Symposium Title: Capturing Change in Behaviour over Time in Individuals with Genetic Syndromes Associated with Intellectual Disability

Chair: Chris Oliver

Discussant: Jennifer Zarcone

Overview: There is clear evidence that individuals with genetic syndromes are at increased risk for adverse behavioural outcomes including challenging behaviour, sleep disorders, repetitive behaviour, mood disorder and poorer adaptive behaviour (McClintock et al., 2003). These behaviours are often viewed as intransient features of the syndrome. However, empirical studies have demonstrated differences in such behaviour not only between syndromes (Arron et al., 2011) but also within syndromes, with variability across individuals with the same diagnosis (Strachan et al., 2009) and within individuals over time (Cochran et al., 2015). As well as the empirical argument for behavioural change there is also a clinical picture that clearly describes these behaviours as varying day to day and week to week, a phenomenon which is important to capture. Traditional cross sectional approaches have been employed to examine the issue of behavioural change, but are insensitive to fluctuations in behaviour over short time scales and are inherently limited when examining behaviour over longer timeframes due to variance from individual differences. Critically, understanding the way behaviour changes has both clinical and theoretical implications. Identifying longer term outcomes enables effective planning for service provision and understanding the emergence and trajectory of behaviour facilitates proactive early intervention. Understanding temporal associations can help to elucidate cause and maintenance of behaviour leading to more complete theoretical models. Adequately capturing change in behaviour in the short and long term requires effective designs, sensitive measurement and robust analysis techniques. This symposium, chaired and moderated by experts in behavioural measurement, will present data from studies capturing changes in behaviour over time in individuals with genetic syndromes, from daily variation through to changes over the course of a decade. Each presentation will describe a different methodological or analytical procedure.

References/Citations:


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Paper 1 of 4

**Paper Title:** Sleep Disorders, Painful Health Conditions and Challenging Behaviour in Children with Smith-Magenis Syndrome (SMS) and Angelman Syndrome (AS): A Temporal Analysis

**Authors:** Caroline Richards⁵, Jayne Trickett⁵, Mary Heald⁵ & Chris Oliver⁵

**Introduction:** Sleep disorders and challenging behaviour are common in individuals with intellectual disabilities (Richdale & Baker, 2014; Emerson et al., 2001). Pain and painful health conditions, whilst often under-identified and under-treated, are also purported to be frequent. There is emerging evidence of bi-directional relationships between painful health conditions, sleep disorders and challenging behaviour (Tudor et al., 2015); these associations warrant further investigation. SMS (caused by loss of material on chromosome 17p11.2) and AS (most commonly caused by a deletion of the UBE3A gene), provide unique populations in which to investigate these putative associations, given the high prevalence of sleep disorders, painful health conditions and challenging behaviour in both groups.

**Methods:** Questionnaire data were collected on pain related behaviour, painful health conditions, challenging behaviour and sleep quality in children with SMS and AS. These data were augmented through novel week-long actigraphy and daily pain and challenging behaviour ratings for children with SMS (N=14) and AS (N=18). These data were analysed to evaluate temporal associations using a multi-level modelling approach.

**Results:** The results revealed that sleep disordered breathing ($r_s=.53$, $p=.002$) and parasomnias ($r_s=.36$, $p=.049$) were associated with the presence of painful health conditions for children with AS. Symptoms of gastrointestinal reflux were associated with poorer sleep quality for children with ($r_s=.63$, $p=.004$) and AS ($r_s=.37$, $p=.038$). Poorer sleep quality was associated with challenging behaviour in both groups ($p<.05$). The results of the actigraphy study support these associations between painful health conditions, challenging behaviour and sleep disorder and reveal temporal relationships between a number of these variables.

**Discussion:** The implications of these results for the assessment and treatment of painful health conditions in interventions for sleep disorders and challenging behaviour are discussed. Application of the methods used in this study, both assessment techniques and statistical analysis will be explored.

