Belgium

[2]Department of Clinical Genetics, Academic Hospital Maastricht, Maastricht, The Netherlands

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We investigated the clinically derived hypothesis of a relatively high incidence of delusional and psychotic disorders in adolescents with juvenile Myotonic Dystrophy type-1 (DM1). Twenty-seven subjects of age 16–25 with juvenile DM1 and their parents were invited to have a clinical psychiatric interview, and to complete an ASEBA behavior checklist (YSR, ASR, CBCL, and ABCL). We diagnosed a Delusional Disorder in 19% of our patients and a Psychotic Disorder not otherwise specified in another 19%. These two groups of patients had a significantly worse level of clinically defined general functioning. It is clinically relevant to investigate in patients with juvenile DM the symptom of delusions and the presence of a delusional and psychotic disorder, and to consider the presence of juvenile DM in youngsters presenting with such a thought disorder. These disorders compromise the general functioning of the subjects and are often to some extent treatable. © 2017 Wiley Periodicals, Inc.

Key words: muscular dystrophy; juvenile myotonic disorder; delusional disorder; psychotic disorder; psychosocial functioning

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INTRODUCTION

We investigated the presence of a higher incidence of delusional and psychotic disorders in adolescents and young adults with juvenile Myotonic Dystrophy type-1 (DM1).

Myotonic dystrophy (DM) is often considered to be the most variable of all human disorders: the age of onset ranges from foetal life to old age and virtually all systems of the body can be affected in some way [Harper, 2001]. The disease is characterized by the skeletal muscle symptoms of myotonia and progressive muscle weakness. Other organs commonly involved are the eyes, heart, lungs, smooth muscles, peripheral nerves, endocrine glands, skeleton, skin, and brain [Harper et al., 2004]. Brain manifestations include somnolence, cognitive impairment, personality features and mental illness [Harper, 2001].

Harley et al. [1993] proposed a classification of four different categories of myotonic dystrophy in relation to age of onset and to clinical symptoms [Steyaert et al., 1997].

(1) The *mild* form of DM with cataract and minimal or no neuromuscular symptoms in middle or older age.
(2) The *classical* or *adult* form with typical neuromuscular symptoms in adolescence or early adult life.
(3) The *juvenile* or *childhood* form: symptoms are present in childhood before the age of 12, but not yet at birth. Learning disabilities are often prominent, while neuromuscular symptoms are rather mild or sometimes even absent [de Die-Smulders, 2004].
(4) The *congenital* form with clinical symptoms present in utero or from birth: hypotonic cerebral palsy, respiratory and/or feeding problems, and mild to moderate developmental delay in survivors.

A second type (type-2) of autosomal dominant inherited DM with a different genetic cause was discovered in 1994 [Ricker et al., 1994], and since then two types of DM are distinguished: DM type-1 and DM type-2.

DM type-1 is an autosomal dominant inherited disorder, caused by a (CTG)*n* repeat expansion mutation in the 3′ untranslated

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*Correspondence to:
Delphine Jacobs, KU Leuven, CBMER Kapucijnenvoer, 35 box 7001, 3000 Leuven, Belgium.
E-mail: delphine.jacobs@kuleuven.be
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region of the DMPK (dystrophia myotonica protein kinase) gene in chromosome 19q13.3 [Brook et al., 1992; Fu et al., 1992; Mahadevan et al., 1992]. There is a direct but moderate correlation between the number of CTG repeats and disease severity, and an inverse moderate correlation between the number of repeats and the age of onset of symptoms. However, an individual's number of repeats only accounts for a fraction of the total variation in disease severity and in age of onset. Myotonic dystrophy patients inherit at least 50 CTG repeats: persons with the classic adult onset form tend to have 200–500 CTG repeats, in the juvenile form, persons tend to have 500–1,000, and congenitally affected individuals typically have at least 1,000 repeats [Monckton and Ashizawa, 2004].

DM type-2 is caused by an unstable CTG expansion on chromosome 3q21.3, which was discovered in 2001 [Liquori et al., 2001].

In our research we focus on the first type of DM: DM type-1 or "DM1." We will use the term "DM," when writing about previous research conducted when this difference was not yet discovered or applied.

DM1 is the most frequent muscular dystrophy in adults (age of at least 18 years), with a prevalence of 5–20 in 100.000 [Hunter et al., 1992; Harper and Rüdel, 1994]. In children (age below 18 years) few data are available about the prevalence. Darin and Tulinius [2000] reported an estimated prevalence of 5 per 100.000 in the western Swedish population under the age of 16.

Cognitive function testing in patients with the *adult* form of DM shows *IQ* levels slightly reduced compared to controls, but not below the normal range. Longitudinal studies do not seem to indicate a deterioration of IQ with advancing age [Harper, 2001]. Nonetheless, Modoni et al. [2004] hypothesised, on the basis of a cross-sectional study, a decline of frontal and temporal cognitive functions in adult forms, which they presumed was related to aging. Censori et al. [1990] found reduced visuospatial, constructional and frontal lobe performance (in adult patients with, at that time, a no further specified form of DM). Meola et al. [2003] reported that patients with the classical adult form of DM1 had significantly lower scores on tests of frontal lobe function ("dysexecutive syndrome") compared to controls. Significantly worse scores were later found on tests measuring flexibility, short-term memory, attention, executive and visuospatial abilities [Antonini et al., 2006; Winblad et al., 2006; Sistiaga et al., 2010; Schneider-Gold et al., 2015]. Significant structural-functional correlations of morphological MRI findings were associated with reduced flexibility of thinking in DM1 [Schneider-Gold et al., 2015].

