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ABSTRACT

INTRODUCTION: Youths with severe and persistent irritability have a particularly high rate of school failures and learning difficulties. The aim of this study was to determine whether inpatient adolescents with Disruptive Mood Dysregulation Disorder (DMDD) have more motor and/or language impairments compared to patients with other psychiatric disorders.

METHODS: A retrospective chart review of all consecutive cases admitted in two adolescent inpatient units between January 2017 and December 2018 was conducted (N=191). All patients received multi-disciplinary clinical and developmental assessments. For a subtest of subjects, additional standardized tests were used to document motor and language impairments. In this clinical chart 53 adolescents with a DMDD (mean age 13.6 ± 1.5, min 12, max 16, 70% males) were compared to patients with a major depressive disorder (MDD, n=64, mean age 15.3 ± 1.6, 52% males) and patients with a non-mood disorder (NMD, n=61, mean age 14.4 ± 1.55, 59% males).

RESULTS: Among inpatients with DMDD, 71% had an associated motor and/or language disorder, with combined forms in around two-thirds of cases. Compared to youths with MDD, participants with DMDD were more likely to have an associated developmental coordination disorder (67% vs. 22%, *OR*=4.7) and a written language disorder (35% vs. 10%, *OR*=4.6). While 31% of inpatients with DMDD had an associated communication/oral language disorder, this rate was not statistically different from those observed in the MDD group (11%, *OR*=3.2). The frequencies of motor and language impairments were not statistically different between participants in the DMDD group and in the NMD group.

CONCLUSION: The high rate of motor and written language disorders found in DMDD patients may partly account for their academic difficulties. Such finding, if confirmed, supports

systematic screening of motor and written language impairments in youths with chronic irritability and suggests remediation potential.

KEYWORDS: disruptive mood dysregulation disorder, chronic irritability, hospitalization, language disorder, communication disorder, learning disabilities, motor disorder, developmental coordination disorder, cognitive impairments, depressive disorder

1. INTRODUCTION

1.1.General information about DMDD

The Disruptive Mood Dysregulation Disorder (DMDD) is a childhood-onset psychiatric disorder newly included in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) [1]. Youths with DMDD suffer from having a chronically irritable mood associated with repeated temper outbursts disproportionate for the developmental level. While the prevalence of DMDD is around 0.8-3.3% in the general population, it is overrepresented in mental health care services, with rates between 8% and 31% across sites [2]. Such a discrepancy is not very surprising as irritability, the core symptom of DMDD, is one of the most common reasons caregivers bring youths to outpatient treatment [3].

1.2.School impairments in DMDD patients

A high level of impairments in school functioning was constantly reported in youths with DMDD in community-based and clinical studies [4-8]. Margulies et al. [8] noted that children with DMDD are eight times more likely to report any problem with his/her teachers and nine

times more likely to be suspended from school compared to healthy children. Other reports have shown that youths with DMDD have lower academic performance compared to youths with other psychiatric disorders [4-7]. The academic difficulties reported by children with DMDD sometimes persist into adulthood. Copeland et al. [9] showed that young adults who received a diagnosis of DMDD at age 10 were about twice as likely to fail to receive a high school diploma and to not go to college compared to those with another childhood-onset psychiatric disorder.

Several factors may affect the level of school functioning in youths with DMDD. School problems may be directly related to child's symptoms. For example, irritability and associated behaviors (e.g., reactive aggressive behavior) could affect the child's relationships with teachers and others schoolmates which could result in persisting conflicts within the classroom making it difficult to ensure a secure and supportive learning environment. Other co-occurring factors associated with DMDD could influence academic success in these patients, such as parental psychiatric problems [7], a high rate of psychosocial adversity and socio-economic difficulties [4], or comorbid psychiatric/developmental disorder [5,10]. Among these factors, the co-occurrence of developmental/learning disabilities are particularly worth identifying in these patients as they represent treatable conditions resulting in educational improvement when adequately addressed.

1.3.*Learning/developmental difficulties in youths with chronic irritability*

Surprisingly, few studies have examined the relationship between DMDD and developmental/learning disorders except for attention deficit disorder [11]. Preliminary evidence for a possible association between DMDD and learning disabilities was gained from case-series [12], chart-review studies [7,13] and epidemiological study [4]. In a large cross

sectional community-based study conducted in 6,483 adolescents, Althoff, et al. (2016) found that parents of adolescents with DMDD symptoms were 1.7 times more likely to report a history of learning difficulties in their child compared to parents of children with an anxiety disorder, a bipolar disorder or an attention deficit disorder. Carlson et al. [12] reported that among inpatients those with any rages were 5.5 times more likely to present a learning/language disorder compared to those without (83% vs. 47%). As noted by the authors, the lack of awareness of learning/developmental disabilities in patients with chronic emotional dysregulation may represent a missed opportunity to provide remediation interventions and ultimately to gain clinical improvement.

