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EDITORIAL

Diagnostic overlap and exploration of risk factors in child psychiatry

Carmen Moreno[1]

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The articles in this ECAP issue shed light on interesting current conundrums in child and adolescent psychiatry. Diagnostic overlap, searches for endophenotypes and exploration of risk factors are common themes.

Canu et al. conducted a comprehensive review including longitudinal studies following up on younger siblings of children with autism spectrum disorder (ASD) to explore the predictive role of non-social characteristics (observable behaviours, cognitive functions and personal characteristics) on subsequent ASD diagnosis [1]. Compared to children with typical development, siblings of ASD children showed slower disengagement of attention and less mature fine motor skills during the first year. Those later developing ASD showed atypical attention disengagement and abnormal fine and gross motor development during the second year of life, too. As non-social abnormalities appear early, targeting them could add to early identification of ASD in a period critical for brain development.

Fuentes et al. developed a multi-stage epidemiological study of the prevalence of ASD among children 7–9 years [2]. They found a 0.59 percent prevalence rate, lower than in other studies, although limitations such as lack of participation need to be considered. However, interestingly, the newly identified cases (18%) were all males with normal IQ and less severe phenotype. While delayed identification of these children with normal intelligence may reflect a later-onset of social skills deviations in this ASD subgroup, the absence of females in the newly diagnosed sample casts doubt on the gender sensitivity of current diagnostic tools.

Bryson et al. used data from a large community cohort of mother–child dyads enriched for adversity risk to examine the role of maternal physiological stress and parenting behaviours in explaining effects of adversity on young children's physiological stress measured via hair cortisol [3]. Although they did not identify any mediating pathways between economic or psychosocial adversity during pregnancy and mothers' or children's physiological stress, they documented an independent association between maternal and child hair cortisol. This finding suggests that endogenous genetic factors, likely through HPA axis activity and cortisol secretion, may play a greater role than exogenous environmental exposures in young children's physiological stress.

Burrell et al. also studied parental influence on offspring outcomes [4]. They used longitudinal data from Norwegian registries to investigate the influence of parental death by external causes before age 18 years and subsequent risk of hospital-treated deliberate self-harm (DHS). Losing a parent to suicide was associated with the highest risk of DHS hospitalisation, followed by death by falls, poisoning or drowning, but they found no association with deaths from other accidents or external causes. The association was stronger for the few cases born after 1998. Although the impact of shared environmental factors and family discord cannot be ruled out, genetic factors linking suicidality and other mental health outcomes may explain in part the association between parental suicide and death from other accidents and increased risk of DHS hospitalisation in offspring.

Rauschenberg et al. used ecologic momentary assessment and found that exposure to bullying victimisation, specifically physical and indirect, modified affective and psychotic reactivity to stress in youth already undergoing mental health treatment [5]. The patients´ siblings lacked the association and controls had an opposite association, i.e. showing less intense negative affect by exposure levels. Although causality could not be determined with this design, biological vulnerability to stress may underlie group differences and represent a risk or resilient mechanism linking bullying exposure and mental health outcomes.

Seernani et al. evaluated children with ADHD, ASD with and without comorbid ADHD, and controls using behavioural and oculomotor parameters of a visual search

✉ Carmen Moreno
cmoreno@hggm.es

[1] Department of Child and Adolescent Psychiatry, Institute of Psychiatry and Mental Health, Hospital General Universitario Gregorio Marañón, IiSGM, CIBERSAM, School of Medicine Complutense University of Madrid, Madrid, Spain

task [6]. They found that ASD cases performed better in visual search, but this effect was not present in ASD cases comorbid with ADHD, who, as ADHD-only cases, showed increased intra-subject variability (ISV), suggesting ISV as a trans-diagnostic phenotype linked to attention-deficit and hyperactivity.

Scaini et al. used the Italian twin registry to explore environmental and genetic contributions to comorbidity between anger and anxiety syndromes [7]. They found that shared, but no unique, environmental influences had small effects on the phenotypic covariation between anger and anxiety in panic/somatic anxiety, generalised anxiety and social anxiety, but genetic effects did not. The results imply that most etiological influences on anxiety and anger, a construct close to irritability, are independent from each other, and lends support for consideration of irritability as a transdiagnostic construct with potential biological underpinnings.

Damiani et al., using data from the International Neuroimaging Data-Sharing Initiative from the NYC ADHD2000 repository, including 93 ADHD and 88 neurotypical controls, found that ADHD cases had a significantly higher resting state functional connectivity between caudate and regions of the salience network implicated in regulation of attentional switches, behavioural performance, inhibitory control and tolerance to reward delays [8]. This hyperconnectivity in ADHD individuals' subcortical-mesolimbic regions may imply that ADHD is a disorder of emotional salience regulation.

Along similar lines, Blanken et al. explored personality features in 178 children with ADHD (mean age 8.2 (1.4)) using the Big Five questionnaire for children [9]. Children were medication free at baseline and were longitudinally assessed over 1 year. Authors found three temperament profiles: two of them irritable/emotionally dysregulated (profile 1 with decreased levels to openness to experience and profile 2 with decreased agreeableness compared to the other groups) and a third one displaying scores on the normative range. Clinical differences emerged between these groups, with higher inattention in profile 1, higher hyperactive-impulsive scores in profile 2, and lowest ADHD severity in profile 3. Among children starting medication between baseline and follow-up (44.6%), emotional instability (profiles 1 and 2) at baseline predicted better response to treatment, regardless of symptom severity. Together, the studies of Damiani et al. and Blanken et al. highlight the presence of emotional dysregulation in ADHD and their potential predictive value for treatment and response.

Wang et al. examined prevalence and risk factors for ADHD in a large cohort ($n=695$) of patients 6–15 years of age with congenital heart disease [10]. In this sample, ADHD prevalence was 12.4%, but prevalence of the inattentive-predominant subtype was high (6.8%). The ADHD inattentive profile was more prevalent in patients with greater clinical severity and with cyanotic illness. Although only 58.7% of parents had sought psychiatric care, this proportion was only 18.2% among children with the ADHD inattentive subtype.

In three large consecutive studies in independent samples ($n=234$, $n=313$, $n=315$) reported together, Dekkers et al. showed that parental knowledge on where, how, and with whom children spend their time mediates the association between ADHD and related domains of impairment, namely risk-taking behaviours, resistance to peer influence and homework problems, although with smaller effect on the latter [11]. Although ADHD symptomatology has a major impact on development of risk-taking behaviours and homework problems, improving parental knowledge should also be included as a treatment target of adolescents with ADHD.

Gvion et al. investigated clinician-related factors that increased the likelihood of treating (vs referring) a suicidal adolescent (12). Interestingly they found that the number of treatment tools available and subjective competence increased willingness to treat suicidal adolescents, whereas a therapists' experience correlated negatively. This highlights the need for better skills and tools for treatment of this population and strategies to prevent clinician burnout.

The articles featured in this ECAP issue highlight the need for addressing diagnostic overlap with biologically-based methods complementary to clinical characterisation. They support the transdiagnostic and prognostic value of irritability among paediatric psychiatric conditions, and suggest the expansion of high-risk consideration to offspring of parents who die by suicide and violent accidents. They also underline the weight of genetic factors in vulnerability to stress and its impact on mental health outcomes of children and adolescents, and call for refining diagnostic tools and screening methods to target paediatric populations in which developmental deviations and mental health problems may remain underdiagnosed.

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