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This Section of *Epidemiology and Psychiatric Sciences* regularly appears in each issue of the Journal to describe relevant studies investigating the relationship between neurobiology and psychosocial psychiatry in major psychoses. The aim of these Editorials is to provide a better understanding of the neural basis of psychopathology and clinical features of these disorders, in order to raise new perspectives in every-day clinical practice.

Paolo Brambilla, *Section Editor* and Michele Tansella, *Editor* EPS

The dysregulation profile in children and adolescents: a potential index for major psychopathology?

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We here review the literature on Child Behaviour Checklist-Dysregulation Profile (CBCL-DP) index, which potentially represents a developmental profile of major psychopathology in early adulthood. The understanding of the neural underpinnings of children and adolescents with altered regulation of affect and behaviour may ultimately help in planning strategies to prevent psychiatric syndromes during development.

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The Child Behaviour Checklist (CBCL) is a widely used questionnaire in research on developmental psychopathology (Achenbach & Rescorla, 2001). It is composed of 118 questions filled by the parents and provides T scores for three general domains (Total, Internalizing and Externalizing problems), eight Empirically Based Syndromes Scales (Anxious/Depressed, Withdrawn/Depressed, Somatic Complaints, Social Problems, Thought Problems, Attention Problems, Rule-Breaking Behaviour and Aggressive Behaviour) and six Diagnostic and Statistical Manual of Mental Disorders (DSM)-oriented scales (Affective Problems, Anxiety Problems, Somatic Problems, Attention Deficit/Hyperactivity Problems, Oppositional Defiant Problems and Conduct Problems). In the past few years, it has been proposed that the sum of T scores in three Syndromes scales (i.e. Aggressive Behaviour, Anxious/Depressed and Attention Problems) could be used to identify CBCL-Juvenile Bipolar Disorder index (CBCL-JBD index; Biederman *et al.* 2009). However, the diagnostic value of this index in detecting JBD has been disconfirmed afterwards because of its low sensitivity and specificity (Volk & Todd, 2007). Recently, the CBCL-JBD index has been renamed as 'CBCL-Dysregulation Profile' (CBCL-DP) index, as it better detects children with 'a persisting deficit of self-regulation of affect and behaviour' (Holtmann *et al.* 2011). Several studies confirmed that CBCL-DP does not represent an early manifestation of JBD and it is not linked to a specific psychiatric diagnosis (Ayer *et al.* 2009), rather it is a developmental risk marker of poor overall functioning in adult life (Holtmann *et al.* 2011, Table 1). In large population-based samples (Ayer *et al.* 2009; Althoff *et al.* 2010, Table 1), this index usually indicates a more severe psychopathology, and studies on clinical populations also confirmed these

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Table 1. *Summary of the studies described in this review*

Study	Sample	Age range	Type of study	Assessment and diagnostic	Findings
Althoff *et al.* (2010)	1576 subjects population-based sample	3–17 at baseline	Longitudinal (14 years)	CIDI CBCL	CBCL-DP was associated with anxiety and disruptive behaviour disorders after controlling for co-occurring disorders in adulthood.
Ayer *et al.* (2009)	2029 subjects population-based sample	6–18	Psychometric	SES CBCL	High overlap between CBCL-DP and CBCL-PTSD scale.
Biederman *et al.* (2009)	204 ADHD	6–18 at baseline	Follow-up (7.4 years)	KSADS-E GAF SAICA SCID SES CBCL	CBCL-DP predicted subsequent diagnoses of BD, major depression and conduct disorder. Associated with impaired psychosocial functioning and psychiatric hospitalization.
Doyle *et al.* (2010)	765 individuals from 154 families enrolled in a linkage study of ADHD	11.1 mean age	Genetic	CBCL KSADS-E	Dysregulation profile is highly inheritable. Peaks on 1p21.1, 6p21.3 and 8q21.13 surpassed the threshold for suggestive linkage.
Halperin *et al.* (2011)	90 ADHD	7–11 at baseline	Follow-up	IOWA Conners DISC K-SADS-PL SCID-II CBCL YSR	CBCL-DP did not significantly predict Axis I disorders, but it significantly predicted the presence of a cluster C personality disorder.
Holtmann *et al.* (2011)	325 young adults at risk for psychiatric illnesses	0.3 at baseline	Longitudinal (19 years)	MEI SCID-I GAF SUQ FTND BDI	CBCL-DP scores in childhood are at increased risk for ADHD, mood and substance use disorders, suicidality and poorer overall functioning.