An increased frequency of *personality* features and disorders is found in *adult* DM1 [Delaporte, 1998; Meola et al., 2003; Winblad et al., 2005; Sistiaga et al., 2010]. Peric et al. [2014] conclude that all the empirically reported traits belong to the anxious or fearful cluster (avoidant, dependent, and obsessive-compulsive) and the odd or eccentric cluster (paranoid, schizotypal, schizoid). Personality disorders were found in around 20% of the patients [Delaporte, 1998; Winblad et al., 2005]. Peric et al. [2014] found significant avoidant and paranoid traits and a negative correlation between paranoid traits and quality of life and educational/professional level. They state that it seems that the personality profile of patients with DM1 results both from the genetic brain abnormality and an incapability to cope with a debilitating disease. Winblad et al. [2005] found that DM1 patients scored significantly higher on the temperament and character inventory dimension harm avoidance, and lower on persistence, self-directedness, and cooperativeness.

Whether *depression* is specifically increased in DM is doubtful [Harper, 2001]. Brumback [1987] considered many of the DM symptoms to have a depressive basis. Others did not find a greater frequency of depression or anxiety than in healthy controls or patients with other muscular dystrophies [Duveneck et al., 1986; Bungener et al., 1998], but significantly lower scores for expressiveness and significantly higher scores for anhedonia. Like Peric et al. [2014], Bungener et al. [1998] contributed this emotional deficit to an adaptive reaction to the threatening implications of the disease, or to the effect of the CNS lesions which occur in DM, or to both. More recently, Antonini et al. [2006] again found mild depression and marked (state and trait) anxiety symptoms in adult DM1 on the basis of Hamilton rating scales. Winblad et al. [2010] scored clinical depression in 32% of the patients with DM1 using the Beck Depression Inventory (BDI). However, a large majority of patients was scoring high on the somatic dimension of the BDI and contrastingly low on content, so few patients would have met a psychiatric criterion of depression due to low scores on the cognitive-emotional dimension.

The *social consequences* of the variety of DM impairments mentioned above have been quantified in the Saguenay study in Quebec: Perron et al. [1989] found a reduced educational level and employment level compared with the general population in the area, and they reported that 57% of families with DM were living below the poverty line. Antonini et al. [2006] reported a severely impaired health-related quality of life in adult DM1 which was negatively influenced by severity and duration of disease as well as by specific cognitive deficits and changes in emotional functioning. Peric et al. [2014] found a negative correlation between paranoid traits and quality of life and educational/professional level.

The cognitive, neuropsychological, and psychiatric profiles of patients with the *juvenile/childhood* form of DM1 were the object of several studies. Full-scale *intelligence* quotient varied from below average to normal, with a significant discrepancy between scales (performance scores lower than verbal scores) and a visual attention and visual–spatial deficit [Goossens et al., 2000; Steyaert et al., 2000; Angeard et al., 2011; Douniol et al., 2012]. Repeat length appeared to be negatively correlated to IQ and neuropsychological functioning. Steyaert et al. [2000] reported that the executive mental functions can be markedly impaired in DM and that for this reason (pre)frontal areas might be involved in the pathophysiology of DM. More than half of the included patients received one or more *child psychiatric diagnoses*, mostly ADHD (inattentive subtype), Anxiety Disorder and Mood Disorder [Goossens et al., 2000; Steyaert et al., 2000; Douniol et al., 2012]. Ekstrom et al. [2008] found a high prevalence of ASD in children with DM1 and intellectual disability (most of them moderate or severe). The frequency of ASD increased with the severity of the form of DM1 and with increasing CTG repeat expansions.

In this research we wanted to test the hypothesis that there is a relatively high incidence of delusional and psychotic disorders in adolescents with juvenile DM. In our juvenile DM patients at the Centre for Human Genetics at UZ Leuven in Belgium, we observed delusional and psychotic disorders in a striking number of adolescents

and young adults. It is of clinical importance to detect these disorders, but patients rarely spontaneously talk about psychotic symptoms [Granö et al., 2016] and clinicians seldom ask about them. This co-occurrence of DM and the symptom of delusions has rarely been described before: Harper [2001] mentioned a "rare occurrence of psychosis, possible coincidental," and Peric et al. [2014] found an higher score on "psychotic delusions" on the Millon Multiaxial Clinical Inventory (MMCI). Also, in relation to these delusional and psychotic disorders, we wanted to investigate the general behavioral and psychosocial functioning of our patients.

MATERIALS AND METHODS

In order to clinically investigate a higher presence of delusional and psychotic disorders in juvenile DM1, a group of adolescents and young adults was asked to fill in a questionnaire, and to have a clinical psychiatric interview.

We assessed cognitive functioning and psychiatric symptoms in adolescents (below 18 years of age) and young adults (18 years or more) with juvenile MD1 attending the Centre for Human Genetics of the University Hospital Leuven.

