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Combined pharmacotherapy-multimodal psychotherapy in children with Disruptive Behavior Disorders



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ABSTRACT

Although multi-component psychotherapeutic interventions are first-line treatments for Disruptive Behavior Disorders (DBD), pharmacotherapy is often associated for more severe patients. Our aim was to explore effectiveness of an associated pharmacotherapy in referred children with DBD receiving a one-year psychotherapeutic intervention. Aggression, callous unemotional (CU) traits and emotional dysregulation were outcome measures. The sample included 144 children, aged 8–12 years, 41 (29%) with an ADHD comorbidity. Fifty-five (38%) patients received an additional pharmacotherapy with one medication, methylphenidate, a second generation antipsychotic, or a mood stabilizer. Data were collected before and after the one-year treatment. According to the Child Behavior Checklist (CBCL), aggressive behaviors, rule-breaking behaviors and emotional dysregulation improved in the whole group, as well as parent- and child-reported CU traits. The hierarchical regression model showed that additional pharmacotherapy significantly predicted lower scores at the CBCL aggressive behaviors and emotional dysregulation, but not CU traits at the end of the treatment. The interaction between methylphenidate and ADHD comorbidity predicted lower aggressive behaviors after the treatment. In summary, this naturalistic investigation suggest that an additional pharmacotherapy significantly improved aggression and emotional dysregulation, but not CU traits. When ADHD was comorbid, methylphenidate was more effective than antipsychotics or mood stabilizers in reducing aggression.

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1. Introduction

Disruptive Behavior Disorders (DBD), including Oppositional Defiant Disorder (ODD) and Conduct Disorder (CD), are among the most represented clinical conditions in child and adolescent mental health settings. There is a long and extensive history of research on DBD, namely regarding the best treatment strategies and the predictors of treatment response (American Psychiatric Association, 2000; Moffitt et al., 2008). Major goals in clinical research of DBD are to develop effective treatment models for improving aggressive and rule breaking behaviors, as well as for defining possible risk factors of poor outcomes or relapses. Consistent findings from clinical studies and meta-analyses indicate that a multi-component intervention, usually including child-oriented sessions, family sessions, interventions at school, and based on cognitive behavioral principles and practices, are usually the

first-line treatment option for DBD (Mc Cart et al., 2006; Eyberg et al., 2008). Evidence from studies on pharmacological treatments in patients with DBD is still poorly informative, although some limited data support efficacy of second generation antipsychotics (SGA), mood stabilizers (MS), and stimulants (Ipser and Stein, 2007; Turgay, 2009; Loy et al., 2012; Gorman et al., 2015). However, considering that in the clinical practice a co-treatment with psychotherapeutic interventions and pharmacotherapy is a frequent strategy, namely in the more severe patients with DBD, there is a dearth of studies exploring the clinical implications of this association. Recent studies suggest that a combination of both psychotherapeutic and pharmacological approaches can improve the outcome of aggressive children and adolescents with DBD (Aman et al., 2014; Gadow et al., 2014).

A critical issue in evaluating the effectiveness of DBD treatments is patient heterogeneity within the same diagnostic category (Klahr and Burt, 2014). Disentangling this diagnostic domain in meaningful clinical subgroups may have significant clinical and treatment implications. At least two subtypes of DBD can be described, one associated with Callous Unemotional (CU) traits and predatory aggressiveness, and another associated with impulsive

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and reactive aggression, often co-occurring with mood and anxiety disorders (Vitiello and Stoff, 1997; Blair, 2013). Compared to patients with impulsive/reactive aggression, children and/or adolescents with CU traits and predatory aggression have been found to be more resistant both to medications (Masi et al., 2006; Masi et al., 2009), and to multi-component interventions (Masi et al. 2011, 2013; Hawes et al., 2014). However, previous studies have suggested that CU traits can decrease during multi-component treatments, including parenting intervention, individual psychotherapy and pharmacotherapy (Kolko and Pardini, 2010; Muratori et al., 2015).

Another important clinical specifier for a DBD subtyping is the co-occurrence of emotional dysregulation, including mood instability, severe irritability, aggression, temper outburst, and hyper-arousal (Masi et al., 2015a, 2015b). The Child Behavior Checklist Dysregulation Profile (CBCL-DP), with simultaneous high values (above two Standard Deviations) in three CBCL syndrome scales (Anxious/Depressed, Attention Problems, and Aggressive Behavior), has been proposed as a possible diagnostic tool for identifying children with Emotional Dysregulation (Faraone et al., 2005; Youngstrom et al., 2005; Volk and Todd, 2007; Holtmann et al., 2011; Mbekou et al., 2014). Previous studies investigated CBCL-DP in DBD (Volk and Todd, 2007; Masi et al., 2015a, 2015b), and found that the CBCL-DP score may be associated with an increased risk of persisting ADHD or superimposed mood disorders. However, to date, implications of this conceptualization on treatment outcome are poorly explored.

Our aim was to address the topic of effectiveness of a combined pharmacotherapy-psychotherapy in children with DBD referred in a clinical setting and treated with a multi-component intervention. This naturalistic investigation compared children receiving the combined treatment and children those receiving the same psychotherapeutic intervention, but not medications. Although it is not possible to draw firm information on the efficacy of the treatments from a naturalistic observation, significant information may stem on effectiveness and course under a specific treatment. In order to explore the specific impact of the two treatment strategies, not only aggressive behavior, but also callous-unemotional traits and emotional dysregulation we selected as outcome measure. In order to explore more specific pharmacological strategies, efficacy of *methylphenidate* was compared with *second generation antipsychotics or mood stabilizers*.

2. Method

2.1. Participants and procedures

In this naturalistic study, a consecutive sample of children initially referred for behavioral problems received a systematic evaluation at the Child and Adolescent Psychiatry and Psychopharmacology Department of our Hospital. At the baseline, trained child psychiatrists administered separately to parents and children a clinical interview, the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL) (Kaufman et al., 1997). Patients also received an assessment of functional impairment, according to the Children Global Assessment Scale (C-GAS) (Shaffer et al., 1983), an evaluation of cognitive abilities with the Wechsler Intelligence Scales for Children – 3rd Ed (WISC-III) (Wechsler, 1991), while parents completed the Child Behavior Checklist (Achenbach and Rescorla, 2001).

The inclusion criteria of the current study were: 1) DSM-IV-TR diagnosis of ODD or CD according to K-SADS-PL; 2) a Full Scale IQ above 85; 3) a CBCL externalizing score above 63. A total of 164 children and families met the inclusion criteria, completed pre-

treatment assessments, and started intervention. Twenty participants (14%) discontinued the treatment (i.e., they stopped treatment without mutual consent, and they did not receive further treatment before the second assessment), and they were not included in the analyses. The final sample included 144 children, age range 8–12 years, 129 (90%) male and 15 (10%) female, 124 (86%) Caucasians and 20 (14%) African. Forty-one (29%) presented a CD diagnosis and 103 (71%) an ODD diagnosis, 41 (29%) had an ADHD comorbidity, and 30 (23%) had a Mood Disorder (MD) comorbidity (including Depressive Disorders and Bipolar Disorders). Regarding socio-economic status (SES), 42 families (29%) presented a low SES according to Hollingshead and Redlich scale (1958).

All the participants were treated with a multi-component intervention (including a child psychotherapy and parent training intervention) based on cognitive behavioral practices and principles (for further details see Masi et al., 2014). The children and parents received the full dosage of the treatment program, with an average child and parent attendance rate of 83%. The integrity of this model was monitored and measured in the following ways: (a) Therapists attended official training in cognitive behavioral psychotherapy; (b) Therapists attended supervision meetings with a certified cognitive behavioral psychotherapy supervisor; (c) During a weekly staff meeting based on case reviews, therapists completed a checklist of objectives delivered within sessions.

One month before the beginning of the multi-component treatment, all the patients were assessed by child psychiatrists, and, when necessary, they received a medication, based on the severity of the clinical picture and the categorical diagnosis. Fifty-five patients (38%) received a pharmacotherapy: methylphenidate was prescribed to 19 patients with ADHD, while 25 patients received a second generation antipsychotic (risperidone or quetiapine), and 11 a mood stabilizer (lithium carbonate or valproic acid). No patients received more than one medication, and each medication was continued during the 12-month multimodal treatment, with possible dosing adjustments, based on efficacy and tolerability.

Data were collected before the multi-component treatment, and at the end of the treatment. Consent was obtained from parents at initial enrollment and at each of the following assessment points. The Ethical Committee of our Hospital approved the study.

2.2. Measures

- *Categorical diagnosis*: at the baseline, trained child psychiatrists with specific experience in child and adolescent psychiatric disorders administered separately to the parents and children the clinical interview K-SADS-PL (Kaufman et al., 1997), which explores the presence or absence of each symptom according to DSM-IV. The K-SADS-PL was double-rated, and the interviewer agreement was 89%.
- *Family socioeconomic status* (SES) was assessed with the Hollingshead and Redlich scale (Hollingshead and Redlich, 1958).
- *Intellectual functioning* was assessed with the Wechsler Intelligence Scales for Children – 3rd Ed (WISC-III) (Wechsler, 1991).
- *Behavior Problems* were explored with the CBCL (Achenbach and Rescorla, 2001) at each time point. The CBCL is a 118 item standardized format, completed by parents for recording behavioral problems and skills in children and adolescents from 6 to 18 years of age. The 118 behavior problem items are aggregated in eight different subscales. Each item is scored on a 3-step response scale. Two subscales (Aggressive behavior and Rule-Breaking behavior) are related to the externalizing domain and were used as measure of behavior problems. Reliability across the time points was .78 for the Aggressive behavior and .85 for

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