Previous studies have shown that youths with chronic irritability performed poorer in stop-signal task, a psychological task measuring motor inhibition, compared to children with other psychiatric disorders [14,15]. Whether difficulties in other components of motor skill (e.g., fine motor skill, imitation, visuo-spatial abilities) exist in youths with chronic irritability has never been investigated. Children with poor motor skills may be more likely to experience chronic negative mood, in particular in school, in response to repeated learning difficulties or peer rejection [16]. However, for children with poor motor skills and depressed mood the exclusion from certain activities involving motor cooperation could result in missed opportunities to refine their emotional regulation strategies in an extra-familial context [17]. Motor remediation or interventions enhancing participation with peers could be useful in this context to break the vicious circle of rejection, depressed mood and poor emotional regulation.

Several lines of research suggest that language difficulties are worth investigating in youths with chronic irritability. Child language delays and behavior problems, especially those involving poorly regulated anger, have been found to be associated both in clinical and non-clinical samples [18-20]. Longitudinal studies have shown direct evidence for relations among growth in language skills, decline in anger reactivity, and increase in self-regulatory strategy

use [21,22]. In the same way, several interventions that teach children to use words to deal with frustration or to improve emotional categorization have shown a positive impact on socio-emotional competence [23,24].

As reading and writing are involved in almost all learning activities in schools, difficulties in these domains could contribute to the high rate of academic failure observed in youths with DMDD. The emergence of reading and writing skills involves the integrity of several acquired competences in language (e.g., phonological awareness) and motor domains (e.g., visuo-spatial, fine motor skill). It is therefore likely that difficulties in one of these domains could affect reading/writing performances.

1.4.*Aims of the study*

We used a retrospective chart review to determine the frequencies of motor and/or language developmental difficulties in inpatients with DMDD. Such developmental difficulties were measured in three ways: (i) the frequency of parent-reported delay and/or abnormal development in the domain considered, (ii) the frequency of associated diagnoses of developmental coordination disorder, communication/oral language disorder, and written language disorder and, (iii) the description of the detailed motor and/or language tests performed in a subset of patients prior or during the hospitalization. Inpatient adolescents with DMDD were compared to inpatients with Major Depressive Disorder without DMDD (MDD group) and to inpatients with non-mood disorder without DMDD (NMD, mainly psychotic and severe neurodevelopmental disorders). We hypothesized that the rate of developmental motor and language disorders would be higher in the DMDD group compared to the MDD group. No apriori-hypothesis was made for the difference between the DMDD and the NMD groups. We expected that DMDD youths would show impairments in multiple developmental domains, i.e.,

many of these patients having a combined form of developmental impairments in line with the observation provided by Carlson et al. [12]. Using an exploratory approach, the difficulties in several components of motor and language abilities were examined in the subsample of DMDD patients who had standardized tests:

- For motor development we paid particular attention to perceptive and motor abilities involved in the development of children's socio-emotional competence: motor imitation involved in contingent early-interaction with caregivers and later with peers [25,26]; fine motor ability [27], and visuo-spatial skill involved in cognitive perspective-taking [17].
- For oral language development, we examined specifically the semantic component of spoken language (vocabulary understanding), considering the relation between lexical enrichment and emotional regulation competencies reported [28,29]. While other aspects of language typically affected in communication/oral language disorder such as phonological awareness and syntax were also examined, the pragmatic component of language was not.
- For written language, we in particular examined the speed and the quality of the reading and the writing, regarded to be strong predictors for school performances [30,31].

2. METHODS

2.1.Study design and setting

Data from the medical records of all patients hospitalized between January 1, 2017 to December 31, 2018 in the two adolescent units of the child and adolescent psychiatric department of a tertiary university care center were extracted (N = 191). Two researchers (a

psychologist and a resident in psychiatry) used a 72-item computerized questionnaire to extract relevant information based on all clinical and paramedical charts available. All data was cross-checked by the senior psychiatrist who directly cared for each adolescent. The inter-rater reliability of the chart review instrument based on the analysis of ten randomly selected files was good ($\kappa = .80$). The data collected encompassed (i) socio-demographic characteristics, (ii) clinical features and symptom severity, (iii) developmental history and associated medical conditions, (iv) school functioning and psychosocial factors. The levels of functioning and symptom severity were assessed using questionnaires routinely used in the units: the Children-Global Assessment of Functioning scale (C-GAF) [32], the Clinical Global Impressions-Severity scale (CGI-S), and the CGI-Improvement Scale (CGI-I) [33]. The study followed general recommendations for retrospective chart review [34]. This project was designated as IRB exempt due to its retrospective design, patient de-identification, and the use of routine questionnaires.

2.2.*Participants*

We used a two-step procedure for the diagnostic of DMDD. Firstly, we carefully reviewed all charts searching for symptoms of chronic irritability (i.e., persistent irritable mood *and/or* anger feeling *and/or* impulsive/reactive/hostile aggressive behavior, *and/or* temper tantrums, for at least 12 months). We also examined the list of patients who required seclusion and/or intra-muscular treatment during the study period. Secondly, clinical data of inpatient adolescents positively screened were abstracted using a specific instrument based on the criteria for the *temper dysregulation disorder with dysphoria*, a research entity developed by the DSM-5 Task Force prior to the publication of the final DMDD criteria [35]. Each item was endorsed as *present* or *absent* or *unknown*. The final diagnostic was endorsed only if participants matched all diagnostic criteria, including duration criteria, cross-domain impairment, and age of onset

(Table S1). The psychometric properties of this *ad-hoc* diagnostic section for DMDD were explored in another sample of 12 to 15 year-old outpatients (internal validity Chronbach's α=0.90, test-retest reliability κ =.87) [36]. All other diagnoses were based on discharge diagnoses and follow the DSM-5 formulation [1].