Subjects

We invited 30 subjects, aged 16–25 years, with DM and without a history of other major somatic disorders, to participate in a systematized clinical assessment of cognitive functioning and psychiatric symptoms. Twenty-seven subjects, 14 women, and 13 men gave their informed consent to participate. The protocol consisted of cognitive testing, a psychiatric interview of the patient (and the parent(s) if the patient accepted them to be present) and a questionnaire filled in by the patient and the parent(s) separately. Two subjects declined to participate for personal reasons, and a third subject could not participate because of incarceration. The clinical diagnosis of DM was confirmed by a previous molecular diagnosis in our Centre of expansion of CTG repeats at the DMPK locus. The Commission of Medical Ethics of UZ Leuven approved the publication of this study.

Psychiatric Interview

The first author (DJ) conducted a structured clinical psychiatric interview based on DSM-IV-TR [American Psychiatric Association, 2000] with the patient (in the presence of his/her parent(s), unless refused) in order to assess (i) the presence of current adolescent psychiatric symptoms and syndromes and (ii) the present social functioning (studies, job, partner and friends, and General Assessment of Functioning score). The clinical data were analysed by two trained clinicians (JS and DJ) and diagnostic classifications were obtained by consensus diagnosis according to DSM-IV criteria. One of these clinicians (DJ) did not have any previous knowledge about the clinical history of the patients. In order to standardize the clinical interview, we used the OPCRIT structure (Operational Criteria Checklist for psychotic and affective disorders) [Craddock et al., 1996], but without generating diagnoses with the computer programs. Instead we generated diagnoses in a clinical psychiatric way, based on the DSM-IV.

Cognitive Testing

All subjects underwent a cognitive test using the WAIS-III [Wechsler Adult Intelligence Scale-III, Dutch version].

Behavioral Measures

The patients and their parents were asked to complete a questionnaire: *Youth Self Report* (YSR) or *Adult Self Report* (ASR), both questionnaires of the ASEBA (Achenbach System of Empirically Based Assessment) [Achenbach and Rescorla, 2001 and 2003], for the patients; and for the parents *Children Behaviour Checklist* (CBCL) or *Adult Behaviour Checklist* (ABCL) (both ASEBA questionnaires, Achenbach and Rescorla, 2001 and 2003). The questionnaires were mailed to the patients and parents,who separately returned them in sealed envelopes at the moment of the clinical assessment. Subjects below 18 of age are called "children," subjects of 18 years and older are called "adults."

The ASEBA questionnaires are highly reliable and valid self-administered measures of behavioral and emotional problems in children and adults [Achenbach and Rescorla, 2001 and 2003]. They were translated into Dutch by Verhulst et al. [1991], but norms for the Dutch population were not available yet at the time this study was undertaken. The results from this checklist are shown in a total problem score, in two subscores for respectively the internalising and externalising problem behavior [Table III], in a profile of clusters with specific problem behavior (under and above 18 years, Tables IV and V) and in competence scales (e.g., activities, social, school and total competence for CBCL and YSR, Table VI). The responses are transformed into T-scores ($X = 50$, s.d. $= 10$) which correspond to percentiles. In the total problem score, and the internalising and externalising subscores, the "borderline range" spans the 84th to 90th percentile. Percentiles of 91 and higher are considered to be of clinical concern [Achenbach and Rescorla, 2001 and 2003]. For the specific problem clusters, the 93th to 97th percentile is "in the borderline range" while the percentiles of 98 and higher are called "in the clinical range." Correlations between ratings by different informants (cross-informant comparisons) are expressed in Q correlations which, like Pearson correlations, range from -1.00 (indicating complete disagreement between two raters) to $+1.00$ (indicating complete agreement between the raters' patterns of scores). Correlations between the 25th and 75th percentiles are considered to indicate an average level of agreement between informants.

Statistical Analysis

Data were analysed with the Systat 10.2 package (SYSTAT Software, Inc. 2006).

RESULTS

Molecular Data

Data on gender, age, size of the CTG-repeat on 19q13.3 and the transmitting parent were already available in the patient records at the Center, and are shown in Table I, as well as full-scale IQ, psychiatric diagnosis and GAF (General Assessment of Functioning).

TABLE I. The Research Subjects Described in Terms of Gender, Age, Number of CTG Repeats on 19q13.3, IQ, Psychiatric Diagnosis and GAF (General Assessment of Functioning)

	Gender	Age	Repeats	Transmitting parent	FSIQ	Diagnosis 1	Diagnosis 2	GAF
1	Male	19	1,900	Mother	97	Delusional disorder	ADHD	55
2	Male	25	1,900	Father	92	Delusional disorder	ADHD	25
3	Male	20	1,200	Father	74	Alcohol abuse		55
4	Female	21	1,900	Father	73	Psychotic disorder	Dysthymic disorder	41
5	Female	19	1,500	Mother	74	Psychotic disorder		35
6	Male	21	1,000	Father	96	—		55
7	Male	18	2,200	Mother	74	PDD-NOS		35
8	Female	20	2,100	Mother	69	PDD-NOS		35
9	Female	16	1,000	Mother	58	Psychotic disorder		31
10	Male	18	960	Father	92	—		59
11	Male	24	2,600	Father	78	ADHD		55
12	Male	21	2,800	Mother	61	—		49
13	Female	16	1,400	Father	91	—		71
14	Female	17	650	Father	94	ADHD		61
15	Male	17	1,100	Mother	75	—		75
16	Male	19	900	Mother	80	Psychotic disorder		35
17	Female	16	1,600	Mother	70	—		41
18	Female	18	2,000	Father	66	Delusional disorder		35
19	Female	25	3,000	Father	63	—		35
20	Male	23	1,500	Mother	91	Delusional disorder	ASS	35
21	Female	21	2,600	Mother	78	—		65
22	Female	19	400	Father	57	Psychotic disorder	ADHD	29
23	Male	20	600	Father	74	—		60
24	Female	19	2,900	Mother	70	—		61
25	Male	22	2,100	Mother	86	Delusional disorder	ASS	35
26	Female	16	400	Father	90	—		81
27	Female	16	1,000	Father	86	—		80

