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Emotional dysregulation, executive functions and callous-unemotional traits in children and adolescents with Oppositional Defiant Disorder/ Conduct Disorder and Autism Spectrum Disorder: a direct comparison

C. Narducci [a,b,c], F. Donno [a,d], A. Milone [e], F. Placini [d,e], J.C. Glennon [f,i], G. Masi [e], D. Coghill [g,h], A. Zuddas [a,d,†], S. Carucci [d,j,*], C. Balia [a,d]

[a] Dept. Biomedical Sciences, Sect. Neuroscience & Clinical Pharmacology, University of Cagliari, Italy
[b] Division of Child and Adolescent Neuropsychiatry, University Hospital of Siena, Siena, Italy
[c] Dept. of Molecular and Developmental Medicine, University of Siena, Siena, Italy
[d] Child & Adolescent Neuropsychiatry Unit, "A.Cao" Paediatric Hospital, Cagliari, Italy
[e] IRCCS Stella Maris Foundation, Scientific Institute of Child Neurology and Psychiatry, Calambrone (Pisa), Italy
[f] Department of Cognitive Neuroscience/Donders Institute, Radboud University Medical Centre, Nijmegen, the Netherlands
[g] Departments of Paediatrics and Psychiatry, Faculty of Medicine, Dentistry and Health Sciences, University of Melbourne, Melbourne, Australia
[h] Murdoch Children's Research Institute, University of Melbourne, Melbourne, Australia
[i] Conway Institute of Biomolecular and Biomedical Research, School of Medicine, University College Dublin, Dublin, Ireland
[j] Dept. Medical Science and Public Health, University of Cagliari, Italy

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ABSTRACT

Background: Autism Spectrum Disorder (ASD), Oppositional Defiant Disorder (ODD) and Conduct Disorder (CD) share many symptomatic dimensions. Emotional dysregulation (ED) and Callous-Unemotional (CU) traits have been described as transdiagnostic symptoms as well as executive dysfunctions. However, few previous studies compared these disorders directly at a clinical and a neuropsychological level.

Methods: 138 children and adolescents aged 10–17 years (n = 63 ODD/CD; n = 35 ASD and n = 40 TDC), with an intelligence quotient ≥80 were included. The three groups were compared on the emotional and behavioural characteristics by the CBCL 6–18 questionnaire (with particular attention to the emotional dysregulation profile), on the CU traits assessed by the ICU questionnaire (parent version), and the executive functioning assessed by the BRIEF parent form.

Results: Compared to controls, ODD/CDs and ASDs, showed a higher proportion of internalizing and externalizing symptoms, greater emotional dysregulation, higher presence of callous-unemotional traits and executive dysfunction. While participants with ODD/CD significantly differed from those with ASD with higher deficits in impulse inhibition as well as greater planning and organization problems, the two populations did not differ in working memory or the ability to initiate or shift as measured by the BRIEF. ED was confirmed as a transdiagnostic symptom, though more highly represented in ODD/CD compared to ASD. CU traits were also seen as cross-disorder problems, confirming deficits in empathy across both disorder groups, albeit with somewhat different profiles: ODD/CDs showed greater callousness and uncaring than ASDs, while they did not statistically differ from them in the unemotionality.

Conclusions: Our study provides a better understanding of the clinical and neuropsychological character of ODD/CD and ASD populations, showing that they present as overlapping entities but with some specific features.

* Corresponding author. Child & Adolescent Neuropsychiatry Unit, "A.Cao" Paediatric Hospital, Cagliari, Italy.
E-mail address: sara.carucci@unica.it (S. Carucci).

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1. Introduction

Autism Spectrum Disorder (ASD), Oppositional Defiant Disorder (ODD), and Conduct Disorder (CD) exhibit shared symptomatic dimensions. Irritability, anger outbursts, poor behavioral control, verbal and physical aggression, rule violations, antisocial behaviors, and behavioral problems are observed both in ODD/CD and ASD (Mayes et al., 2012; Kaat and Lecavalier, 2013; Mazurek et al., 2013). Nonetheless, the neuropsychological substrates underlying these behaviors may vary significantly (Balia et al., 2018). For some individuals with ASD, disruptive behaviors have been linked to a preference for sameness, which results in difficulties adapting to different contexts, demands, novelties, or changes in routines or habits. For others, these behaviors appear to be associated with a desire to gain or maintain access to restricted/repetitive interests or objects (Reese et al., 2005; Georgiades et al., 2011). In ODD/CD, disruptive behaviors are the core symptoms and can be considered as part of a pattern of problematic interactions with others (American Psychiatric Association, 2013). In fact, according to one conceptual model, individuals with ODD/CD often exhibit oppositional or aggressive behaviors as they perceive them to be the only viable response to situations they misinterpret as unreasonable or aversive. This may be due to an attribution bias which itself is explained by underlying neurobiological vulnerabilities and environmental influences, such as negative parenting (Blair, 2013).

The presence of Callous-Unemotional (CU) traits (a clinical specifier in the context of CD) (American Psychiatric Association, 2013) appears to be a transdiagnostic construct with increased prevalence not only in CD, as expected, but also in other disorders such as ODD and ASD (Carter Leno et al., 2015; Herpers et al., 2016; Tkalcec et al., 2023). CU traits refer to a specific subgroup of affective and interpersonal characteristics, including lack of empathy and guilt, insensitivity to others' feelings, shallow and deficient affect, unconcern for performance, and the callous use of others for one's own personal interest. CU traits are considered to be associated with a high risk of psychopathy and antisocial behavior. A common tool for assessing CU traits in children and adolescents is the Inventory of Callous-Unemotional Traits (ICU) (Frick, 2004). The psychometric properties, such as factorial structure and internal consistency of the ICU, are well established (Essau et al., 2006; Kimonis et al., 2008).