**References/Citations:**

Paper 2 of 4

**Paper Title:** The Temporal Associations of Difficult Behaviours in Tuberous Sclerosis Complex

**Authors:** Stacey Bissell⁵, Lucy Wilde⁵, Chris Oliver⁵

**Introduction:** Tuberous sclerosis complex (TSC) is a genetic disorder associated with benign tumour growth, as a result of mutations affecting the TSC1 or TSC2 genes. In addition to clinical characteristics, such as epilepsy and intellectual disability, there are a number of common difficult behaviours reported in TSC, including self-injury and aggression. Such externalising behaviours are relatively well understood within an operant theory framework of behaviour. However, there are other difficult behaviours in TSC, which may be ‘non-operant’ in nature that require further investigation as currently their aetiology and phenomenology are poorly understood. It is unclear both how these behaviours manifest (temporal sequences) and how they...
developed with age. These behaviours include overactivity, impulsivity, temper outbursts, non-compliant behaviours, and repetitive and inflexible behaviours (de Vries, Hunt, & Bolton, 2007; Hunt, 1993; Prather & de Vries, 2004).

**Methods:** To understand more about the potential antecedents, consequences, and change over time of these five less well understood behaviours in TSC, the Difficult Behaviours Interview was developed. This in-depth semi-structured interview covers five aspects of the behaviour: an operationalised definition, history, current behavioural status, antecedents and consequences, and impact of the behaviour. Caregivers of children aged 4-15 years with TSC completed the interview together with informant-based measures of adaptive ability and TSC specific associated behaviours (TAND Checklist; de Vries et al., 2015).

**Results:** Caregiver descriptions delineated the emergence and development of overactivity, impulsivity, temper outbursts, non-compliant behaviours, and repetitive and inflexible behaviours. Overall, behaviours were described as emerging early in development, with the manifestation of behaviour being influenced by broader developmental milestones. Common antecedents for behaviour included both fatigue and environmental unpredictability. Significant variability was identified in the temporal sequence of behavioural manifestation, together with variability in antecedents and consequences identified by caregivers.

**Discussion:** The Difficult Behaviours Interview is a promising tool to gain an in-depth understanding of behaviours that are currently less well defined in TSC, including history and temporal sequences. Use of this tool alongside standardised questionnaire measures of behaviour provides more in-depth insight into an individual's behavioural history, and the possible cognitive, biological and environmental factors affecting the behaviour over time. Such information will be particularly useful to parents and professionals when considering tailored behavioural interventions that may be relevant to their child.

**References:**


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**Paper Title:** The Lifespan Trajectory of Mood, Interest and Pleasure in Cornelia de Lange Syndrome

**Authors:** Laura Groves⁴, Jo Moss⁴, ⁵, Lisa Nelson⁴, Chris Stinton⁶, Chris Oliver⁴

**Introduction:** Cornelia de Lange syndrome (CdLS) is a rare genetic disorder associated with intellectual disability as well as a number of physical, health and behavioural difficulties. Low mood is often described in individuals with CdLS, with prevalence estimates ranging from 11-50%. Studies also report that low mood may worsen as individuals age, however there are few studies utilizing longitudinal methodologies to investigate this. In addition, there is limited research assessing what behavioural characteristics may be associated with low mood in CdLS which could be informative for clinical practice. Previous research in CdLS and that from the idiopathic autism literature has shown level of ability, autism spectrum disorder (ASD) symptomology and insistence on sameness are correlated with emotional difficulties (Fortuna et al., 2015; Nelson, Moss & Oliver, 2014). In this study we aimed to assess the trajectory of mood in CdLS, as well as what behavioural characteristics may be associated with this.

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Methods: Caregivers of individuals with CdLS (n = 44; M_age=18.39) and Fragile X syndrome (FXS; n = 95; M_age=17.29) completed questionnaires at Time 1 as well as 3 and 7 years later (Time 2 and Time 3). The questionnaires assessed participants’ mood and interest and pleasure (IP) (Mood, Interest and Pleasure Questionnaire; Ross & Oliver, 2003), severity of ASD characteristics (Social Communication Questionnaire; Rutter et al., 2003) and insistence on sameness (Repetitive Behaviour Questionnaire; Moss et al., 2009). To investigate the trajectory of mood and IP scores latent growth curve models were fitted to the data with participants’ exact ages inputted as individually-varying time points. Spearman’s Rho correlations were employed to explore what behavioural characteristics at Time 1 were associated with mood and IP scores at Time 1 and at outcome seven years later (Time 3).