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Jucksch *et al.* (2011)	9024 clinical subjects	4–18	High DP *v.* other clinical samples	GAPD Psychosocial axis of ICD-10 (consensus among clinicians) CBCL	CBCL-DP subjects were significantly more impaired and had more psychosocial adversities than other subgroups.
Meyer *et al.* (2008)	74 offspring of parents with mood disorders	1.5–7	Longitudinal (23 years)	CAS	CBCL-DP had significantly lower levels of social and occupational functioning. They were at risk for anxiety disorders, ADHD, cluster B personality disorders and BD, drug abuse and suicidal ideation.
	27 controls			DICA SCID-I IPDE GAF CBCL	
Rich *et al.* (2011)	20 BD	8–17	Neuroimaging (MEG)	KSADS-PL	SMD youth showed greater arousal after negative feedback than both BD and controls, and they responded to negative feedback with significantly greater activation of the ACC and MFG than controls.
	20 severe mood dysregulation		Affective Posner Task.	CDRS	
	20 controls			YMRS CGAS	
Spencer *et al.* (2011)	197 ADHD	6–18	Group comparison	KSADS-E	Higher CBCL-DP in ADHD is associated with higher rates of psychiatric comorbidity and with significant impairment in social function.
	224 controls			SAICA CBCL	

ACC, anterior cingulate cortex; BDI, Beck Depression Inventory; CAS, Child Assessment Schedule; CDRS, Children's Depression Rating Scale; CGAS, Children's Global Assessment Scale; CIDI, Composite International Diagnostic Interview; DICA, Diagnostic Interview for Children and Adolescents; DISC, Diagnostic Interview Schedule for Children; FTND, Fagerström Test for Nicotine Dependence; GAF, Global Assessment of Functioning; GAPD, Global Assessment of Psychosocial Disability; IPDE, International Personality Disorder Examination; KSADS-E, Epidemiological version of Kiddie-Schedule for Affective Disorder and Schizophrenia for Children; MEG, Magneto-Encephalography; MEI, Mannheim Parent Interview; MEL, Munich Events List; SAICA, Social Adjustment Inventory for Children and Adolescents; SES, Socio-Economic Status; SCID, Structured Clinical Interview for DSM-IV; SMD, Severe Mood Dysregulation; SUQ, Substance Use Questionnaire; YMRS, Young Mania Rating Scale; YSR, Youth Self-Report.

results. Most of the studies on clinical subjects involved Attention Deficit Hyperactivity Disorder (ADHD). Spencer *et al.* (2011, Table 1) found that children with ADHD and CBCL-DP were more socially impaired and they had increased probability of comorbid disorders (such as anxiety and disruptive behaviour disorders) compared to non-CBCL-DP ADHD. Consistent findings were reported by follow-up studies on ADHD children (Biederman *et al.* 2009; Halperin *et al.* 2011, Table 1).

Studies on heterogeneous clinical populations found results in the same direction. Meyer *et al.* (2008) analysing data from a 23 years longitudinal study on at-risk youth for psychiatric disorders (i.e. offspring of parents with mood disorders), found that CBCL-DP during childhood is associated with later anxiety disorders, ADHD, cluster-B personality disorders, bipolar disorder (BD), drug abuse and suicidal ideation (Table 1). Similar results were found on 9024 clinical subjects with non-specified psychiatric pathologies (Jucksch *et al.* 2011) and on 325 children that presented risk factors associated with obstetric complications and psychosocial status (Holtmann *et al.* 2011, Table 1).

As to the neurobiological bases of this syndrome, so far few studies have investigated the biological and neural substrates of the CBCL-DP. It has been shown that this profile is highly inheritable (Doyle *et al.* 2010) and that it is associated with genetic regions found in adult BD, schizophrenia, autism and ADHD, like 1p21 (Table 1).

In parallel studies, Rich *et al.* (2011) using the magnetoencephalography (MEG) compared children with Severe Mood Dysregulation (SMD), characterized by abnormal mood, hyper-arousal and increased reactivity to negative emotional stimuli, being therefore very similar to the CBCL-DP (Leibenluft, 2011), to children with BD and controls during a Posner Affective Task. This task consists of a modified Posner Task, in which error feedbacks are modified to elicit frustration. The authors found that SMD youth showed greater arousal following negative feedback than both BD and controls, and they responded to negative feedback with significantly greater activation of the anterior cingulate cortex (ACC) and the medial frontal gyrus (MFG) than controls, while BD youth showed dysfunction in the superior frontal gyrus (SFG) and insula (Table 1). It seems therefore that specific cerebral substrates are involved in childhood SMD, thus supporting the hypothesis of a specific syndrome not related to JBD (Leibenluft, 2011).

In conclusion, there is evidence that the CBCL-DP represents a useful index for identifying children and adolescents at risk for psychiatric problems in early adulthood. Given the ease of administration of the CBCL and its widespread use, this could become a powerful and low-cost tool to detect children who need early intervention for the prevention of mental illnesses, reducing the subsequent cost of treatment for psychiatric disorders (Kessler *et al.* 2009). However, few studies have been carried out so far to explore the potential neurobiological bases of patients with CBCL-DP. More neuroimaging investigations, coupled with neuropsychology and genetics, are therefore expected to further delineate the neural underpinnings of CBCL-DP, which may ultimately help in planning specific strategies to prevent major psychopathology during development.

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