



# Aetiological developmental models of symptoms of mental disorders in children: are we focussing on the relevant aspects in relation to individual diagnosis and intervention?

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There is a long history of empirical research testing biologically or psychosocially oriented models to explain the incidence and prevalence of mental disorders, first, in adults since around the nineteenth century and, more recently, also in children since around mid of the twentieth century. Many early models focussed on single or just a few factors, which were expected to explain most of the variance in behaviour, impairment or psychopathology associated with mental disorders, accommodating the human mind's cognitive bias of seeking causality. By integrating current advances in genetics, epigenetics, neuroscience (including neurocognitive, behavioural and interpersonal aspects) as well as computational basic science, aetiological models of mental disorders, diagnostic and intervention approaches for mental disorders in children and adolescents may be considerably revised in the future.

In the present issue, results of clinical and population based, cross-sectional (Arnaud et al., Pauli-Pott et al., Treier et al., Tetteh et al. in this issue) as well as longitudinal studies (Andreassen et al., Carr et al., Cheng et al., Houmann et al., Leppänen et al., Panagi et al., Schettler et al., Sivertsen et al., Tanaka et al. in this issue) from childhood to adolescence or adulthood are reported. Especially the authors of the longitudinal studies have made a huge and costly effort to ascertain large samples and longitudinally re-assess their initial study population, resulting in retention rates around 70% in most studies. The results are most often reported either as correlations (dimensional measures) or as odds ratios (categorical measures), which are statistical measures of protective or risk effects across all individuals of

the respective study sample, adjusted for the effect of other, so called “confounding” variables. They cannot prove causality, even not based on longitudinal study results nor can the individual's longitudinal outcome be predicted based on these measures. Still, results of the studies in this issue are highly relevant with regard to primary prevention on the population level of head injuries in children (Carr et al. in this issue) as well as indicated prevention of mental disorders in the population of preterm children (Leppänen et al. in this issue) or in children with long-term physical health conditions (Panagi et al. in this issue). They also show, that on the group level, psychopathological internalising as well as externalising symptoms show a relatively high stability over time in around 10% of older school aged children and youth (Cheng et al., Sivertsen et al. in this issue). In addition, most of the studies in the present issue found that increased symptoms of internalising (Sun et al., Tanaka et al. in this issue) or externalising psychopathology (Arnaud et al., Vanzella-Yang et al., in this issue) as well as emotion dysregulation (Paschke et al., Treier et al., in this issue) or reduced executive function abilities (Andreassen et al.) in childhood predicted longitudinal outcomes in various domains, such as substance use, educational achievement or chronicity of mental disorder symptoms.

Based on the findings of the articles in this issue, several aspects related to improved targeted diagnosis, prevention and intervention in the preschool and school age years may be discussed.

First, early intervention in preschool and school age, which effectively increases the child's emotion regulation and executive function abilities, and reduces her/his mental disorder symptoms needs to be implemented on a broad societal level. The systematic review of Sampaio et al. (in this issue) reports strong evidence for cost-effectiveness of parent trainings in the preschool and school age on mental disorder symptom reduction, especially for children with elevated externalising symptoms (targeted prevention and early

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intervention), but also on anxiety (primary prevention). It may be assumed, based on additional studies, that executive function abilities are also improved by early parent trainings [1]. In contrast, it is less clear, if these parent trainings also may improve the child's emotion regulation strategies. Given the strong association of preschool emotion regulation abilities with adolescent emotion regulation [2], parent trainings during preschool age should be tested for their efficacy and cost-effectiveness to also improve emotion regulation in the future. The efficacy and cost-effectiveness of parent trainings also point to another, often neglected, aspect in child mental health, the relevance of interpersonal relationships for their individual development and psychopathology. In young children, especially the relations and interaction with adults, including parents, is of relevance, in older children from preschool age on also with their peers, and additionally from adolescence onwards, the larger society [3, 4].