Results: Overall, individuals with CdLS had lower levels of mood and similar levels of IP compared to individuals with FXS. Growth curve analyses revealed mood in CdLS and FXS and IP in FXS remained stable across the lifespan, however a significant decrease in levels of IP in CdLS was found (est. = -0.16, SE=0.03, p<0.001). Spearman’s Rho correlations found a range of behaviours were associated with MIPQ scores at Time 1 including severity of repetitive behaviour with mood (r_s=-.51, p<0.001), and ASD severity and insistence on sameness with IP (r_s=-.59, p<0.001 and r_s=-.41, p<0.01). However, only ASD severity and insistence on sameness remained significantly correlated with Time 3 IP scores (r_s=-.48, p<0.01 and r_s=-.42, p<0.01).

Discussion: These findings show that mood and interest and pleasure differed in severity, trajectory and were associated with different behavioural profiles in CdLS. This suggests that these constructs may be dissociable in CdLS and have a qualitatively different presentation to individuals with FXS. Furthermore, the finding that certain Time 1 behavioural characteristics were associated with IP scores up to seven years later could support the early identification of this in clinical practice.

References

Paper Title: A Ten Year Longitudinal Study of Behaviour in Smith-Magenis Syndrome

Authors: Lucy Wilde⁷, Suzanne Whittall⁷, Hannah Callaghan⁷, Jenny Sloneem⁸, Chris Oliver⁷, Alice Welham⁷,⁹.

Introduction: Smith-Magenis syndrome (SMS) has a particularly striking behavioural phenotype. Sleep disturbance is described as one of the cardinal features of the disorder (Gropman, Elsea, Duncan & Smith, 2007), self-injurious and aggressive behaviour are common (prevalence of up to 90%) and temper outbursts, impulsivity and stereotyped behaviours are also characteristic (Arron et al., 2011, Dykens & Smith, 1998, Martin et al., 2006). Adaptive functioning in SMS is reported to be less than might be predicted from either age or cognitive ability (Udwin et al., 2001). While the behavioural phenotype of SMS is now relatively well delineated, much less is known about how behaviours change with age. This question has acquired particular clinical importance as those diagnosed as children early in the syndrome’s history have reached adulthood.

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Methods: The current study is a 10 year follow-up of a sample of individuals with Smith-Magenis syndrome (n = 32), aged between 6-39 years (MDN 10.5, IQR 10.25) at time one (T1). At T1 a range of measures of behaviour were completed, including informant report of adaptive communication abilities, challenging behaviour, repetitive behaviour and behaviours associated with ADHD. These measures (in addition to novel measures of quality of life and mental health) were repeated at time two (T2). Participants were contacted on average 10 years after the initial study (range 9-11 years), resulting in 15 participants (47% of the original sample). In this sample 7 (47%) were female, and ages ranged from 15 to 42 years (MDN 22, IQR 10.5).

Results: Scores on the behavioural assessments were compared between T1 and T2 to assess change with age. Average frequency, severity and management difficulty of aggressive behaviour decreased from T1 to T2, as did frequency of destructive behaviour. Fewer difficulties relating to hyperactivity were also evident at T2. For repetitive behaviour, insistence on sameness increased, as did overall level of repetitive behaviour. As expected raw scores on adaptive communication increased from T1 to T2, however standardised scores significantly decreased over time (Z=-2.826, p=0.005) indicating that ability in relation to same-age peers declined.

Discussion: Findings suggest that the picture of age related behavioural outcomes in SMS may be quite mixed. Encouragingly, several of the behavioural difficulties associated with the syndrome appear to reduce in severity with age, including aspects of challenging behaviour and features of ADHD. Conversely, other behaviours appear to gain prominence with age, e.g. repetitive behaviour. Adaptive communication gains are shown; however the gap between individuals with SMS and their typically developing peers seems to increase with age. These findings are discussed in the context of the significant variability that was shown across individuals.

References/Citations: