The search for core symptoms: will this help clinical decision making?

Heterogeneity is the rule rather than the exception in neurodevelopmental disorders. Our nosological frameworks allow us to group together children who share symptom patterns, and who, we assume, also share underlying biological and environmental vulnerabilities that are unique to that particular diagnostic category. These same children, however, will often vary considerably on any number of other developmental traits that may be shared with other diagnostic groups, and may well be as important for prognosis and treatment as the core symptoms that defined the group. Autism spectrum disorder (ASD) is a perfect example. Diagnosis is based on the presence of both social communication deficits and a restricted repertoire of interests and behaviours (APA, 2013). Yet within ASD there is enormous variation in other developmental processes and some, such as the development of spoken language before school entry, are key predictors of long-term well-being and later independence (cf. Thurm, Manwaring, Swineford, & Farmer, 2015). The causal relationships between core symptoms and ancillary symptoms are hotly contested and a matter of both theoretical and clinical interest. We now know that the genetic liabilities that give rise to language impairment within ASD are also implicated in the language deficits that characterise a number of other seemingly disparate developmental disorders (Rodenas-Cuardrado, Ho & Vernes, 2014). But what does this knowledge mean for research and clinical practice? How should we approach the heterogeneity that dominates our clinical reality?

Given this clinical picture, I'm often intrigued by the considerable research effort that goes into refining assessment in order to achieve ever more homogeneous sub-groups within a particular diagnostic category. The main assumptions that drive this approach are (a) that improved measurement will identify syndrome-specific symptom profiles; (b) that these in turn will signal distinct causal pathways distinguished by unique underlying neurobiological mechanisms; and (c) that identification of neurobiological mechanisms will inform diagnosis-specific approaches to treatment. Somer et al. (this issue) exemplify this approach to refining diagnostic criteria. They

investigated the factor structure of a commonly used diagnostic instrument, the ADOS, in order to identify core dimensions of social communication deficit that are unique to ASD, and those aspects of social communication impairment that may be present to varying degrees in other neurodevelopmental disorders. A real strength of the paper is the comparison of symptom profiles in ASD to a heterogeneous, non-ASD group with a variety of developmental diagnoses. Given the controversy that surrounds the new DSM5 category 'social (pragmatic) communication disorder' (Norbury, 2014), this paper provides a welcome delineation of potential qualitative differences in social communication that could aid differential diagnosis. Specifically, 'basic social-communication' behaviours, (which included eye contact, facial expressions and gesture) were separated from 'interaction quality' behaviours (including rapport, conversation and reciprocal social communication), and a third factor which reflected restricted interests and repetitive behaviours. Furthermore, while basic social-communication behaviours were not significantly correlated with child characteristics such as age or gender, interaction quality behaviours were, though the effect size is small. Verbal ability was not included in the correlational analysis, and in terms of differential diagnosis, it is important that future investigations consider how verbal and non-verbal pragmatic skills co-vary with structural language competence.

The authors suggest that an important implication of their work is the ability to isolate basic social communication symptoms that are relatively specific to ASD and less subject to broader developmental influences such as language or cognition in order to facilitate efforts to identify ASD-specific aetiologies. I see equal value in attempting to understand what is common across diagnostic boundaries, and how more 'disorder general' vulnerabilities shape both core features and clinical outcomes. A quick survey of this current issue of JCPP suggests that language, non-verbal ability, executive function and anxiety are traits that are variably compromised across most developmental disorders and add significantly to prediction of long term outcome, above and beyond core symptoms. Robust measurement of core and ancillary traits remains important, but their association with a particular diagnostic category is perhaps less so.

In particular, I want to consider what implications for treatment arise from finding relatively 'pure' symptom profiles linked to particular genetic and/or neurobiological mechanisms. Assuming we are able to identify a reasonably homogeneous group of children with ASD with respect to basic social communication profiles, in our current knowledge state identification of the genetic and neural markers of basic social communication deficit is unlikely to inform our strategies for treating core social communication symptoms. Another issue is that a group homogeneous for core symptoms may well be heterogeneous for other traits. For example, groups of children similar with respect to core autism symptomatology may have significantly different levels of language competence (Loucas et al. 2008). These differences may influence response to treatment, and may suggest different approaches to treating core symptoms is warranted, depending on the child's level of language competence. In addition, Somer et al. acknowledge that non-core symptoms may in fact be the preferred intervention target, especially if deficits in, for example, interaction quality yield more functional impairment in social adaptation and academic achievement. Clinicians often assume that treatment of language and communication in ASD requires a qualitatively different framework to intervention for similar concerns in other populations, such as those with specific language impairment (Bishop et al. 2016). However, there is little, if any, hard evidence at the moment that this is the case. Assessing treatment effects in 'pure' diagnostic groups will no doubt limit sample size; it may be worth asking whether particular traits influence response to treatment in larger, more diverse clinical samples.

Another challenge in the pursuit of core symptoms, is that the presence or quality these symptoms is likely to fluctuate over development and perhaps in response to external environmental factors such as family experience, schooling or intervention. Clinicians must therefore incorporate heterogeneity and issues of developmental timing into treatment planning. This is illustrated by three studies in the current issue that focus on conduct disorder. We are reminded by Wall et al. (this issue), that a reasonably straightforward measure of behaviour, the presence or otherwise of callous-unemotional (CU) traits, appears differentiate sub-groups of children with

conduct disorder that arise from at least partially distinct genetic influences. Of clinical relevance, it has been suggested that these sub-groups respond differently to conventional treatment approaches, and may thus require differentiated approaches to treatment and outcome measurement (cf. Hyde, Waller & Burt, 2014). Nevertheless, Wall et al. demonstrate that even when sub-groups are more homogeneous on a measure of CU traits, they may still vary significantly with regard to expression of conduct problems. In addition, other child-level factors such as executive dysfunction and concomitant hyper-activity/impulsivity, as well as environmental factors such as parenting behaviours were important predictors of whether or not children with high-CU traits engaged in significant amounts of anti-social behaviour. Furthermore, Short et al. (this issue) demonstrate that non-verbal cognitive abilities and concomitant anxiety disorder may modulate emotion recognition processing in individuals with conduct disorder. It would therefore seem that measurement of additional factors is at least as important as classifying children into appropriate sub-groups in treatment planning and in understanding individual differences in treatment response.

Staying with conduct problems for the moment, Powers, Bierman & Coffman (this issue) consider issues of intervention timing, with a focus on educational placement. Their results highlight the unintended negative consequences of restrictive educational placements on key adolescent outcomes including conduct problems, depressive symptoms, and non-completion of high school. Importantly, placement in a restrictive setting during primary school had negligible impact on adolescent outcomes. In contrast, placement during secondary school increased risk for poor outcome, but especially for those children with better cognitive performance. Unfortunately, CU traits were not measured in this population, so we are unsure whether this adds another dimension to our understanding of adolescent outcomes for children with early-onset conduct problems. Nevertheless, these findings raise important challenges for clinical and educational services as they indicate a need to accommodate these young people within mainstream education settings without compromising the learning environment of other children. Clearly, treatment programmes based in

education settings are urgently needed. Those that take account of additional child-level and environmental factors that may moderate education experience would be especially informative.

A different clinical group was investigated by Hiller et al. (this issue) but this group highlights an additional consideration: is intervention always necessary, or is there sufficient natural variation in outcome to warrant a period of 'watchful waiting'? Hiller et al. focused on children who have been exposed to trauma and show symptoms of post-traumatic stress disorder (PTSD). This group is extremely heterogeneous given the wide variation in pre-morbid child status and the nature of the trauma experienced. Hiller et al. used meta-analysis to elucidate the extent to which spontaneous recovery is possible in the year following exposure to trauma; encouragingly, prevalence of PTSD was reduced by approximately 50% in the first six months following the traumatic event. This good news was tempered by the additional finding that there was very little change in either prevalence or symptom severity after six months. The obvious clinical implication from this work is that a 'watchful waiting' approach may be the most clinically appropriate action to take in the immediate aftermath of a trauma, with screening and assessment after six months more likely to identify those children with persistent PTSD in need of intervention. Two caveats to this conclusion are worth noting. First, the authors note that children experiencing very high levels of distress in the acute phase may well require immediate clinical attention. Second, as is often the case in developmental conditions, although we know that many children will show significant symptom improvement without clinical intervention, our abilities to predict with any certainty who will resolve and who will present with persistent need is still far from perfect. Here again, individual differences in child characteristics such as anxiety, and environmental influences such as the child's social networks may increase prediction and inform intervention targets (Hiller et al).

Refining diagnostic tools is an important endeavour as clinical decisions rely on tools that are reliable, valid and sensitive to differences between people and sensitive to measuring change (developmental or in response to specific inputs). Refining clinical tools in order to identify more

homogeneous sub-groups, or to facilitate discovery of neurobiological markers may be less likely to translate into better clinical care. Instead, embracing heterogeneity within a diagnostic category and encouraging cross-disorder comparisons of shared traits may ultimately yield more clinically applicable outcomes. The papers in this volume demonstrate that variables such as child language, cognition and affect, environmental experiences and developmental timing, are as important as core symptom profiles in understanding the developmental course and potential for change following clinical or educational input.

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