Despite its' transdiagnostic nature, we know little about CU traits in disorders other than CD and about their implications for severity and functional adaptation. High CU traits have been reported in both ODD/CD and ASD and although CU traits can present similarly at a superficial level in both populations, this may be the result of different processes (Carter Leno et al., 2015). Similarly to the different neuropsychological bases for empathy deficits across both disorders (mainly emotional empathy deficit in ODD/CDs versus cognitive empathy deficit in ASDs) (Decety and Moriguchi, 2007; Lamm et al., 2016), CU traits might also have different underlying mechanisms in these populations.

In individuals with ODD or CD, the presence of CU traits has been associated with reduced attention to peripheral prosocial cues, leading to impaired socio-emotional processing (Castagna et al., 2025), as well as with selective deficits in affective domains, such as the ability to care about others' feelings. These may be indicative of impaired affective empathy (Decety and Moriguchi, 2007; Lamm et al., 2016).

Some authors have associated CU traits in individuals with ASD with deficits in cognitive empathy (theory of mind), that is, the ability to understand what others are thinking and to take their mental states into account (Decety and Moriguchi, 2007; Carter Leno et al., 2015; Lamm et al., 2016). Others have proposed a "double hit" hypothesis, suggesting that the presence of CU traits requires not only deficits in cognitive empathy, but also additional impairments in emotional processing associated with CU dimensions (Rogers et al., 2006).

To date, only a few studies have examined the profile of CU traits in ASD, and even fewer have directly compared the CU dimension across ODD/CD and ASD populations (Carter Leno et al., 2015; Herpers et al., 2016; Tkalcec et al., 2023). As a result, it remains unclear whether the underlying neuropsychological bases of psychopathic traits and the specific subdimensions of CU traits involved are shared across the two disorders (Carter Leno et al., 2015; Herpers et al., 2016; Tkalcec et al., 2023). This has important implications for the development of tailored care pathways.

Emotional dysregulation (ED) is another cross-disorder trait widely described in ASD, ODD and CD (Muratori et al., 2017; Joshi et al., 2018; Bierens et al., 2023). ED is defined as a poor ability to inhibit inappropriate behaviors (emotional impulsivity) and a deficient emotional self-regulation (impaired regulation of emotional states, excessive and inappropriate emotional expressions, high excitability and lability and slow return to baseline). Successful emotion regulation is associated with good mental and somatic health, more effective social relationships, and more productive academic and work functioning. Conversely, ED may potentially be relevant for the development of psychopathology and predict a longer treatment course and worse prognosis (Muratori et al., 2017; Joshi et al., 2018; Bierens et al., 2023). Among various instruments to assess ED, the Child Behavior Checklist (CBCL) (Achenbach, T. M. and Rescorla, L. A., 2001), a widely used measure for developmental psychopathology, represents a possible tool for identifying ED in children and adolescents, using an elevation in three syndrome scales (Anxiety/Depression, Aggression, Attention). This profile, called ED Profile, is positively correlated with objective indices of ED (Tonacci et al., 2019) and has been used in previous studies investigating ED in youth (Masi et al., 2015; Sesso et al., 2020).

In addition, executive dysfunctions have been described in both ODD/CD and ASD. In ASD, the most frequent deficits include planning, cognitive flexibility (mostly reported in terms of errors of perseveration), set shifting, working memory, sustained or selective attention and response inhibition (Chien et al., 2014, 2015; Craig et al., 2016). Similarly, alterations in selective attention, working memory, flexibility, planning, and inhibitory control have been observed in ODD/CD patients along with alteration in sensitivity to rewards and punishments, resulting in misleading decision-making (Fairchild et al., 2009; Matthys et al., 2013; Johnson et al., 2015; Blair et al., 2018). Additionally, this population exhibits longer reaction time during response inhibition tasks, such as "Stop Task", and an increase in intra-individual response time variability (Hobson et al., 2011).

Few studies have directly compared ODD/CD and ASD. Those focusing on emotional topics such as the processing of the emotional valence of stimuli (Herpers et al., 2019) or emotional face recognition (Bours et al., 2018), did not find differences between the two groups. As individuals with ODD/CD or ASD demonstrated pronounced difficulties in distinguishing between neutral and positive images when compared to controls, the authors hypothesized a reduced sensitivity to positive stimuli or a lack of a "positive perception bias". They suggested that youths with ODD/CD or ASD may share a diminished capacity for detecting emotional valence (Herpers et al., 2019). Bours and colleagues further reported that male adolescents with either ASD or ODD/CD spent less time looking at the eyes of faces expressing fear, anger, happiness, or neutrality, and exhibited a nominally longer latency in fixating on the eyes of fearful faces relative to controls (Bours et al., 2018).

As far as we are aware, a comprehensive and direct comparison of the clinical and neuropsychological similarities and differences between the two disorders is still lacking.

The main objective of this study was to perform a multidimensional assessment of children and adolescents with ODD/CD, ASD, and typically developing controls (TDC). The assessment included cognitive profile, emotional and behavioral characteristics, CU traits, and executive functioning. The aim was to delineate the clinical and neuropsychological profiles of ODD/CD and ASD, and to identify shared or distinct domains across the groups. An accurate characterization of the clinical and neuropsychological profiles of specific populations may facilitate the identification of distinct and shared neurocognitive and neuropsychological endophenotypes. This could contribute to improving and refining the current mental disorders classification system and enhancing their

assessment, thus leading to the development of more specific and targeted intervention strategies. Such an approach aligns with the perspective of transitioning from the molecular bases to the clinical endophenotype, and, ultimately, to the therapeutic targets (Craig et al., 2016).

2. Materials and methods

2.1. Participants

138 children and adolescents aged 10–17 years (n = 63 ODD/CD; n = 35 ASD and n = 40 TDC), with an intelligence quotient (IQ) ≥80, were enrolled in the study. Participants with ODD or CD were grouped together, as in previous studies (Bours et al., 2018; Herpers et al., 2019) since both disorders are closely linked and ODD can be considered either prodromal to CD or a subsyndromal form of CD (American Psychiatric Association, 2013).