Psychiatric Syndromes

We found that 15 subjects qualified for one or more DSM-IV-diagnoses (Table II). Five subjects were found to have a Delusional Disorder and five persons met the criteria for a Psychotic Disorder not otherwise specified (we will refer to these two groups as one group named "thought disorders," cf. Sadock and Sadock, 2005, p. 858). Five subjects fulfilled the criteria for Attention Deficit Hyperactivity Disorder (ADHD), four subjects had a diagnosis of pervasive developmental disorder: two of autistic disorder (AD) and two of pervasive developmental disorder not otherwise specified (PDD-NOS). One person received the diagnosis of Alcohol Abuse and one woman suffered from a Dysthymic Disorder since she had been subject to the loss of a first-degree relative. Twelve subjects did not qualify for any DSM-IV diagnosis (Table II).

The two autistic individuals also had a delusional disorder. Their delusions were of the grandiose type. The three subjects without autism had delusions of the grandiose type, the paranoid type and the erotomanic type, respectively.

Intelligence

All the patients had intelligence levels in the normal, borderline or mildly intellectually disabled range. The Full Scale IQ-scores range from 57 to 97, mean FSIQ 78,1. Six persons (22%) scored in the intellectually disabled range (2 SD below the mean). There is no significant difference between the mean Verbal (79.7) and mean Performal IQ (77.7).

When comparing the FSIQ of subjects without psychiatric diagnosis (mean FSIQ 78.8) to those with a psychiatric diagnosis (mean FSIQ 77.6), we found no statistical difference. Neither did we find a significant difference in FSIQ when comparing the group without thought disorders (mean FSIQ 78.5) to the one with thought disorders (mean FSIQ 77.4).

TABLE II. Number and Percentage of Each Psychiatric Diagnosis on the Total of 27 Subjects

Diagnosis	N = 27 (%)
Delusional disorder	5 (19)
Psychotic disorder	5 (19)
ADHD	5 (19)
Autistic disorder	2 (7)
PDD-NOS	2 (7)
Alcohol abuse	1 (4)
Dysthymic disorder	1 (4)
No diagnosis	12 (44)

Behavioral and Emotional Functioning

The mean *General Assessment of Functioning* (*GAF*) score for the entire group was 49 (s.d. 16; range 21–85). The GAF scores differed significantly between the groups with or without thought disorders: 35,6 (SD 8) versus 57.2 (SD 15) ($P < 0.001$) and between the groups with or without a psychiatric diagnosis: 38.5 respectively 62.7 ($P < 0.001$).

For the ASEBA questionnaires we will indicate the number of "clinical cases." According to ASEBA research and guidelines, centile 91 or higher for Total Problem Score, Internalizing and Externalizing subscales coincides with clinical caseness, while centile 98 or higher coincides with clinical caseness for the specific problem clusters.

Internalising problems seemed to be more common in our subjects than in the general population, according to the parent-rated *ASEBA* questionnaires: the parents of 9 out of 27 patients (33%, 8 adults, and 1 child) attributed rates in the clinical range (Table III). Compared to the proportion in the general population (10%) this was a significant difference (binomial distribution test for above or under cut-off $P < 0.001$). The proportion of externalising problems (7.4%) and of total problems (14.8%) did not significantly differ from the general population, nor did the number of clinical scores on the specific problem clusters (Table III). The following specific problem clusters contained one, two or three clinical cases in the adult subjects: "anxious/depressed," "withdrawn," "somatic problems," "thought problems," and "social problems (Table IV), but again this did not differ significantly from the proportion in the general population. In children, we found no clinical problem clusters, when scored by themselves or by the parents (Table V) (except once "social problems" rated by the parents). When comparing the Achenbach results between the groups with or without thought disorder we did not find any significant differences.

Subjects reported very few problems on the Achenbach Self Report questionnaires, and the proportion with scores in the clinical range did not differ from the normal population. The degree of agreement between the ratings by the parents and by the patients (self report) was in the average range.

Social and Professional Functioning

Eleven patients (41%) were (or had been) attending mainstream education schools, 16 (59%) (had) attended special education schools. In the general Flemish population, 3.89% of teenagers attend special education secondary schools (source: ond.vlaanderen.be/onderwijsstatistieken 2005–2006). Hence, in our group we found a 15-fold increase in attendance of special school services compared to the general population. Eleven subjects had completed school or had dropped out early from school, and were working or looking for a job; none of them had a job (or were searching for a job) on the regular job market. Fifteen subjects (51.85%) had a "satisfactory" social, life, which we defined clinically in comparison to matched individuals of the same age, taking into account their general somatic and psychosocial condition. Six subjects (22.22%) were in a more or less stable relationship; none of them had a psychiatric diagnosis at the moment of this study.

