**Paper Title**: Examining the properties of response inhibition paradigms in children with rare genetic syndromes associated with intellectual disability

**Authors**: Mr Rory O’Sullivan[[1]](#footnote-1), Dr Stacey Bissell1, Dr Catherine Laverty1, Dr Rory Devine1, Dr Hayley Crawford[[2]](#footnote-2), Prof Andrew Bagshaw1,[[3]](#footnote-3), Prof Caroline Richards1

**Introduction**:

Impulsivity is common in many rare genetic syndromes associated with intellectual disability, such as Smith-Magenis syndrome (Oliver et al., 2011), Fragile X syndrome (Richards et al., 2017), Cornelia de Lange syndrome (Srivastava et al., 2014), and tuberous sclerosis complex (de Vries et al., 2018). Contemporary aetiologic models of impulsivity refer, at least in part, to deficits in response inhibition (Bari & Robbins, 2013) which are also heightened in individuals with intellectual disabilities (Bexkens et al., 2014). Response inhibition is assessed via objective paradigms, such as Go/No-Go, continuous performance, and stop-signal tasks. However, the measurement properties of these paradigms require further examination in children with rare genetic syndromes to ensure rigorous assessment of response inhibition. Therefore, this study examined multiple properties of response inhibition paradigms, including: the distinction between ‘hot’ and ‘cold’ paradigms, correspondence with behavioral impulsivity ratings, practice/fatigue effects, and test-retest reliability.

**Methods**:

27 children aged 4-15 years with Smith-Magenis syndrome (N=6), Fragile X syndrome (N=6), Cornelia de Lange syndrome (N=9), and tuberous sclerosis complex (N=6) took part in remote sleep assessments lasting 10 days. Throughout the assessments, parents/caregivers completed daily ratings of impulsivity, overactivity, daytime sleepiness, and bedtime resistance. On 4-5 days of the sleep assessment, children completed a standardized battery of ‘hot’ (prohibition task) and ‘cold’ (Go/No-Go task) response inhibition paradigms. Concordance was examined (i) between the response inhibition paradigms, and (ii) between daily impulsivity ratings and response inhibition estimates collected on the same day. To test practice/fatigue effects, mean response inhibition estimates were compared between each administration iteration (i.e. first administration, second administration, etc.). Finally, to examine test-retest reliability, performance on the response inhibition paradigms was compared between the first and second administration.

**Results**:

Response inhibition estimates did not converge between the prohibition (‘hot’) and Go/No-Go (‘cold’) tasks. However, response inhibition deficits, estimated by the prohibition task, positively predicted daily impulsivity ratings. The mean scores from each paradigm did not significantly differ between the administration iterations, although a visual trend towards lower Go/No-Go response inhibition deficits was noted towards the later administrations. Good test-retest reliability was demonstrated for each response inhibition paradigm.

**Discussion**:

In summary, the current findings (i) supported the distinction between ‘hot’ and ‘cold’ response inhibition paradigms; (ii) highlighted that behavioural impulsivity may be linked to response inhibition deficits, contributing to models of cause; (iii) indicated that practice effects may occur for the Go/No-Go task, which future studies should mitigate against; and (iv) demonstrated good test-retest reliability for the response inhibition paradigms.

This work is now being replicated and extended in a large sample of ~100 individuals with rare genetic syndromes (Research into Executive Functions in Individuals with Additional Needs, REFINE). REFINE will examine multiple executive functions via play-based, objective paradigms and address multiple measurement properties (e.g. test-retest reliability, reliability of caregiver and researcher administration, and convergence with informant-report executive functioning estimates).

**References**:

Bari, A., & Robbins, T. W. (2013). Inhibition and impulsivity: behavioral and neural basis of response control. *Progress in Neurobiology, 108,* 44-79.

Bexkens, A., Ruzzano, L., Collot d'Escury‐Koenigs, A. M. L., Van der Molen, M. W., & Huizenga, H. M. (2014). Inhibition deficits in individuals with intellectual disability: A meta‐regression analysis. *Journal of Intellectual Disability Research*, *58*(1), 3-16.

De Vries, P. J., Belousova, E., Benedik, M. P., Carter, T., Cottin, V., Curatolo, P., ... & Jansen, A. C. (2018). TSC-associated neuropsychiatric disorders (TAND): findings from the TOSCA natural history study. *Orphanet Journal of Rare Diseases*, *13*, 1-13.

Oliver, C., Berg, K., Moss, J., Arron, K., & Burbidge, C. (2011). Delineation of behavioral phenotypes in genetic syndromes: characteristics of autism spectrum disorder, affect and hyperactivity. *Journal of Autism and Developmental Disorders, 41,* 1019-1032.

Richards, C., Powis, L., Moss, J., Stinton, C., Nelson, L., & Oliver, C. (2017). Prospective study of autism phenomenology and the behavioural phenotype of Phelan–McDermid syndrome: comparison to fragile X syndrome, Down syndrome and idiopathic autism spectrum disorder. *Journal of Neurodevelopmental Disorders, 9*(1), 1-15.

Srivastava, S., Landy‐Schmitt, C., Clark, B., Kline, A. D., Specht, M., & Grados, M. A. (2014). Autism traits in children and adolescents with Cornelia de Lange syndrome. *American Journal of Medical Genetics Part A, 164*(6), 1400-1410.

1. School of Psychology, University of Birmingham [↑](#footnote-ref-1)
2. Warwick Medical School, University of Warwick [↑](#footnote-ref-2)
3. Centre for Human Brain Health, University of Birmingham [↑](#footnote-ref-3)