Participants diagnosed with ODD/CD were recruited within the Multidisciplinary Approaches to Translational Research In Conduct Syndromes WP6-1 (MATRICS_WP6-1) trial (Balia et al., 2021), a multicenter, phase II, control design, and acute, placebo-controlled, single-blind, challenge clinical study. The trial was conducted at two Italian sites (Cagliari University Hospital and IRCCS Stella Maris, Pisa) in accordance with the Declaration of Helsinki and the good clinical practice (GCP) parameters, between February 2018 and November 2019. The study protocol, informed consents, and any other appropriate documents were submitted to the national competent authority Italian Drug Agency (AIFA) and to the local ethical review boards (Independent Ethics Committee of the Cagliari University Hospital and Ethics Committee of the Tuscany Region). The study was approved by the AIFA on July 4, 2017. Approval from the local ethical review boards was obtained on December 29, 2017 for the Cagliari site and on January 22, 2018 for Pisa (Tuscany) site (EudraCT registration number: 2015-001916-37).

ASD participants were enrolled at the University Hospital of Cagliari, between March 2018 and November 2019, within the Neuropsychological Characterization of Autism Spectrum Disorder without Intellectual Disability (CNeSA) clinical study (Donno et al., 2023), a single-center, case-control, spontaneous study that was approved from the Independent Ethics Committee of the Cagliari University Hospital on March 28, 2018 (protocol number: PG/2018/4421). The TDC group was the same for the MATRICS_WP 6–1 and CNeSA studies and was identified in communities among friends or classmates of the clinical group participants. Participation to the study was on a voluntary basis. Before any study procedure, parents or a legally authorized representative of the subject signed the informed consent. Children and adolescents provided their written assent.

Inclusion criteria for the ODD/CD group required a formal diagnosis of ODD or CD according to DSM-5 and documented by the semi-structured Kiddie-Schedule for Affective Disorders and Schizophrenia-Present And Lifetime Version (K-SADS-PL) interview (Kaufman et al., 1997); significant levels of aggression, measured by a T score of ≥70 at the aggression or delinquency subscale of the Teacher Report Form (TRF), Youth Self Report (YSR), or Child Behavior Checklist 6–18 (CBCL 6–18) (Achenbach, T. M. and Rescorla, L. A., 2001) or a score of ≥27 on the *Disruptive-Total* (D-Total) index of the Nisonger-Child Behavior Rating Form (NCBRF-TIQ) (Aman et al., 2008). The NCBRF-TIQ is a 66-item clinician-administered questionnaire completed by parents or caregivers to assess behavioral functioning in children and adolescents with disruptive behavior disorders; the D-Total index is a total composite score for disruptive behavior derived from the Oppositional and the Conduct Problems subscales.

Participants were included in the ASD group if they met the diagnostic criteria for ASD according to the DSM-5, confirmed through the administration of gold-standard instruments for ASD assessment: the Autism Diagnostic Observation Schedule, Second Edition (ADOS-2) (Lord et al., 2012), and the Autism Diagnostic Interview–Revised (ADI-R) (Lord et al., 1994).

Subjects with an IQ < 80, or with a primary diagnosis of schizophrenia-related disorders, bipolar disorder, depression or anxiety, and subjects on any psychotropic medications within the last six months before screening visit were not allowed to be enrolled in the study. For further information about inclusion and exclusion criteria, see the detailed studies protocols (Balia et al., 2021; Donno et al., 2023).

2.2. Screening, clinical and neuropsychological assessment

Hereafter are reported only the evaluations, questionnaires, and rating scales relevant for this study (for further information see the above-mentioned studies protocols (Balia et al., 2021; Donno et al., 2023)).

The assessment included the following:

- Wechsler Intelligence Scale for Children-Fourth Edition (WISC-IV) (Wechsler, D., 2003) or Wechsler Adult Intelligence Scale- Fourth Edition (WAIS-IV) (Wechsler, D., 2008) administered to assess global intelligence functioning. The cognitive evaluation was not assessed if performed within the previous 2 years.
- Child Behavior Checklist for ages 6–18 (CBCL 6–18) (Achenbach, T. M. and Rescorla, L. A., 2001): this questionnaire was employed to assess emotional and behavioral functioning. The questionnaire includes two sets of main scales: the syndrome scales and the DSM-Oriented ones. The syndrome scales comprise eight categories: *Anxious/Depressed*, *Withdrawn/Depressed*, *Somatic Complaints*, *Social Problems*, *Thought Problems*, *Attention Problems*, *Rule-Breaking Behavior*, and *Aggressive Behavior*. From these, three summary scales are derived: *Internalizing Problems* and *Externalizing Problems* are calculated by grouping specific syndrome scales, while the *Total Problems* score is obtained by summing all items from the syndrome scales. The reliability coefficients (Cronbach's alpha) are 0.80, 0.88 and 0.92 respectively (Achenbach, T. M. and Rescorla, L. A., 2001). The DSM-Oriented Scales include six domains: *Affective Problems*, *Anxiety Problems*, *Somatic Problems*, *Attention Deficit/Hyperactivity Problems*, *Oppositional Defiant Problems* and *Conduct Problems*. Additionally, the questionnaire comprises three additional scales: *Sluggish Cognitive Time Problems*, *Obsessive-Compulsive Problems* and *Stress Problems*. To avoid redundancy in assessment, the present study focused on the syndrome scales, the summary scales, and two additional scales mentioned above (*Sluggish Cognitive Time Problems* and *Obsessive-Compulsive Problems)*. Furthermore, we considered the ED Profile, as indicated in prior studies (Masi et al., 2015; Sesso et al., 2020), obtained by summing the scores on the syndromic scales of *Attention Problems*, *Aggressive Behavior* and *Anxious/Depressed*.
- ICU (Frick, 2004; Essau et al., 2006): a 24-item parent questionnaire to comprehensively assess CU traits including three subscales (*Callousness*, *Uncaring*, and *Unemotional*) and a summary scale (*Total*). Responses are scored on a 4-point Likert scale, ranging from 0 (not at all) to 3 (definitely true). The Cronbach's alpha coefficients range from 0.74 to 0.85 for the Total score, from 0.71 to 0.88 for the *Callousness* subscale, from 0.78 to 0.84 for the *Uncaring* subscale, and from 0.45 to 0.77 for the *Unemotional* subscale (Essau et al., 2006; Kimonis et al., 2008; Roose et al., 2010).
- Behavior Rating Inventory of Executive Function (BRIEF) (Gioia, G. A et al., 2000): an 86-item parent form questionnaire to assess "real life" executive function (EF) for children and adolescents aged 5–18, allowing the identification of clinically relevant manifestations across various contexts such as home and school. BRIEF evaluates nine factors associated with specific EFs: *Inhibit*, *Self-Monitor*, *Shift*, *Emotional Control*, *Initiate*, *Working Memory*, *Plan/Organize*, *Task Monitor* and *Organization of Materials*. Additionally, it provides three composite scales: the *Behavioral Regulation Index (BRI)*, encompassing *Inhibit*, *Shift*, and *Emotional Control*; the *Metacognition Index (MI)*, including *Initiate*, *Working Memory*, *Plan/Organize*, *Organization of Materials*, and *Task Monitor*; the *Global Executive Composite (GEC)* score, derived from the sum of the three composite indexes.

Cronbach's alpha values for the primary indexes are typically high, ranging from 0.80 to 0.98. Specifically, the *GEC* often shows excellent reliability of 0.97, while the *BRI* and *MI* of 0.90–0.95 Individual subscales may have slightly lower alpha values, but above 0.70 (Gioia, G. A et al., 2000).

2.3. Statistical analysis

Statistical analyses were performed using the statistical software Statistical Package for Social Science (SPSS), version 29.0 for Windows (SPSS, 2022). Descriptive analyses of the demographic and clinical characteristics of the two clinical samples and of the TDCs group were performed.

Multivariate analysis of variance (MANOVA) tests, with post-hoc Bonferroni correction, has been used to compare the three groups (ODD/CD, ASD and TDC). A logarithmic transformation (Logarithm 10, Lg10) was applied to normalize the distributions in case of data not meeting assumptions of normality.

3. Results

3.1. Sample characteristics

The clinical and demographic characteristics of the total sample are shown in Table 1. No significant differences between groups were found in terms of age and sex so the three groups were considered homogeneous for age and sex. Mean age was 13.90 ± 2.46 years in the ASD, 13.29 ± 1.94 in the ODD/CD and 12.85 ± 1.65 in the TDC group, with a male prevalence in each group (88.6 % in ASD, 82.5 % in ODD/CD and 95 % in TDC). Among the clinical groups, we found a not negligible comorbidity with ADHD: 17.1 % of ASD and almost all the ODD/CD sample equal to 95.2 %.

IQ mean value (105.94 ± 14.8 in ASD, 98.78 ± 11.3 in ODD/CD and 116.85 ± 10.67 in TDC) resulted significantly lower in the two clinical groups compared to TDC ($p < .001$) and in ODD/CD compared to the ASD population ($p = .026$).

In the visuo-perceptual reasoning index (PRI) (mean value: 112.57 ± 15.5 in ASD, 104.14 ± 12 in ODD/CD and 118.45 ± 11.81 in TDC), ODD/CD reported significantly lower scores compared to both ASD ($p < .008$) and TDC ($p < .001$). The verbal comprehension (VCI) as well as the working memory index (WMI) and processing speed index (PSI) were not significantly different in the two clinical groups although both diverge from the TDC (VCI: $p < .001$ for ODD/CD and $p = .027$ for ASD; WMI: $p < .001$ for ODD/CD and $p = .004$ for ASD; PSI: $p < .001$ for ODD/CD and $p < .001$ for ASD).

Table 1
Clinical and demographic characteristics of the whole sample.

	ASD (n = 35)	ODD/CD (n = 63)	TDC (n = 40)
Males n (%)	31 (88.6 %)	52 (82.5 %)	38 (95 %)
Females n (%)	4 (11.4 %)	11 (17.5 %)	2 (5 %)
ADHD n (%)	6 (17.1 %)	60 (95.2 %)	–
ODD n (%)	–	53 (84.1 %)	–
CD n (%)	–	2 (3.2 %)	–
ODD + CD n (%)	–	8 (12.7 %)	–
Age at V-1 visit (years) mean (±SD)	13.90 (±2.46)	13.29 (±1.94)	12.85 (±1.65)
IQ [a] mean (±SD)	105.94 (±14.8)	98.78 (±11.3)	116.85 (±10.67)
VCI [a] mean (±SD)	109.49 (±13.9)	104.05 (±13.2)	115.95 (±9.63)
PRI [a] mean (±SD)	112.57 (±15.5)	104.14 (±12)	118.45± (11.81)
WMI [a] mean (±SD)	96.15 (±17.8)	89.42 (±13.7)	105.03 (±12.70)
PSI [a] mean (±SD)	91.27 (±12.8)	91.90 (±13.2)	106.85 (±12.46)

The missing Wechsler scales data are due to the fact that for some patients it was necessary to carry out another type of cognitive test due to poor collaboration.
[a] (evaluation with Wechsler scales available in 59 out of the 63 ODD/CD, in 33 out of the 35 ASD and in the 40 TDC).

3.2. ICU questionnaire

Both clinical groups differed significantly from the TDC group in each subscale (Table 2).

ODD/CDs showed significantly higher mean value scores in the *Callousness* (14.75 ± 5.73) and *Total* (38.05 ± 10.19) subscales ($p < .001$) compared to ASD patients (8.77 ± 5.65 and 26.74 ± 12.26 respectively). In the *Uncaring* subscale (mean value 15.69 ± 5.14 in ODD/CD and 11.71 ± 5.49 in ASD), the resulting p value was 0.004. No differences between the two groups were found for the *Unemotionality* subscale.

3.3. CBCL 6–18 questionnaire (Table 3)

Both ODD/CD and ASD subjects showed significantly higher scores in all subscales when compared to TDC, but clinically significant mean scores (T scores above 70) were found only within the ODD/CD group in the *Aggressive Behavior*, *Oppositional Defiant Disorder Problems* and *Total Problems* subscales, as expected according to the inclusion criteria.

Significant statistical differences ($p < .001$) were observed in the syndromic subscales *Rule-Breaking Behavior*, *Aggressive Behavior* and *Externalizing Problems* within the ODD/CD group exhibiting greater impairment than the ASD group. Additionally, the ODD/CD group scored significantly higher, compared to ASDs, in the syndromic subscales *Attention Problems* ($p = .004$) and *Total Problems* ($p = .005$).

Interestingly, neither of the two clinical groups showed mean scores exceeding the clinical cut-off of 210 for the ED profile. Nonetheless, both ODD/CDs and ASDs had significantly higher scores than the TDC group ($p < .001$; $p < .001$ respectively), with a significant difference between the ODD/CD group and the ASD group ($p < .001$).

3.4. BRIEF questionnaire (Table 4)

Significantly higher scores were found in the ODD/CD group, compared to the ASDs, in the *Organization of Materials* ($p = .002$), *Inhibit* ($p = .012$), *Plan/Organize* ($p = .043$), *MI* ($p = .045$) and *GEC* ($p = .044$), while no significant differences were evidenced in the *Emotional Control*. Both clinical groups reported significant higher scores ($p < .001$) than controls in all subscales.

4. Discussion

This study aimed to explore the overlapping and specific features related to emotional and behavioral functioning, emotional dysregulation profiles, CU traits and real-world executive functioning in individuals diagnosed with ODD/CD or ASD. To date, few previous studies (Bours et al., 2018; Herpers et al., 2019) directly compared similarities and differences for the two disorders.

The two clinical groups with ODD/CD or ASD exhibited a M:F ratio of 4:1 and 7:1 respectively. Our findings are consistent with existing literature indicating a higher prevalence of CD, ODD, and ASD in males. Specifically, studies have reported a male-to-female ratio of approximately 2:1 for CD (American Psychiatric Association, 2013; Fairchild et al., 2019), ranging from 1.4:1 to 1.8:1 for ODD (American Psychiatric Association, 2013; Sacco et al., 2024), and an overall male-to-female prevalence ratio of 4.2 for ASD, with site-specific ratios varying from 3.3 to 5.2 (Maenner et al., 2023).

In our sample, the male prevalence was notably higher than reported in the literature. This discrepancy is likely attributable to our inclusion criteria. For the ODD/CD group, we specifically selected individuals exhibiting marked physical aggression, a characteristic more commonly observed in males. In contrast, females often display relational aggression, such as efforts to disrupt social relationships, rather than overt physical aggression (Rucklidge, 2010). The high comorbidity of ADHD

Table 2
Comparisons between ASD, ODD/CD and TDC groups on the ICU questionnaire.

ICU mean (±SD)	ASD (n = 31)	ODD/CD (n = 61)	TDC (n = 37)	p[a]	Effect Size[b]
Callousness	8.77 (±5.65)	14.75 (±5.73)	4.22 (±2.63)	**<.001** p < .001 ODD/CD > ASD p < .001 ODD/CD > TDC p<.001 ASD>TDC	**0.52**
Unemotionality	6.26 (±3.45)	7.31 (±3.22)	3.84 (±2.14)	**<.001** p < .001 ODD/CD > TDC p = .003 ASD > TDC	**0.21**
Uncaring	11.71 (±5.49)	15.69 (±5.14)	7.00 (±3.18)	**<.001** p = .004 ODD/CD > ASD p < .001 ODD/CD > TDC p<.001 ASD>TDC	**0.39**
Total [cut off =30]	26.74 (±12.26)	38.05 (±10.19)	15.05 (±5.68)	**<.001** p < .001 ODD/CD > ASD p < .001 ODD/CD > TDC p<.001 ASD>TDC	**0.50**

[a] p value at the top refers to the general significance resulting from the comparison between the three groups, while below is reported the significance of the comparison between pairs of groups.
[b] Effect sizes refer to the general comparison between the three groups.

in our ODD/CD sample may also have influenced the observed male predominance. Indeed, literature suggests a male-to-female ratio in ADHD ranging from 2:1 to 10:1, with an average of 4:1 (Mowlem et al., 2019). Regarding the ASD cohort, the inclusion of high-functioning individuals may have contributed to an underrepresentation of females. Females with higher IQ, fewer stereotypical behaviors, and less pronounced behavioral difficulties are frequently underdiagnosed or diagnosed later in adulthood due to subtler symptom presentation that is not captured by standard diagnostic tools (Dworzynski et al., 2012; Begeer et al., 2013). Females are also reported to have greater social camouflaging abilities (Tierney et al., 2016).

The comorbidity rate between ADHD and ODD/CD was 95.2 % in the ODD/CD group and 17.1 % in the ASD group. The rate in the ODD/CD group is consistent with existing literature, which identifies ODD/CD as one of the most frequent comorbid conditions associated with ADHD, with high rates of co-occurrence (Cuffe et al., 2020).

Given that almost all patients with ODD/CD in our sample also had ADHD, this group should be basically considered, at least for the majority, representative of the phenotype ADHD + ODD + CD. Therefore, the results achieved should be interpreted starting from this assumption. This, while it may be considered a limitation, on the other hand makes the sample as representative as possible of the "real-world scenario", given the high comorbidity of ADHD and ODD/CD seen in clinical settings. There is an existing literature highlighting that, because of this substantial comorbidity between ADHD and ODD, the distinction between the disorders, continues to be a matter of debate (Ghosh et al., 2017).