[Insert Figure 1 about here]

2.3. Measurements

All patients hospitalized in the adolescent units received a multidimensional psychiatric and developmental assessment based on repeated family interviews, clinical interviews and observations of participants in various contexts, including in the hospital school center. Standardized assessments performed prior to the hospitalization were systematically collected and reread.

In-depth motor assessment encompassed four standardized tests ascertaining different components of motor activity:

- The Movement Assessment Battery for Children 2nd edition (MABC-2) is a comprehensive measurement of motor skills used for the detection of movement difficulty in children [37] or as a diagnostic tool for developmental coordination disorder [38]. The test comprises 11 items grouped in 3 subtests: *Manual Dexterity*, *Aiming and Catching*, and *Balance*. The raw scores are converted to percentile rank: a score between the 6th and 15th percentile represents a risk of having a movement difficulty and a score at or below the 5th percentile represents significant movement difficulty. Psychometric properties are good and MABC-2 AB3 version was standardized for youths between 3-16 years.
- The Developmental Test of Visual Perception, 2nd edition (DTVP-2) is a

comprehensive visual-perceptual evaluation [39] which encompasses eight subtests that measure different visual perceptual and visual-motor parameters. The raw scores are calculated as the sum of each subtest, which can be converted into percentiles. Sums of standard scores can be converted to two composite quotients: the motor-reduced visual perception quotient (visual-cognitive aspect) and the visual-motor integration quotient (visual-motor aspect). Psychometrics properties of the DTPV-2 are good [39,40], and the scores were standardized for youths between 4-10 years.

- The Manual and Digital Gnosopraxia Test (EMG) is a specific measure of manual praxis based on gesture imitation for hands and digits [41]. This is a modified version of Bergès, Lézine [42]. A total composite score is based on success rate for gesture imitation and motor planification.
- The Brief assessment of writing skill in adolescent (BHK-ado) [30] is a French adaptation for adolescents of the BHK test created by Hamstra-Bletz [43]. The test consists of a copy of a standardized test during five minutes on a blank paper. Analyses of writing ability is based on nine items measuring the quality of the writing and speed. Psychometric properties were assessed in a French sample of adolescents [44].

In-depth language assessment encompassed several tests ascertaining different components of language activity. For oral language, phonological skill was measured based on the performances at two items (repetition of the logatom, suppression of the last phonem) of the *Evaluation des Fonctions cognitives et des Apprentissages* (EDA) [45]. Syntax and morphology skills were ascertained based on two items of the EDA (syntax understanding, sentence completion). The semantics component of oral language was assessed in two ways: with two items of the EDA for the receptive domain (lexical understanding, picture designation) and with the Peabody Picture Vocabulary Test (PPVT) [46] for the expressive domain. Different tests were used for the assessment of written language. Reading skills were ascertained with the

LMC-R test [47], the *L2MA-2* test [48], *Odédys 2* [49] or *Evaléo 6-15* [31]. Writing skills were based on two items of the EDA (dictation and text transcription), *Alouette-R* test [50] or the *Batterie d'Evaluation de la Lecture et de l'Orthographe* (*BELO) test* [51]. The choice of the appropriate test was left to the speech therapist.

The indication for performing additional tests (e.g., sensory-processing, attentional, logico-mathematic) was discussed case-by-case during weekly multidisciplinary meetings (including two child psychiatrists, a psychologist, a motor therapist, a speech therapist and two schoolteachers). The scores at the different tests were standardized based on the scores of typically developing same-age adolescents' performances such as provided by manuals. Results were reported as Standard Deviation (SD) or percentile. Standard errors have been transformed in confidence intervals to facilitate the interpretation of the results. When several standardized assessments were available, only the last one was reported.

2.4.*Statistical analyses*

For the description of the sample, ANOVA or Kruskall-Wallis tests were used to compare quantitative variables and Chi-squared or Fisher's exact tests for qualitative variables, depending on assumptions validity. Quantitative variables were described using mean and standard deviation and qualitative variables using number and percentage of occurrences. Odd-Ratios (*OR*) were presented with their confidence intervals and Cramer's ϕ (Phi) correlation coefficients for effect sizes.

To document the association between motor impairments and DMDD, a Fisher's exact test was used to compare the proportions of inpatient adolescents with developmental coordination disorder between the DMDD group, the MDD group, and the NMD group. A similar analysis was performed to compare the proportions of parent-reported delays in motor development

between the DMDD, MDD, and NMD groups. Univariate analyses were used to describe the results of the battery of motor tests conducted in the subset of inpatients with DMDD who had in-depth motor assessment (n=24).

To document the association between language impairments and DMDD, a Fisher's exact test was used to compare the proportions of inpatient adolescents with communication/oral language disorder and written language disorder between the DMDD group, the MDD group, and the NMD group. A similar analysis was performed to compare the proportions of parent-reported delays in language development between the DMDD, MDD, and NMD groups. Univariate analyses were used to detail the results of the battery of language tests conducted in the subset of inpatients with DMDD who had in-depth language assessment (n=29).

Analyses were run on R 3.4.0 and a p-value less than 0.05 was considered significant. Applying the Bonferroni correction for planned comparisons for the first two aims of the study this p-value was divided by 15. The corrected threshold for statistical significance was therefore 0.0038. We proceeded to subgroups analyses to determine whether the rates of developmental motor and language disorders differed in DMDD patients with regards to the ADHD status (Table S2).

3. RESULTS

3.1.Description of the sample

Among the 191 inpatient adolescents consecutively admitted during the study period, 67 were positively screened for chronic irritability and 53 matched all criteria for DMDD. All inpatients with chronic irritability without DMDD (n=14, Mean age 14.4 ± 1.9, 64% males) had severe neurodevelopmental conditions and/or chronic psychiatric disorders (intellectual

disability n=11, autistic spectrum disorder n=4, organic neurological disorder n=7, schizophrenia disorder n=2, bipolar disorder n=3, chronic tic disorder n=1).

As presented in Table 1, inpatients with DMDD were mostly boys and were younger than inpatients in the MDD and NMD groups. The most frequent psychiatric disorders associated with DMDD were disruptive behavioral disorder, anxiety disorder and attention deficit disorder. The C-GAF score at admission, the CGI-S score, and the CGI-I score were not statistically different among the three groups.

[Insert Table 1, about here]

3.2.Motor developmental difficulties

In our clinical chart, 67% of the DMDD inpatients had an associated developmental coordination disorder which represents 80% of those who had in-depth motor assessment (23/29) and 20% of those who did not (5/24). The rate of developmental coordination disorder was higher in the DMDD group than in the MDD group (*OR*= 4.66 95% CI: 2.09, 10.41, ϕ = .32, $p < .001$) but was not statistically different from the NMD group (*OR*= 1.76 95% CI: 0.84, 3.70, $\phi = .29$, $p = .559$) (Table 2). The frequency of parent-reported delay and/or abnormal motor development was higher in the DMDD group compared to the two other groups.

Inpatient adolescents with DMDD who had in-depth motor assessment had problematic scores in tests measuring fine motor skills such as the EMG manual imitation score and the sub-score of the MABC-2 for manual dexterity. They had scores in the normal range for the tests ascertaining gross motor skills (i.e., the MABC-2 total score) and visuo-spatial skills (i.e., the DTVP-2) and scored low in the BHK-ado, a test of graphism and writing ability.

[Insert Table 2, about here]

[Insert Table 3, about here]

3.3. Language developmental difficulties

In our clinical chart, 31% of the DMDD inpatients had an associated communication/oral language disorder; this represent 47% of those who had in-depth language assessment (11/24) and 0% of those who did not (0/29). Considering corrected p-value, the rate of communication/oral language disorder was not statistically different between the DMDD and the MDD groups (*OR*= 3.21 95% CI: 1.20, 8.61, ϕ = .22, *p*= .019) or between the DMDD and the NMD group (*OR*= 1.61 95% CI: 0.67, 3.84, ϕ = .15, *p*= .367) (Table 2). Parent-reported delay and/or abnormal language development were not statistically different among the three groups.

As presented in Table 4, inpatients with DMDD who had in-depth language assessment had low scores in tests measuring phonological awareness (repetition of logatom, suppression of the last phonem), syntax and sematic expression (sentence completion, picture denomination). However, tests measuring the receptive component of spoken language (lexical understanding, picture designation, syntax understanding) were in the normal range.

[Insert Table 4, about here]

In our clinical chart, 35% of DMDD inpatients had a written language disorder; this represents 50% of those who had in-depth language assessment (12/24) and 11% of those who did not (3/29). The rate of written language disorder was higher in the DMDD group than in the MDD group (*OR*= 4.56 95% CI: 1.65, 12.64, ϕ = .59, *p*= .002) but not statistically different compared to inpatients in the NMD group (*OR*= 4.33 95% CI: 1.56, 12.02, ϕ = .58, *p*= .005) (Table 2).

Inpatients with DMDD who had in-depth language assessment had scores in tests measuring reading ability and writing skill between -1 and -2 SD (Table 4).

3.4. Combined developmental difficulties

Around 71% of inpatients with DMDD had an associated motor and/or language developmental disorder. A combined form of motor and/or language disorders concerns almost 46% inpatients with DMDD which is higher than in the MDD and NMD groups (Table 2). Only two subjects with DMDD had a written language disorder without also having a communication/oral language disorder.

