

## Back to basics in behavioural phenotypes

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## **Back to basics in behavioural phenotypes: insights from developing a detailed understanding of behaviour**

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The 22<sup>nd</sup> SSBP Educational Day and Research Symposium focuses around the theme, ‘Back to basics in behavioural phenotypes: insights from developing a detailed understanding of behaviour’. The theme of the conference was inspired by an editorial published in the *Journal of Intellectual Disability Research* in 2017 (Oliver, 2017), titled ‘*The importance of knowing when to be precise.*’ It was argued that, at this point in the development of behavioural phenotype research, where we are seeing the synthesis of disciplines such as genetics, psychiatry and psychology, it is more important than ever to place emphasis on precise behavioural measurement. Importantly, researchers need to be careful to avoid clustering behaviours together under collective terms such as “challenging behaviour.” A lack of precision could preclude discovery of fine-grained associations between different levels of functioning, which are potentially lucrative for furthering our understanding of mechanisms and progressing towards intervention. For example, recent research has highlighted that in Tuberous sclerosis complex, whilst both self-injury and aggression “challenging behaviors” are associated with impulsivity, self-injury is also associated with gastric health problems and communication difficulties, and aggression is also associated with compulsive behaviour (Wilde et al., 2017). Thus, describing behaviour in detail identifies both shared and divergent pathways to mechanism and ultimately intervention. Once evaluating potentially efficacious interventions, decades of work in pharmacological treatment trials has highlighted the major limitations in many of the most commonly used behavioural measures, which fail to detect important subtle changes that may become even more clinically meaningful in the longer term (Berry-Kravis et al., 2017). The speakers at this year’s conference remind us of the importance of precision by providing numerous examples of how careful behavioural phenotyping is providing new insights into pathways from gene to behaviour.

The *Educational day* addresses key methodological approaches, which have the potential to increase our understanding of behavioural phenotypes and facilitate pathways to intervention. Each of these approaches benefits in a specific way from a detailed understanding of behaviour. A. Stanfield’s keynote introduces how, with a detailed understanding of an individual’s genetic, cognitive and/or behavioural profile, we can better target pharmacological treatments to benefit particular individuals. L. Gallagher’s keynote builds on this, introducing how developing neurodevelopmental disorder carrier cohorts based on genetic profiles can progress work on understanding behaviour and treatment. Importantly, in such work that takes a person’s genetics as the starting point, we observe commonalities in behaviour linked to different genetic profiles, suggesting shared pathways to behaviour, which may be addressed at intervention. Highlighting this issue, A. Meyer-Lindenberg’s keynote addresses the transdiagnostic nature of neurodevelopmental disorders and associated behavioural phenotypes. Of course, no individual exists in a vacuum, although a cursory look at the behavioural phenotype literature may lead us to underestimate the complex roles of multiple layers of the environment. R. Hasting’s keynote helps to redress this dearth by discussing the role of family systems in rare genetic syndromes. Finally, A. Waller’s keynote provides an insight into how advancing knowledge of even idiosyncratic behaviour profiles can be put to effective use for informing the design of digital assistive technology interventions if one employs an iterative user-centred collaborative design approach.

The *Research symposium* kicks off with the *Careful phenotyping* session, led by a keynote from C. Oliver, who demonstrates advances in understanding of behavioural phenotypes in several rare genetic syndromes, which have been led by behavioural precision. But at the same time cautions against a splitting dogma, arguing that certain research, intervention and policy contexts may at times benefit from lumping – flexibility is key. Other presentations in this symposium focus on how specific genetic mechanisms linked to fragile X (Baker et al., 2019), Lesch Nyhan (Harris, 2019) syndromes and neurofibromatosis type I (Ottenhof et al., 2019) can be linked to differences in cognitive and behavioural profiles when one is careful about splitting at a genetic level.

M Thomas' keynote provides an insightful take on precision when aiming for effective intervention, discussing how computational modelling approaches can be harnessed to help us to understand intervention mechanisms in sufficient detail to know who will benefit when. This provides an excellent foundation for the *Treatment approaches for behavioural phenotypes* session. J Wolstencroft and colleagues begin to illustrate how population characteristics must be considered carefully in intervention design, by discussing the feasibility testing of a social skills training approach for adolescents with Turner syndrome, which was originally developed for autistic adolescents. S. Blackwell and colleagues take us further down the route of intervention design led by precisely defined behavioural phenotypes. They discuss the iterative collaborative design of an early intervention – together with children with Prader-Willi, fragile X syndromes or autism and their families – that tackles a specific aspect of the behavioural phenotype (resistance to change) and associated pathway (cognitive flexibility or lack thereof), which may be shared across these disorders.

In her keynote, G. Sherif, discusses how the availability of genetic testing is now providing the means to study the pathways between gene, brain, cognition and behaviour earlier in development, and the opportunities this may give for targeted intervention. G. Sherif will also remind us of the importance of developmental context when studying developmental disorders. Later in the research symposium, D. Fidler provides further examples of the importance of early developmental skills in predicting outcomes, with a focus on the foundations of goal-directed behaviour in Down syndrome. The importance of developmental context and longitudinal research is echoed throughout the *development of cognition* and the *social cognition* sessions. For example, K. Ellis and colleagues describe the application of a developmentally scaled battery of social cognition tasks to examine the interplay between early social cognition skills and social behaviour across genetic syndromes, and H. Crawford and colleagues discuss associations between impulsivity and aggressive behaviours in a longitudinal research study with fragile X syndrome.

Just as in many life science fields, Western European and North American populations are over-represented in the behavioural phenotype literature. If behavioural precision is important, then it would be unwise to ignore the role of global cultural context on behaviour. This becomes particularly pertinent if we consider how advancing genetics technologies are allowing rarer and rarer genetic neurodevelopmental disorders to be identified, and global collaboration could therefore be essential for true understanding of a disorder. Yet, we are frequently left without the means to explore such cultural impact. Leading the *Health and disease* session, C. Silvestre de Paula joins the conference from São Paulo, discussing diagnoses and service use linked to neurodevelopmental disorders in Brazil and five other Latin American countries. Only careful consideration of work like this and a concerted effort to collaborate across more than traditional borders, will allow us to tackle this global challenge on a global scale. In an impressive demonstration of how health and disease outcomes might be improved via collaborative efforts, later in this symposium R. Hithersay and colleagues report longitudinal data

from a large sample of aging adults with Down syndrome. They show that changes in performance on memory and attention tests may potentially act as early indicators of dementia.

Drawing further parallels between behavioural phenotype research and global health challenges, we are reminded of why further research into mental health in individuals with intellectual disability is needed by researchers such as K. Gray and colleagues, who provide evidence of elevated prevalence of mental health difficulties in adults with autism, including those with intellectual disabilities. There is growing awareness that individuals with intellectual disabilities are often excluded from research into mental health outcomes (Russell et al. 2019). Accordingly, we hear from researchers who are addressing this gap, such as L. Groves who illustrates how attentional control theory may provide insight into anxiety in Cornelia de Lange syndrome.

Emphasising an important theme that comes through in several guises throughout the conference, in the final keynote J. Rodgers focuses on how tailoring assessment and intervention approaches to individual difference is paramount. Indeed, when behavioural precision is recognised as important and meaningful, it is in many respects easier to think about tailoring assessment and intervention to individual difference. However – as the speakers in the conference demonstrate – even recognising that individual variability is ubiquitous, precise behavioural phenotyping can identify commonalities across individuals that are extremely useful for elucidating mechanisms of health, disorder and intervention.

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