Regarding the morbidity between ADHD and ASD, previous studies have highlighted that the prevalence of psychiatric comorbidities, including ADHD, within ASD populations, is highly variable and influenced by several factors. These include the diagnostic tools employed, and several sample characteristics, including age and cognitive level (Lai et al., 2019; Hossain et al., 2020; Fucà et al., 2023). The time when the study was conducted may also contribute to this variability, given that, prior to the DSM-5 (American Psychiatric Association, 2013), the two conditions were considered mutually exclusive and a comorbid diagnosis of ASD and ADHD was not permitted. Rates of ADHD comorbidity reported in clinical studies range from 35.3 % (Khachadourian et al., 2023) to over 70 % (Joshi et al., 2014), and are usually higher in studies that did not stratify ASD samples by age or cognitive functioning. A recent meta-analysis (Lai et al., 2019) that included 100 heterogeneous studies, reported the overall rate of comorbidity as 28 %. It is worth noting that our ASD sample consisted of a specific subgroup, namely high-functioning adolescents with a mean age of 13.9 years. Our findings are consistent with those of another Italian study (Fucà et al., 2023) conducted during a comparable recruitment period and involving a similar sample. That study analyzed psychiatric comorbidities in a high-functioning ASD cohort stratified by age and reported ADHD comorbidity rates of 20 % in children aged 3–5 years, 21 % in those aged 6–11 years, and 7 % in adolescents aged 13–18 years.

Our analysis of CU traits revealed that both ODD/CD and ASD show significantly higher CU traits than TDC (with higher scores on each ICU subscale and on the total score). However, when we compared the two clinical groups, we found that, compared to those with ASD, those with an ODD/CD diagnosis had higher scores on the total ICU scale and were more callous and uncaring. The exception was *Unemotionality* where those with ODD/CD were not more unemotional than those with ASD.

As far as we know, this is the first study to directly compare CU traits in the ODD/CD and ASD populations. A recent study included adolescents, 11–18 years of age, with ADHD (without specifying comorbidities), age-matched ASD subjects and a TDC group (Chang et al., 2021). Both individuals with ASD and those with ADHD showed significantly higher scores than controls across most of the ICU subscales. There were few differences between the two clinical groups, except for the *Unemotionality* subscale. Those with ASD scored significantly higher for *Unemotionality* than those with ADHD, and there were no differences between ADHD and TDC. The findings reported by Chang and collaborators suggest the possibility that while those with ASD may present a pronounced impairment in the *Unemotionality* dimension, those with ADHD do not. These findings suggest that the high comorbidity with ADHD in our ODD/CD sample may not explain the findings on *Unemotionality* in our study, and that the impairments in this dimension may be related to the primary diagnoses of ODD/CD and ASD, rather than the ADHD. Similarly, the higher scores of the ODD/CD sample on *Callousness* and *Uncaring* dimensions may be independent of the comorbidity with ADHD.

The hypothesis of a significant impairment in the *Unemotionality* subscale in those with ASD is also supported by the findings of another previous study in which adolescents with ASD showed an association between CU traits and impaired fear recognition, potentially mediated by unemotionality (Carter Leno et al., 2015). Also studies that have examined the presence of alexithymia—which refers to marked difficulties in identifying, describing, expressing, and regulating one's own emotions—also pointed toward an impairment in the emotional domain in children and adolescents with ASD (Griffin et al., 2016; Trevisan et al., 2016).

Surprisingly, in our study, we did not find a greater impairment in ASD, compared to ODD/CD, in the *Unemotionality* subscale. On the contrary, the two groups did not differ in this dimension. In our sample, the absence of a statistically significant difference between the two clinical groups in the *Unemotionality* dimension, does not appear to reflect greater impairment in the ASD group compared to the ODD/CD

Table 3
Comparisons between ASD, ODD/CD and TDC groups on the CBCL 6–18 questionnaire.

CBCL 6–18 mean (±SD)	ASD (n = 32)	ODD/CD (n = 60)	TDC (n = 38)	p[a]	Effect Size[b]
Anxious/ Depressed	63.78 (±8.95)	64.60 (±9.88)	52.97 (±5.06)	**<.001** p < .001 ODD/CD > TDC p<.001 ASD>TDC	**0.33**
Withdrawn/ Depressed	67.91 (±11.00)	64.25 (±9.83)	53.71 (±5.19)	**<.001** p < .001 ODD/CD > TDC p<.001 ASD>TDC	**0.34**
Somatic Complaints	62.34 (±11.46)	59.23 (±7.74)	53.68 (±4.29)	**<.001** p < .001 ODD/CD > TDC p<.001 ASD>TDC	**0.13**
Social Problems	65.53 (±8.23)	64.80 (±8.83)	52.05 (±3.41)	**<.001** p < .001 ODD/CD > TDC p<.001 ASD>TDC	**0.48**
Thought Problems	63.38 (±8.33)	62.72 (±8.64)	51.63 (±3.31)	**<.001** p < .001 ODD/CD > TDC p<.001 ASD>TDC	**0.41**
Attention Problems	62.53 (±9.22)	69.25 (±8.89)	51.84 (±3.49)	**<.001** p = .004 ODD/CD > ASD p < .001 ODD/CD > TDC p<.001 ASD>TDC	**0.56**
Rule-Breaking Behavior	56.00 (±6.83)	67.58 (±6.44)	51.21 (±2.94)	**<.001** p < .001 ODD/CD > ASD p < .001 ODD/CD > TDC p = .003 ASD > TDC	**0.63**
Aggressive Behavior	59.22 (±8.36)	74.75 (±9.07)	51.03 (±1.78)	**<.001** p < .001 ODD/CD > ASD p < .001 ODD/CD > TDC p<.001 ASD>TDC	**0.71**
Internalizing Problems	65.94 (±9.82)	64.62 (±8.79)	48.05 (±9.62)	**<.001** p < .001 ODD/CD > TDC p<.001 ASD>TDC	**0.39**
Externalizing Problems	56.47 (±9.81)	71.40 (±6.30)	43.53 (±7.27)	**<.001** p < .001 ODD/CD > ASD p < .001 ODD/CD > TDC p<.001 ASD>TDC	**0.70**
Total Problems	63.66 (±8.51)	69.77 (±6.58)	42.63 (±10.41)	**<.001** p = .005 ODD/CD > ASD p < .001 ODD/CD > TDC p<.001 ASD>TDC	**0.62**
Sluggish Problems	63.81 ± 7.53	60.28 ± 8.71	52.11 ± 4.62	**<.001** p < .001 ODD/CD > TDC p<.001 ASD>TDC	**0.29**
Obsessive-Compulsive Problems	63.87 ± 8.72	60.75 ± 9.89	52.24 ± 4.58	**<.001** p < .001 ODD/CD > TDC p<.001 ASD>TDC	**0.30**
Emotional Dysregulation Profile	185.53 ± 21.11	208.60 ± 21.89	155.84 ± 8.50	**<.001** p < .001 ODD/CD > ASD p < .001 ODD/CD > TDC p<.001 ASD>TDC	**0.65**

[a] p value at the top refers to the general significance resulting from the comparison between the three groups, while below is reported the significance of the comparison between pairs of groups.
[b] Effect sizes refer to the general comparison between the three groups.

group. Rather, it seems to be attributable to a lower level of impairment in this area among individuals with ODD/CD, compared to that observed in the *Callous* and *Uncaring* subscales which reduced the difference between the two clinical groups on this dimension. Nevertheless, we believe that our findings should be replicated in a larger ASD sample to better investigate the *Unemotionality* component.

Interestingly, both those with ODD/CD and those with ASD exhibited deficits in empathy and emotionality area; however, the underlying mechanisms remain poorly understood and may differ. This would have a substantial implication in terms of the development of care pathways for these populations (Maguire et al., 2024). While our study does not allow for a firm conclusion regarding underpinning mechanisms, it highlights the importance of assessing CU traits in both disorders. Indeed, we think that CU traits may not be an intrinsic component of ASD symptomatology per se, but rather represent a distinct and trans-diagnostic construct, even within ASD, identifying subgroups of patients with more severe behavioral problems and an elevated risk of antisocial behavior. Including the ICU questionnaire, both total and subscale scores, in the neuropsychiatric assessment of these clinical populations, could assist clinicians in tailoring rehabilitation interventions to specific impaired subdimensions, regardless of the formal diagnosis.

Comparisons of the externalizing spectrum subscales of CBCL 6–18 questionnaire data revealed a consistent trend of greater impairment in the ODD/DC group compared to individuals with ASD. Conversely, the two clinical groups presented a reversed profile in the internalizing spectrum subscales (withdrawal, somatic problems, social problems), as well as in *Obsessive-Compulsive Problems* and *Sluggish Cognitive Time Problems* albeit not in a statistically significant manner. These findings suggest a greater prevalence of internalizing problems in individuals with ASD and of externalizing problems in those with ODD/CD. This matches the findings from a previous Italian study (Sesso et al., 2020) in which the comparison between two groups of patients (aged 6–18 years)

Table 4
Comparisons between ASD, ODD/CD and TDC groups on the BRIEF scale.

BRIEF mean (±SD)	ASD (n = 32)	ODD/CD (n = 57)	TDC (n = 38)	p[a]	Effect Size[b]
Inhibit	62.59 ± 12.38	72.91 ± 14.14	42.74 ± 7.94	**<.001** p = .012 ODD/CD > ASD p < .001 ODD/CD > TDC p<.001 ASD>TDC	**0.59**
Emotional Control	63.41 ± 13.27	68.53 ± 11.67	44.26 ± 9.34	**<.001** p < .001 ODD/CD > TDC p<.001 ASD>TDC	**0.43**
Shift	64.81 ± 11.32	61.47 ± 12.41	41.66 ± 6.73	**<.001** p < .001 ODD/CD > TDC p<.001 ASD>TDC	**0.50**
Initiate	64.09 ± 12.83	66.46 ± 10.73	42.84 ± 7.92	**<.001** p < .001 ODD/CD > TDC p<.001 ASD>TDC	**0.48**
Working Memory	62.00 ± 16.24	65.70 ± 11.05	38.92 ± 7.24	**<.001** p < .001 ODD/CD > TDC p<.001 ASD>TDC	**0.50**
Plan/Organize	60.28 ± 14.77	67.46 ± 9.48	41.11 ± 6.50	**<.001** p = .043 ODD/CD > ASD p < .001 ODD/CD > TDC p<.001 ASD>TDC	**0.50**
Organization of Materials	52.06 ± 11.62	60.58 ± 10.26	42.32 ± 7.90	**<.001** p = .002 ODD/CD > ASD p < .001 ODD/CD > TDC p<.001 ASD>TDC	**0.37**
Monitor	60.84 ± 11.73	66.95 ± 9.84	42.37 ± 8.47	**<.001** p < .001 ODD/CD > TDC p<.001 ASD>TDC	**0.51**
Behavioural Regulation Index	66.00 ± 12.32	71.58 ± 12.99	42.03 ± 7.20	**<.001** p < .001 ODD/CD > TDC p<.001 ASD>TDC	**0.56**
Metacognition Index	61.53 ± 14.07	68.84 ± 9.79	42.89 ± 13.37	**<.001** p = .045 ODD/CD > ASD p < .001 ODD/CD > TDC p<.001 ASD>TDC	**0.43**
Global Executive Composite	64.63 ± 13.31	71.25 ± 11.06	40.18 ± 7.69	**<.001** p = .044 ODD/CD > ASD p < .001 ODD/CD > TDC p<.001 ASD>TDC	**0.57**

[a] p value at the top refers to the general significance resulting from the comparison between the three groups, while below is reported the significance of the comparison between pairs of groups.
[b] Effect sizes refer to the general comparison between the three groups.

with ADHD + ASD and ADHD + ODD/CD revealed a similar profile. As for the ED profile, we found a greater impairment in both clinical groups compared with TDCs, with significantly higher scores in the ODD/CDs when comparing with ASDs, which is also in accordance with the previous literature (Sesso et al., 2020).