Subjects with a psychiatric diagnosis were receiving or had been receiving special education significantly more often than subjects without psychiatric diagnosis: 13 in 15 (86.66%), respectively 4 in 12 (33.33%) (chi-square: $P = 0.004$). We observed a similar but non-significant trend for special education and the presence of thought disorder: 8 in 10 subjects (80%) with thought disorder had attended special education, while 9 in 17 (52.94%) had attended special education in the group without thought disorder (chi-square $P = 0.16$). Also, in the thought disorder group 2 subjects (20%) had a "satisfactory" social life, while this was the case for 12 in 17 subjects (70.58%) without thought disorder (chi-square: $P = 0.011$) (Table VI).

The social functioning scores according to the Achenbach questionnaires of both adults and children did not reveal any additional data.

TABLE III. Number of Clinical Cases in 27 Patients for Internalizing, Externalizing, and Total Problem Score

	Internalizing	Externalizing	Total
Self report	2	1	1
Parent report	9 (33%); $P < 0.001$	2	4

DISCUSSION

We investigated the presence of a high incidence of *delusional and psychotic disorders* in adolescents and young adults with juvenile Myotonic Dystrophy type-1 (DM1). Our clinical impression of an unusually high prevalence of delusional and psychotic disorders in the juvenile DM patients known at the Centre for Human Genetics was confirmed: 10 out of 27 subjects (37%) met DSM-IV criteria for either Delusional Disorder or Psychotic Disorder not otherwise specified. To our knowledge this had not been demonstrated before. The patients had all been referred to our Centre and diagnosed with DM1 years before, for physiological problems but not for psychiatric problems (only one patient was referred because of psychiatric symptoms). The subjects with a thought disorder at the moment of assessment seemed to have developed it during their teenage years. Guided by our hypothesis we explicitly assessed our patients for symptoms related to delusional and psychotic disorders during the standard clinical psychiatric interview. One of the two interviewers was not aware of the patients' complaints and psychiatric history and we assume this limited the ascertainment bias (DJ conducted the interviews and all the answers and clinical diagnoses were discussed with JS as a supervisor).

Delusional disorder has an estimated prevalence of only 0,03% in the general population [Smith and Buckley, 2006] and the age of onset is generally in the mid- to late 30s. It mostly has an insidious onset and functioning tends to be preserved [Sadock and Sadock, 2005]. The lifetime prevalence of all psychotic disorders has been reported to be 3.06%, and 0.18% for delusional disorder [Perälä, 2007].

Other quite frequent psychiatric diagnoses in our group of juvenile DM patients are ADHD and ASD. This finding is partly

TABLE IV. Number of Clinical Cases for Each Pproblem Cluster in 20 Adults, Self Report (ASR), and Parent Report (ABCL)

	Anxious/depressed	Withdrawn	Somatic problems	Thought problems	Attention problems	Aggressive	Rule breaking	Intrusive
Self	1	1	0	1	0	0	0	0
Parent	3	2	2	0	0	0	0	0

a replication of findings of earlier studies mentioned above on the psychiatric diagnoses in children with juvenile DM. In contrast with these studies (e.g., 25% of anxiety disorders in Steyaert et al., 2000) we did not encounter any patient with an anxiety disorder. This corresponds to the general clinical finding that most children with anxiety disorders do not have an anxiety disorder in adulthood [Rutter, 1994].

Two patients both had ASD and a delusional disorder. This disorder was of the grandiose type, while in autistic persons *without* DM, systematised delusions are rare: an affective deregulation caused by environmental stress usually precedes a psychotic decompensation in the autistic population. The thoughts generally continue to be hyperformal and logical, although idiosyncratic [Peeters and Vertommen, 2007].

The mean level of *clinically assessed global, social, educational and professional functioning* of our patients, as defined by the DSM-IV Global Assessment of Functioning, was low (in accordance with Perron et al., 1989) and there was a significant difference in functioning between the group with thought disorder and the one without thought disorder.

The *ASEBA questionnaires* revealed a significantly higher prevalence of internalising problems for the entire group of juvenile DM1 patients. When comparing the Achenbach results between the groups with or without thought disorder we didn't find any significant differences. The Achenbach scores for social and professional functioning did not reveal any supplementary interesting information because they were higher than our own clinical rates on functioning. Both our patients and their parents seemed to overestimate the functioning of the affected young people in comparison to average young people.

We had the clinical impression that patients and their parents *experienced* the patient's muscular handicap *as less impairing* than clinically assessed. In patients with the adult form of DM, previous studies mentioned above found avoidant personality traits (e.g., Meola et al., 2003) and a certain type of emotional deficit [Bungener et al., 1998], the latter being contributed by the authors to either an adaptive reaction to the fact of suffering from a progressive disease, or to the effect of the CNS lesions in DM, or to both. We wonder whether our patients' different experience of their impairment should be considered as a lower degree of self-evaluation capacities (a function of (pre)frontal areas thought to be involved in the pathophysiology of DM as described above), or rather an adaptive way of coping with an impairing and potentially life-threatening disease. The parents' underestimation of the impairment of their children with juvenile DM was even more enigmatic. We suppose that the smoothly progressive effects of the DM disease on the patients' somatic and psychic health and on their functioning might imply that parents "grow" into it, in the sense that their expectations and norms are gradually adapted to the health status of their children. Another explanation may be that one parent of each couple of parents suffers from DM1 himself of herself, and for this reason might display the same lower degree of self-evaluation capacities or the same type of predominant coping strategy as hypothesised for DM patients in the research above mentioned. Ekstrom et al. [2008] similarly noticed a tendency in parents to recognize and report fewer symptoms and problems in the interviews than what was clinically observed.

About the *causes of delusional disorders* very little is known [Munro, 1999; Sadock and Sadock, 2005] and existing theories primarily focus on persecutory delusions. Psychodynamic theories postulate that paranoia is a protective psychological response to different types of stress or conflict that represent a profound threat to self-esteem or to the self, which might be the case in a life-threatening disease, especially when experienced somatic and/or psychic health is low or when general functioning is compromised by the disease. Research by cognitive psychologists suggests that people with persecutory delusions show perceptual and cognitive anomalies (they would selectively attend to threatening information, jump to conclusions on the basis of insufficient information, attribute negative events to external personal causes, and have difficulty in envisaging others' intentions and motivations).

It would be interesting to compare our results to findings in patients with other neurological and motor diseases.

Concerning the *implications* of the diagnosis of a delusional disorder, there is little research to rely on: there are no randomised

TABLE V. Number of Clinical Cases for Each Problem Cluster in Seven Children, Self Report (YSR), and Parent Report (CBCL)

	Anxious/depressed	Withdrawn	Somatic problems	Thought problems	Attention problems	Aggressive	Rule breaking	Social problems
Self	0	0	0	0	0	0	0	0
Parent	0	0	0	0	0	0	0	1

TABLE VI. Clinically Obtained Number and Percentage on 27 Subjects of Level of Functioning in Matters of: Educational Level —Having a Stable Relationship with a Partner—Engagement

	N = 27 n (%)	
Mainstream education	11	(41)
Relationship with partner	6	(22)
Social life	14	(52)
Regular job market	Not at school (N = 11)	Still at school (N = 16)
	0 (0)	/

controlled trials on psychopharmacological treatment [Skelton et al., 2015] and only one small RCT study on cognitive-behavioral treatment [O'Connor et al., 2007]. It is suggested that antipsychotics could be efficacious, but, due to their lack of insight in their condition and of experienced impairment, patients rarely present themselves voluntarily for treatment.

This study has several *limitations*. We used a cross-sectional design and did not compare our patient group to a clinical contrast group. The functioning of our subjects was not measured by a specific questionnaire but clinically assessed. DJ was the interviewer of the participants while JS as DJ's supervisor discussed these interviews with DJ; JS was the participants' treating physician professional who was aware of the previous psychiatric history. However, because this research is to our knowledge the first to demonstrate the high prevalence of thought disorders in juvenile DM1, our results are valuable as they have important clinical implications. As such, our study can form the basis for further research into the prevalence of thought disorders in juvenile DM1 by using a longitudinal design.

CONCLUSION

Our finding of an unusually high prevalence of thought disorders (delusional disorder and psychotic disorder not otherwise specified) in juvenile DM1 can be of clinical importance in two ways. First, clinicians should consider the presence of juvenile DM1 in adolescents and young adults presenting with only the psychiatric symptoms of disturbances of thought content. Second, it is advised to systematically investigate the presence of thought disorders in patients with juvenile DM. Inquiring about symptoms of thought disorders is often not a part of a routine psychiatric interview. Nevertheless, we demonstrated that this group functions at a significantly lower level than juvenile DM patients without a thought disorder. For this reason it is of clinical interest to detect this particular subgroup of patients, even more so because thought disorders are potentially treatable conditions.

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REFERENCES

Achenbach T, Rescorla L. 2001. Manual for the ASEBA School-Age Forms & Profiles. Burlington, VT: University of Vermont, Research Center for Children, Youth & Families (Dutch translation: Verhulst FC & van de Ende J. Erasmus MS—Sophia Kinderziekenhuis, Postbus2060, 3000 CB Rotterdam, www.aseba.nl).

Achenbach T, Rescorla L. 2003. Manual for the ASEBA Adult Forms & Profiles. Burlington, VT: University of Vermont, Research Center for Children, Youth & Families (Dutch translation: Verhulst FC & van de Ende J. Erasmus MS—Sophia Kinderziekenhuis, Postbus 2060, 3000 CB Rotterdam, www.aseba.nl).

American Psychiatric Association. 2000. Diagnostic and Statistical Manual of Mental Disorders, 4th edition, Text Revision (DSM-IV-TR), 4e. Arlington, VA: American Psychiatric Association.

Angeard N, Gargiulo M, Jacquette A, Radvanyi H, Eymard B, Héron D. 2011. Cognitive profile in childhood myotonic dystrophy type 1: Is there a global impairment? Neuromuscul Disord 17:451–458.