4. DISCUSSION

4.1.Interpretation of the main finding

We found a very high rate of developmental motor and language disorders in inpatients with DMDD (71%) compared to inpatients with MDD or NMD (respectively, 28% and 36%). As a comparison, a 7% rate of learning disabilities was reported among the DMDD youths in the chart-review of 6-17-year-old inpatients conducted by Tufan et al. [13]. A 19% rate of learning disabilities was reported in DMDD patients in a Canadian 7 to17-year-old outpatient sample particularly enriched in mood disorders, although this rate was not statistically different from subjects with major depressive disorder (11%) [7].

This finding should be interpreted in the light of the risk of sampling bias. Most of the participants' hospitalizations were planned to provide a second opinion and adequate treatments for severe forms of psychiatric disorders. This may explain why this sample is particularly enriched in complex forms of psychiatric and developmental disorders. In addition, our

department includes an expert center for learning disabilities which had referred some patients. Furthermore, only adolescents were included in this research, unlike previous studies reporting the rate of learning disabilities in all DMDD patients [13,12,7]. By doing that, we may have selected a sample of particular severity as many prepubertal children with DMDD have only a transitory course of symptoms [6]

Several competing hypotheses could explain the high rate of co-occurrence between motor and/or language disorders and DMDD. Aberrancies in the motor and language domains could co-occur with irritability i) because they increase the frequency of frustrating events, in particular academic failure and difficult peer-relations [16,22], ii) because they are associated with delay in emotion-regulation skills [27,21], or iii) due to shared risk factors [7,52]. The results presented here do not allow us to distinguish between these three possibilities.

In our research we found that youths with DMDD had low scores in motor tasks testing motor imitation and fine motor skills. In contrast, balance and visuo-spatial skills were in the normal range. Such findings, while preliminary, are interesting considering the role of imitation in the emergence of young children's socio-emotional competence [26]. Difficulties in imitating facial emotion has been also associated with impairments in emotional recognition [53] and poor emotional awareness [54], two difficulties reported in DMDD patients [2]. The relatively good performance of DMDD in visuo-spatial tasks should be interpreted with caution, considering a possible ceiling effect for the DTVP-2 test, as the normative scores were extracted from a children sample.

We found that almost a third of DMDD patients had an associated communication/oral language disorder. However, using a more stringent criteria for statistical significance the difference between the patients with DMDD and the two other clinical control groups were no longer significant. In-depth language assessment tests showed that the subsample with DMDD

and oral language impairments were particularly affected in the expressive domain of language (e.g., ascertained with the PPVT test) while they had scores in the normal range for the receptive domain (lexical understanding, picture denomination of the EDA test). This reflects the importance of considering not only the theoretical knowledge of youths' vocabulary but also how the lexical terms are actually used in everyday situations in youth with emotional problems and oral language impairments [55]. Suboptimal scores in other components of spoken language skills (i.e., phonology, syntax) were consistent with the relations reported between these components and early behavioral problems [56].

As the content of many therapeutic interventions for emotional disorders in adolescents are delivered orally (e.g., structured psychotherapies, group interventions, psychoeducation, family-focused interventions), a low level of oral language competence may also be worth identifying in youths with DMDD as it could moderate the response to therapeutic interventions. It remains to be seen whether interventions focusing on enhancing verbal emotional expression that proved effective in improving socio-emotional competence in children [23] could be successfully applied to DMDD patients with difficulties in oral language skills.

Youths with DMDD were particularly impaired in reading and writing competency (i.e., BHK-ado, dictation, text transcriptions) in line with our initial hypothesis. Nearly one third of DMDD patients had a written language disorder, and the lowest scores in standardized language tests were observed for tasks ascertaining reading and writing skills. In addition to the difficulties in phonology reported in DMDD subjects here, DMDD patients may be affected in several cognitives domains involved in the reading process such as attention [2] and inhibition [14,15]. Logically, the combination of reading/spelling difficulties and fine motor/graphism problems (i.e., as ascertained by the item *Manual Dexterity* of the MABC-2) in DMDD subjects results in poor writing performance This is particularly true for DMDD patients, as many of

them have combined forms of learning/developmental disorders. The difficulties in text transcription based on visual or auditory informations could affect all learning activities, accounting for the low level of academic achievement observed in DMDD patients [4-8] .

4.2.Limitations

First, and as previously mentioned, this sample reflects adolescents referred in a tertiary university care referral center. How these findings apply to adolescents with less severe symptoms remains to be studied. A non-irritable ADHD sample might have been also worth including as a comparison group to account for the confounding effect of ADHD. Second, this chart-review study may be prone to a measuring bias, due to missing or incomplete charts. Standardized assessments were only performed in a subgroup of non-randomly selected patients resulting in a possible sampling bias and an overestimation the rates of motor and language impairments. To limit this risk, the link between DMDD and developmental motor and language disorders was estimated by combining different measures: rates of DSM-5 psychiatric disorders, parent-reported information, and profile of impairments based on standardized tests in subsets of patients. Third, the diagnostic of DMDD was set up retrospectively on the basis of the temper dysregulation with dysphoria disorder whose diagnostic criteria differ slightly from DMDD. The use of this proxy diagnostic procedure was regarded as acceptable as all patients with temper dysregulation with dysphoria would match the less stringent DMDD criteria.

4.3.Clinical and research implications

If confirmed, this work will support the use of standardized screening assessment for developmental difficulties in help-seeking populations of adolescents with DMDD. Further

studies would help to elucidate how difficulties in motor and language domains play a role in the propensity to anger reaction and temper outbursts observed in DMDD youths. For example, longitudinal studies of preschool children with repeated assessment of developmental steps, anger reactivity and behavioral measures could provide opportunities to understand the temporal interplay between these dimensions. Such studies may contribute to the development of promising therapeutic opportunities to reduce the academic difficulties of youths with DMDD.

4.4.Conclusion

In the current study, we found that a vast majority of inpatient youths with DMDD presented an associated diagnosis of developmental motor and written language disorders. Most of these adolescents with DMDD had combined forms of developmental impairments. Considering the current lack of therapeutic opportunity for DMDD youths, awareness of these associated conditions could be beneficial. Clinicians and researchers should remain careful that behavioral expressions of anger do not distract them from the bigger picture of developmental impairments in DMDD patients.

LIST OF ABBREVIATIONS USED: Disruptive Mood Dysregulation Disorder (DMDD); Bipolar Disorder (BD); Adjustment Disorder (AD); Post-Traumatic Stress Disorder (PTSD); Attention Deficit Hyperactivity Disorder (ADHD); Disruptive Behavioral Disorder (DBD); Tourette Syndrome (TS); Brief Psychotic Disorder (BPD); Intellectual Disability (ID); Autistic Spectrum Disorder (ASD); Children-Global Assessment Scale (CGAS); Clinical Global Impressions–Severity (CGI-S); Clinical Global Impressions–Improvement (CGI-I); Wechsler Intelligence Scale for Children - Fourth Edition (WISC-IV); Wechsler Intelligence

Scale for Children - Fifth Edition (WISC-V); Movement Assessment Battery for Children 2nd edition (MABC-2); Manual and Digital Gnosopraxia Test (EMG); Developmental Test of Visual Perception 2nd edition (DTVP-2); Brief assessment of writing skill in adolescent (BHK-ado); Evaluation des Fonctions cognitives et des Apprentissages (EMA); Peabody Picture Vocabulary Test (PPVT).

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FIGURES CAPTIONS

Figure 1. Flow-chart of the sample

All consecutive patients hospitalized in adolescent units between January 1st 2017 - December 31st 2018 (N=191)

Chronic irritability?

No n=124

Clinical control groups

Non mood disorder (n=61)

MDD group (n=64)

Yes n=67

DMDD criteria?

No

n=11
Excuded from analyses

Yes

DMDD group (n=53)

Comparions between the three groups

- Socio-demographic characteristics
- Clinical features and symptom severity
- Developmental history and medical conditions associated
- School functioning
- Psychosocial factors

In-depth assessment in a subset of patients (based on tests performed during or prior the hospitalization)

Motor standardized tests (n=29)

Language standardized tests (n=24)

Table 1. Description of the subjects with DMDD, MDD and non-mood disorder

	DMDD (n=53)	MDD (n=64)	NMD (n=61)	*p-value*
Socio-demographic characteristics				
Gender, female, n (%)	16 (30%)	31 (48%)	25 (41%)	.134 †
Age (y) (mean ±SD)	13.58 ± 1.49 [a]	15.33 ±1.65 [b]	14.42±1.55 [b]	<.001†††**
Socio-economic status, high and middle, n (%)	31 (59%)	51 (80%)	48 (79%)	.017 †
School functioning and psychosocial factors				
Prior grade repetition, n (%)	15 (28%)	13 (20%)	9 (15%)	.204.201 ††
School non-attendance above 3 months, n (%)	24 (45%)	32 (51%)	20 (33%)	.118.139 ††
School adaptations, n (%)	36 (68%)	29 (46%)	31 (51%)	.050 †
Special educational facilities, n (%)	14 (26%) [a]	6 (10%) [b]	7 (12%) [b]	.025.030 †† *
Foster care placement, n (%)	17 (32%) [a]	7 (11%) [b]	4 (7%) [b]	<.001 †† **
Home educative assistance/report to child-protection agencies, n (%)	32 (60%) [a]	19 (30%) [b]	27 (44%) [ab]	.004 † **
Developmental history and medical conditions associated				
Complicated pregnancy, n (%)	13 (32%) [a]	16 (25%) [a]	5 (9%) [b]	.022.020 †† *
Acute fetal distress, n (%)	11 (26%)	12 (19%)	7 (13%)	.226.349 ††
Neurological disorder, n (%)	9 (17%) [ab]	4 (6%) [b]	13 (22%) [a]	.045.035 †† *
Chronic somatic condition (non-neurological), n (%)	29 (55%)	21 (33%)	24 (40%)	.054 †
Comorbid psychiatric disorders, %				
ADHD	23 (43%) [a]	4 (6%) [b]	5 (8%) [b]	<.001 †† **
ASD	3 (6%)	3 (5%)	14 (23%)	.001
ANX	29 (55%)	37 (58%)	23 (38%)	.057.061 ††
ASD	3 (6%) [b]	3 (5%) [b]	14 (23%) [a]	.003 †† **
DBD	36 (68%) [a]	6 (9%) [b]	11 (18%) [b]	<.001 †† **
ED	1 (2%)	5 (8%)	1 (2%)	.226 ††
ID	0 [b]	9 (14%) [a]	13 (22%) [a]	<.002001 †† **
SPD	0 [b]	3 (5%) [b]	22 (36%) [a]	<.001 .004†† **
STRDTSD	16 (30%)	13 (20%)	23 (38%)	.100 ††
TTS	5 (9%)	1 (2%)	6 (10%)	.084 ††
Number of psychiatric diagnoses at discharge (mean ±SD)	2.7 ±0.99 [a]	2.09 ±0.94 [b]	1.52 ±0.65 [c]	<.001†††**
Severity and treatment response				
History of admission in inpatient structure, n (%)	33 (62%) [a]	29 (45%) [ab]	18 (30%) [b]	.002 † **
C-GAF at admission (mean ±SD)	38.17 ±10.69	38.44 ±11.68	36.44 ±14.41	.422 †††
C-GAF at discharge (mean ±SD)	58.30 ± 10.59	62.52 ± 13.15	60.23 ±13.33	.091 †††