Until now, no studies have compared the neuropsychological functioning of these two clinical populations through the BRIEF questionnaire. In the current study, ODD/CD patients showed a greater impairment in the area of inhibition when compared to the ASD group similarly to what has been reported in other studies comparing the ADHD and ASD populations (Happé et al., 2006; Sinzig et al., 2008; Lawson et al., 2015; Craig et al., 2016). Contrary to what was expected, we did not find a greater impairment, in individuals with ASD, in the *Shift* and *Plan/Organize* areas when compared with the ODD/CD ones, despite studies confirming a greater impairment in these areas in the ASD subjects (Carter Leno et al., 2015). In the current study, no differences have been found between ODD/CDs and ASDs in the *Working Memory* and *Initiate* areas, accordingly to studies that have highlighted that *Working Memory* and *Initiate* are little distinctive in discriminating between ADHD and ASD (Craig et al., 2016).

5. Limitations

The present study has several limitations: first the small sample size and the high heterogeneity of the samples (the combination of ODD and CD together and the high prevalence of ADHD comorbidity in both groups) prevent the stratification of the subjects to find specific clinical endophenotypes. Furthermore, the high comorbidity of ADHD in the ODD/CD sample could lead to the hypothesis that most of the results come from the presence of ADHD. In future studies, this issue could be overcome by enlarging the sample size of the ODD/CD without ADHD comorbidity. This could allow for a valid comparison between pure ODD/CD and ODD/CD plus ADHD groups and, thus, assess if any bias is introduced by the presence of ADHD in the sample. Finally, the presence of statistically significant differences in terms of IQ level between the two populations could have influenced some results, given the possible role of IQ on executive functioning and behavioral profile.

6. Conclusions

This study provides a further contribution to a better understanding of the clinical and neuropsychological characterization of ODD/CD and ASD, representing two largely overlapping entities although presenting some peculiarities both at clinical and neuropsychological level.

At clinical level, both ASD and ODD/CD are characterized by internalizing symptoms, with higher scores in the ASD group although not to a statistically significant extent, and both are characterized by externalizing features, with higher statistically significant scores in the ODD/CD group. Moreover, from a neuropsychological perspective, ODD/CD individuals differ from ASDs, presenting greater inhibition, planning and organization problems. However, these two populations do not seem to differ in terms of working memory, initiation or shifting

abilities.

Emotional dysregulation is confirmed as a potential transdiagnostic symptom, although more clearly seen in those with ODD/CD. This highlights the importance of addressing this dimension as a treatment target in both disorders. The CU traits profile indicates that ODD/CD differs from ASD with higher levels of callousness and uncaring while they do not statistically differ in unemotionality. This emphasizes that both groups present with substantial difficulties with emotional expressivity. Such findings could allow us to develop more specific, appropriate, and tailored treatments for ODD/CDs and ASDs and the importance of investigating this dimension regardless of the diagnostic label.

In the future, it will be important to extend the neuropsychological characterization of patients with ODD/CD and with ASD by analyzing the results obtained from the two clinical populations in the neuropsychological tasks from the CANTAB and Emoticom batteries.

CRediT authorship contribution statement

C. Narducci: Writing – review & editing, Writing – original draft, Formal analysis, Data curation. **F. Donno:** Writing – review & editing, Formal analysis, Data curation. **A. Milone:** Writing – review & editing, Data curation. **F. Placini:** Writing – review & editing, Data curation. **J. C. Glennon:** Writing – review & editing, Supervision, Conceptualization. **G. Masi:** Writing – review & editing, Supervision, Data curation. **D. Coghill:** Writing – review & editing, Supervision, Conceptualization. **A. Zuddas:** Conceptualization. **S. Carucci:** Writing – review & editing, Supervision, Data curation. **C. Balia:** Writing – review & editing, Supervision, Formal analysis, Data curation.

Informed consent

Informed consent was obtained from all subjects' parents/legal guardians before starting any study procedure; patients and control subjects were also provided informed consent and signed assent documents according to the national law.

Data availability statement

All data are available upon reasonable request emailed to the corresponding author.

Ethics approval

MATRICS_WP6-1 study was conducted according to the guidelines of the Declaration of Helsinki and approved by the national competent authority AIFA (Agenzia Italiana del Farmaco) on July 4, 2017. Approval from the local ethical review boards (Comitato Etico Indipendente of the Cagliari University Hospital and Comitato Etico per la Sperimentazione Clinica of the Tuscany Region) was obtained on December 29, 2017 for the Cagliari site and on January 22, 2018 for Pisa (Tuscany) site. EudraCT registration number: 2015-001916-37.

CNeSA clinical study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Independent Ethics Committee of the Cagliari University Hospital on March 28, 2018 (protocol number: PG/2018/4421).

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Declaration of competing interest

C.N., A.M., F.P and J.C.G. declare no conflicts of interest; F.D.: sub-investigator in clinical trials sponsored by Lundbeck and as an independent rater in clinical trials sponsored by Servier, Acadia and Bioproject; G.M.: Advisory board for Angelini; speaker for Lundbeck, Otsuka, Humana; Institutional Grants Angelini, Humana and Laborest; D.C. served on advisory boards, gave lectures, or received travel grants within the last 5 years from MEDICE, Novartis, Servier, and Shire/Takeda; and has received royalties from Cambridge University Press and Oxford University Press; S.C.: collaborations within projects from the European Union (7th Framework Program) and as a sub-investigator in sponsored clinical trials by Lundbeck, Otsuka, Janssen Cilag, Angelini, and Acadia; C.B: collaborations within projects from the European Union (7th Framework Program) and as a sub-investigator in sponsored clinical trials by Lundbeck, Otsuka, Janssen Cilag, Angelini, and Acadia.

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