Antonini G, Soscia F, Giubilei F, De Carolis A, Gragnani F, Morino S, Ruberto A, Tatarelli R. 2006. Health-related quality of life in myotonic dystrophy type 1 and its relationship with cognitive and emotional functioning. J Rehabil Med 38:181–185.

Brook JD, McCurrach ME, Harley HG, Buckler AJ, Church D, Aburatani H, Hunter K, Stanton VP, Thirion J-P, Hudson T, Sohn R, Zemelman B, Snell RG, Rundle SA, Crow S, Davies J, Shelbourne P, Buxton J, Jones C, Juvonen V, Johnson K, Harper PS, Shaw DJ, Housman DE. 1992. Molecular basis of myotonic dystrophy: Expansion of a trinucleotide (CTG) repeat at the 3′ end of a transcript encoding a protein kinase family member. Cell 68:799–808.

Brumback R. 1987. Disturbed personality and psychosocial adjustment in myotonic dystrophy: Relationship to intellectual/cognitive function and underlying affective disorder (depression). Psychol Rep 60:783–796.

Bungener C, Jouvent R, Delaporte C. 1998. Psychopathological and emotional deficits in myotonic dystrophy. J Neurol Neurosurg Psychiatry 65:353–356.

Censori M, Danni L, Del Pesce M, Provinciali L. 1990. Neuropsychological profile in myotonic dystrophy. J Neurol 237:251–256.

Craddock M, Asherson P, Owen MJ, Williams J, McGuffin P, Farmer AE. 1996. Concurrent validity of the OPCRIT diagnostic system. Comparison of OPCRIT diagnoses with consensus best-estimate lifetime diagnoses. Br J Psychiatry 169:58–63.

Darin N, Tulinius M. 2000. Neuromuscular disorders in childhood: A descriptive epidemiological study from western Sweden. Neuromuscul Disord 10:1–9.

de Die-Smulders CE. 2004. Congenital and childhood-onset myotonic dystrophy. Myotonic dystrophy: Present management, future therapy. Oxford: Oxford University Press. pp 162–175.

Delaporte C. 1998. Personality patterns in patients with myotonic dystrophy. Arch Neurol 55:635–640.

Douniol M, Jacquette A, Cohen D, Bodeau N, Rachidi L, Angeard N, Cuisset J-M, Vallée L, Eymard B, Plaza M, Héron D, Guilé J-M. 2012. Psychiatric and cognitive phenotype of childhood myotonic dystrophy type 1. Dev Med Child Neurol 54:905–911.

Duveneck MJ, Portwood MM, Wicks JJ, Lieberman JS. 1986. Depression in myotonic muscular dystrophy. Arch Phys Med Rehabil 67:875–877.

Ekstrom A-B, Hakenäs-Plate L, Samuelsson L, Tulinius M, Wentz E. 2008. Autism spectrum conditons in myotonic dystrophy type 1: A study on 57 individuals with congenital and childhood forms. Am J Med Genet Part B 147B:918–926.

Fu Y-H, Pizzuti A, Fenwick G, Jr., King J, Rajnarayan S, Dunne PW, Pubel J, Nasser GA, Ashizawa T, De Jong P, Wieringa B, Korneluk R, Perryman MB, Epstein HF, Thomas Caskey C. 1992. An unstable triplet repeat in a gene related to myotonic muscular dystrophy. Science 255:1256.

Goossens E, Steyaert J, de Die-Smulders C, Willekens D, Fryns J-P. 2000. Emotional and behavioral profile and child psychiatric diagnosis in the childhood type of myotonic dystrophy. Genet Couns 11:317–327.

Granö N, Kallionpää S, Karjalainen M, Roine M, Ranta K, Heinimaa M. 2016. Discrepancy between self-reported and interviewed psychosis risk symptoms: Auditory distortions are the most reliably reported symptom by self-report. Early Intervent Psychiatry 10(2):129–136.

Harley HG, Rundle SA, MacMillan JC, Myring J, Brook JC, Crow S, Reardon W, Fenton I, Shaw DJ, Harper PS. 1993. Size of the unstable CTG repeat sequence in relation to phenotype and parental transmission in myotonic dystrophy. Am J Hum Genet 52:1164–1174.

Harper P, Rudel R. 1994. Myotonic dystrophy. In: Nagel AG, Franzini-Armstrong M, editors. Myology. New York: McGraw-Hill.

Harper P, van Engelen B, Eymard B, Wilcox D. 2004. Myotonic dystrophy: Present management, future therapy. New York: Oxford University Press.

Harper P. 2001. Myotonic dystrophy, 3rd edition. London: WB Saunders.

Hunter A, Tsilfidis C, Mettler G, Jacob P, Mahadevan M, Surh L, Korneluk R. 1992. The correlation of age of onset with CTG trinucleotide repeat amplification in myotonic dystrophy. J Med Genet 29:774–779.

Liquori CL, Ricker K, Moseley ML, Jacobsen JF, Kress W, Naylor SL, Day JW, Ranum LPW. 2001. Myotonic dystrophy type 2 caused by a CCTG expansion in intron 1 of ZNF9. Science 293:864–867.

Mahadevan M, Tsilfidis C, Sabourin L, Shutler G, Amaniya C, Jansen G, Neville C, Narang M, Barcelo J, O'Hoy K, Leblond S, Earle-MacDonald J, De Jong PJ, Wieringa B, Korneluk RG. 1992. Myotonic dystrophy mutation: An unstable CTG repeat in the 3′ untranslated region of the gene. Science 255:1253.

Meola G, Sansone V, Perani D, Scarone S, Cappa S, Dragoni C, Cattaneo E, Cotelli M, Gobbo C, Fazio F, Siciliano G, Mancuso M, Vitelli E, Zhang S, Krahe R, Moxley R. 2003. Executive dysfunction and avoidant personality trait in myotonic dystrophy type 1 (DM-1) and in proximal myotonic myopathy (PROMM/DM-2). Neuromuscul Disord 13:813–821.

Modoni A, Silvestri G, Grazia Pomponi M, Mangiola F, Tonali PA, Marra C. 2004. Characterization of the pattern of cognitive impairment in myotonic dystrophy type 1. Arch Neurol 61:1943–1947.

Monckton D, Ashizawa T. 2004. Molecular aspects of mytonic dystrophy: our current understanding. In: Harper P, van Engelen B, Eymard B, Wilcox D, editors. Oxford: Oxford University Press. pp 14–38.

Munro A. 1999. Delusional disorder: Paranoia and related illnesses. Cambridge: Cambridge university press.

O'Connor K, Stip E, Pélissier M-C, Aardema F, et al. 2007. Treating delusional disorder: A comparison of cognitive-Behavioural therapy and attention placebo control. Can J Psychiatry 52:182–190.

Peeters W, Vertommen S. 2007. Autismespectrumstoornissen en relevante differentiaaldiagnostiek bij normaalbegaafde volwassenen: Diagnostische overwegingen aan de grens van het spectrum. Tijdschrift Klinische Psychologie 37:45–59.

Perälä J. 2007. Lifetime prevalence of psychotic and bipolar I disorders in a general population. Arch Gen Psychiatry 64:19–28.

Peric S, Sreckov M, Basta I, Lavrnic D, Vujnic M, Marjanovic I, Rakocevic Stojanovic V. 2014. Dependent and paranoid personality patterns in myotonic dystrophy type 1. Acta Neurol Scand 129:219–225.

Perron M, Veillette S, Mathieu J. 1989. [Myotonic dystrophy: I. Socioeconomic and residential characteristics of the patients]. Can J Neurolog Sci 16:109–113.

Ricker K, Koch MC, Lehmann-Horn F, Pongratz D, Otto M, Heine R, Moxley RT. 1994. Proximal myotonic myopathy: A new dominant disorder with myotonia, muscle weakness, and cataracts. Neurology 44:1448–1448.

Rutter M, et al. 1994. Child and adolescent psychiatry: modern approaches, 3rd edition In: Michael R, et al, editor. London: Blackwell.

Sadock BJ, Sadock VA. 2005. Kaplan and Sadock's Comprehensive textbook of psychiatry 8th edition. Philadelphia: Lippincott Williams and Wilkins.

Schneider-Gold C, Bellenberg B, Prehn C, Krogias C, Schneider R, Klein J, Gold R, Lukas C. 2015. Cortical and subcortical grey and white matter atrophy in myotonic dystrophies type 1 and 2 is associated with cognitive impairment, depression and daytime sleepiness. PLoS One 10:e0130352.

Sistiaga A, Urreta I, Jodar M, Cobo AM, Emparanza J, Otaegui D, Poza JJ, Merino JJ, Imaz H, Martí-Massó JF, López de Munain A. 2010. Cognitive/personality pattern and triplet expansion size in adult myotonic dystrophy type 1 (DM1): CTG repeats, cognition and personality in DM1. Psychol Med 40:487–495.

Skelton M, Khokhar WA, Thacker SP. 2015. Treatments for delusional disorder. In: Cochrane Database of Systematic Reviews. John Wiley & Sons, Ltd.

Smith DA, Buckley PF. 2006. Pharmacotherapy of delusional disorders in the context of offending and the potential for compulsory treatment. Behav Sci Law 24:351–367.

Steyaert J, Umans S, Willekens D, Legius E, Pijkels E, de Die-Smulders C, Van den Berghe H, Fryns J-P. 1997. A study of the cognitive and psychological profile in 16 children with congenital or juvenile myotonic dystrophy. Clin Genet 52:135–141.

Steyaert J, De Die-Smulders C, Fryns J-P, Goossens E, Willekens D. 2000. Behavioral phenotype in childhood type of dystrophia myotonica. Am J Med Genet 96:888–889.

Verhulst F, Van der Ende J, Koot H. 1991. Handleiding voor de CBCL/4-18.

Wechsler D. 2004. WAIS-III-Nederlandstalige bewerking.

Winblad S, Lindberg C, Hansen S. 2005. Temperament and character in patients with classical myotonic dystrophy type 1 (DM-1). Neuromuscular Disord 15:287–292.

Winblad S, Lindberg C, Hansen S. 2006. Cognitive deficits and CTG repeat expansion size in classical myotonic dystrophy type 1 (DM1). Behav Brain Funct 2:16.

Winblad S, Jensen C, Månsson J-E, Samuelsson L, Lindberg C. 2010. Depression in Myotonic Dystrophy type 1: Clinical and neuronal correlates. Behav Brain Funct 6:25.