CGI-S at admission (mean ±SD)	4.96 ± 0.90	4.83 ±1.00	5.02 ±1.27	.313 †††
CGI-I at discharge (mean ±SD)	2.64 ± 0.68	2.44 ±0.90	2.56 ±1.01	.067 †††

Note:
† Chi-2 test; †† Fisher exact test; ††† Kruskal-Wallis test; * indicates $p < .05$. ** indicates $p < .01$. [a-bc] Means in a row without a common superscript letter differ ($p < .05$).
Disruptive Mood Dysregulation Disorder (DMDD); Anxiety Disorder (ANX); Adjustment Disorder (AD); Attention Deficit Hyperactivity Disorder (ADHD); Anxiety Disorder (ANX); Autistic Spectrum Disorder (ASD); Disruptive Behavioral Disorder (DBD); Eating Disorder (ED); Intellectual Disability (ID); Schizophrenia and other psychotic disorder (SPD); Trauma and Stress-Related and Trauma Related Disorder (STSRD); Attention Deficit Hyperactivity Disorder (ADHD); Disruptive Behavioral Disorder (DBD); Tics and Tourette Syndrome (TTS); Schizophrenia and other psychotic disorder (SPD); Intellectual Disability (ID); Autistic Spectrum Disorder (ASD); Children-Global Assessment Scale (CGAS); Clinical Global Impressions–Severity (CGI-S); Clinical Global Impressions–Improvement (CGI-I).

Table 2. Prevalence of motor and language impairments in the DMDD, MDD and NDM groups

		DMDD (n=53)	MDD (n=64)	NMD (n=61)	*Comparisons between the 3 groups p-value*[1]
Motor developmental difficulties					
	Parent-report delay and/or abnormal motor development	32 (67%) [a]	16 (27%) [b]	27 (47%) [a]	<.001††**
	Associated developmental coordination disorder	30 (67%) [a]	14 (22%) [b]	26 (29%) [a]	<.001††**
Language developmental difficulties					
	Parent-report delay and/or abnormal language development	20 (40%)	14 (23%)	20 (35%)	.124††
	Associated communication/oral language disorder	15 (31%)	7 (11%)	12 (21%)	.05637††
	Associated written language disorder	17 (35%) [a]	6 (10%) [b]	6 (11%) [b]	.001.002††**
Combined developmental difficulties					
	Any motor or language disorders, n (%)	35 (75%) [a]	18 (29%) [b]	20 (36%) [b]	<.001††**
	Two combined motor or language disorders[2]	15 (33%) [a]	5 (8%) [b]	6 (11%) [b]	.001.005††**
	Three combined motor or language disorders	6 (13%)	2 (3%)	4 (7%)	.128††

Note:
† Chi-2 test; †† Fisher exact test; * indicates p <.05. ** indicates p < .01. [a-b] Means in a row without a common superscript letter differ (p < .05).
[1] Statistical comparisons between each group (DMDD vs. MDD, and DMDD vs. NMD) are presented in the plain text.
[2] All subjects with communication/oral language disorder had reading difficulties. The difference between a mixed language disorder (oral + written) and the sequela of communication/oral language disorder on reading or writing abilities require further analyses not presented here.

Table 3. Detailed motor difficulties in the subset of DMDD patients with in-depth motor assessments (n=29/53)

Tests		Mean performance of DMDD youths compared to standardized scores in non-clinical population *
Gross motor skills		
	MABC-2: Manual dexterity	14th percentiles, 95% CI [13, 15] **
	MABC-2: Aiming and Catching	36th percentiles, 95% CI [34, 38]
	MABC-2: Balance	27th percentiles, 95% CI [25, 28]
	MABC-2 : total score	18th percentiles, 95% CI [16, 20]
Fine motor skills		
	EMG : Manual imitation	-1.4 SD, 95% CI [-1.5, -1.3] **
	EMG : Digital imitation	+0.1 SD, 95% CI [0.0, 0.2]
Visuo-spatial skills		
	DTVP-2: Motor-reduced visual perception quotient	63th percentiles, 95% CI [61, 65]
	DTVP-2: Visual-motor integration quotient	48th percentiles, 95% CI [45, 50]
Graphism		
	BHK-ado, SD	-1.8 SD, 95% CI [-2.0, -1.7] **

Note:

* Standardized scores in same-age non-clinical sample were provided by the manuals for each test. MABC-2: Movement Assessment Battery for Children 2nd edition (Henderson 2007), EMG: Manual and Digital Gnosopraxia Test (Vaivre-Douret 2011), DTVP-2: Developmental Test of Visual Perception 2nd edition (Hammill 1993), BHK-ado: Brief assessment of writing skill in adolescent (Charles 2003)

** Scores in the problematic or pathologic ranges

Table 4. Detailed language difficulties in the subset of DMDD patients with in-depth language assessments (n=24/53)

Tests	Mean performance of DMDD youths compared to standardized scores in non-clinical population *
Spoken language : phonology	
EDA : Repetition logatom	-0.3 SD, 95% CI [-0.5, -0.1]
EDA : Suppression of the last phonem	-1.4 SD, 95% CI [-1.6, -1.2]
Spoken language : syntax and morphology	
EDA : Syntax understanding	-0.7 SD, 95% CI [-0.8, -0.6]
EDA : Sentence completion	- 1.0 SD, 95% CI [-1.3, -0.7]
Spoken language : semantics	
EDA : Lexical understanding	69th percentiles, 95% CI [56, 82]
EDA : Picture designation	40th percentiles, 95% CI [37, 43]
PPVT : Picture denomination	-2.0 SD, 95% CI [-2.3, -1.8]
Written language : reading	
Reading regular words	-1.5 SD, 95% CI [-1.7, -1.3]
Reading irregular words	-2.0 SD, 95% CI [-2,3, -1.8]
Reading pseudo-words	-2.2 SD, 95% CI [-2.5, -2.0]
Written language : writing	
Dictation	-1.4 SD, 95% CI [-1.6, -1.2]
Text transcription	-1.6 SD, 95% CI [-1.8, -1.4]

Note:

* Standardized scores in same-age non-clinical sample were provided by the manuals for each test. EDA (Billard 2012), PPVT: Peabody Picture Vocabulary Test (Dunn 2007), LMC-R (Khomsi 2003).

** Scores in the problematic or pathologic ranges

Table S1. Algorithm for the diagnosis of DMDD in the current study

Diagnostic criteria:	***Clinical description:***
A1	The temper outbursts are manifest verbally and/or behaviorally, such as in the form of verbal rages, or physical aggression towards people or property
A2	The reaction is grossly out of proportion in intensity or duration to the situation or provocation. *and* The responses are inconsistent with developmental level.
B	The temper outbursts occur, on average, three or more times per week
C1	Nearly every day, the mood between temper outbursts is persistently negative (irritable, angry, and/or sad).
C2	The negative mood is observable by others (e.g., parents, teachers, peers).
D	Criteria A-C have been present for at least 12 months. Throughout that time, the person has never been without the symptoms of Criteria A-C for more than 3 months at a time.
E	The temper outbursts and/or negative mood are present in at least two settings (at home, at school, or with peers) and must be severe in at least in one setting.
F	Chronological age is at least 6 years (or equivalent developmental level).
G	The onset is before age 10 years.
H	There has never been a distinct period lasting more than 1 day during which the full symptom criteria, except duration, for a manic or hypomanic episode have been met.
I	The behaviors do not occur exclusively during the course of a Psychotic or Mood Disorder (e.g., Major Depressive Disorder, Dysthymic Disorder, Bipolar Disorder) and are not better accounted for by another mental disorder (e.g., Pervasive Developmental Disorder, post-traumatic stress disorder, separation anxiety disorder)
Diagnostic procedure:	
A DMDD diagnosis was positively endorsed if the subjects **presented at least eleven positive answers** to the diagnostic criteria described above. The final formulation for DMDD diagnostic criteria (1) are similar to those developed for TDDD (34) except for two changes: (i) the mood between the temper outbursts is persistently irritable or angry most of the day in DMDD. In TDDD the item was endorsed positively if the mood was angry, irritable and/or sad. (ii) A new exclusion criterion was introduced for DMDD '*The symptoms are not attributable to the physiological effects of a substance or to another medical or neurological condition*'.	

Table S2 Subgroups analyses to compare the rate of motor and language impairments in DMDD with and without associated ADHD

	DMDD/ ADHD+ (n=22)	DMDD/ ADHD- (n=31)	*p-value*
Any developmental motor or language disorders, n (%)	18 (86%)	15 (62%)	**.013**
Communication/oral language disorder	9 (41%)	7 (23%)	.152
Written language disorder	8 (36%)	9 (29%)	.573
Developmental coordination disorder	14 (63%)	14 (45%)	.184
Two combined motor or language disorders *	7 (33%)	7 (29%)	.452
Three combined motor or language disorders	4 (19%)	4 (17%)	.597