Second, medication also is effective in reducing externalising symptoms, especially symptoms of inattention, hyperactivity and impulsivity. Vertessen et al. (in this issue) found a linear dose–response-relationship of response to methylphenidate during a randomised-controlled trial in most, but not all children with attention-deficit/hyperactivity disorder (ADHD). Houmann et al. (in this issue) reported a longitudinal association of response to methylphenidate treatment at 3 and 12 weeks of methylphenidate initiation on the 3 year outcome of hyperactivity, impulsivity and oppositional-defiant behaviour in school aged children with ADHD. A recent meta-analysis has found increased efficacy and reduced likelihood of discontinuations with increasing stimulant doses in randomised-controlled trials of methylphenidate in children and youth [5]. Thus, clinicians should carefully review early response to methylphenidate treatment within the first 3 weeks, and titrate the dosage flexibly to the needs of the individual child with ADHD, either below or beyond recommended maximum doses.

Third, working in the mental health care sector, especially in inpatient wards, professionals are seeing many children and youth with an accumulation of psychopathological symptoms as well as a multitude of biological, individual and psychosocial risk factors. These highly burdened children and youth, who often show a chronic course of their mental disorders and associated behavioural symptoms, coming along with a strongly reduced quality of life in regard to most dimensions, are well described in the article by Kandsberger et al. (in this issue), focusing on emergency admissions to an acute child and youth mental health care ward. Many of these children show an accumulation of disorder specific as well as cross-disorder symptoms, such as attention problems (Vanzella-Yang et al. in this issue), impulsivity, impaired executive function (Arnaud et al., Andreassen et al. in this issue), dissociative symptoms (Tanaka et al. in this issue), emotion

dysregulation (Schettler et al., Treier et al. in this issue), aggression (Carr et al., Cheng et al. in this issue), anxiety, pathological gaming (Schettler et al. in this issue), substance use (Arnaud et al. in this issue), self-harm (Tanaka et al., Tetteh et al. in this issue) or suicidality (Tetteh et al. in this issue). Still, many studies are focussing on single symptoms or diagnoses only, thus, it remains unclear, if their results may be generalised to the most severely affected children and youth.

To improve early detection, diagnosis and care for children at highest risk for a chronic course of many comorbid mental disorders and associated symptoms, there is thus a need to develop and test developmental science informed predictive, individualised multilevel models. These will go far beyond the current mental disorder classification systems. For example, applying ICD-11 criteria (<https://icd.who.int/browse11/l-m/en>), some of the above discussed co-occurring symptoms are combined into categorical diagnoses. Other impairing symptoms, such as non-suicidal self-injury (NSSI) or suicidality can be documented under “Symptoms, signs or clinical findings, not elsewhere classified”, “External causes of morbidity or mortality” or “Factors influencing health status or contact with health services”. In clinical practise, these impairing symptoms are often a reason for emergency admissions, but do not constitute a diagnosis. Thus, based on the current classification systems, presenting symptoms of the individual child or youth are categorised into different entities, which are often studied separately, such as conduct disorder, aggressive symptoms (Cheng et al., in this issue), NSSI or suicidality (Tanaka et al., Tetteh et al. in this issue), despite clear evidence of high rates of comorbidity and co-occurrence [6]. Clinically meaningful individualised aetiological models thus may necessitate other diagnostic approaches. To differentiate children at risk for or with mental disorders from typically developing children from an early age on, normative models of behavioural, cognitive, emotional, and social development in various domains, including biological measures, may be helpful. For example, brain imaging studies have started to elicit biologically defined subtypes within the same diagnosis or across diagnostic categories based on normative modelling [7]. These models may be also applied to other dimensional measures, similar to growth charts or IQ tests. Based on culturally sensitive normative models, children may be assigned to a profile of characteristics in several dimensions, including also interpersonal characteristics [8, 9]. This multidimensional approach will allow to individually describe deviations from typical development on various levels, and could also be integrated within the domains of the RDoC initiative (<https://www.nimh.nih.gov/research/research-funded-by-nimh/rdoc>). The contribution of each diagnostic level to the individual's quality of life, educational achievement or emotional wellbeing may then be individually assigned, and

targeted intervention approaches may be chosen based on the respective multidimensional profile.

To establish and test such innovative diagnostic models, large sample across several countries with comparable and high-dimensional measures are necessary, including also biological measures, such as genetic information [10]. Open science recommendations will be highly supportive in establishing large collaborative networks which will allow to advance developmentally based, personalised diagnosis and intervention approaches for children and youth.

## Declarations

**Conflict of interest** Christine M. Freitag is Editor for European Child and Adolescent Psychiatry.

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