

Institute for Children and Young People's Mental Health

at King's College London & Maudsley Hospital

Our specialist Centre for Interventional Paediatric Psychopharmacology Research Team (CIPPRT), led by Professor Paramala Santosh focusses on translational research that includes conducting clinical trials in rare diseases such as Rett Syndrome; developing Patient Centred Outcome Measures (PCOMs) for a range of clinical situations such as medication related suicidality, transition decision making, web-based structured medication review, profiling neuropsychiatric symptoms, and assessing mental health in autism.

Recently, we have set up the world's first Centre for Personalised Medicine for Rett Syndrome (CPMRS), which focusses on providing holistic specialist care, conduct clinical trials, developing digital health strategies to monitor and manage patients, whilst conducting research.

Research focuses on psychopharmacology and paediatric neurodegeneration in a number of rare disorders, digital health monitoring using the HealthTracker™ platform, and sensor-based monitoring of autonomic function using wearable technology. The digital health strategies have been used to assess and manage Emotional, Behavioural and Autonomic Dysregulation (EBAD), which is common in complex multiple co-occurring developmental disorders, head injury, and many rare disorders. Machine learning strategies have been used to assist in predicting suicidal behaviours as part of research.

The CIPPRT links up with the Centre for Interventional Paediatric Psychopharmacology and Rare Diseases (CIPPRD), a Tier 4 national service, which treats extremely ill patients with complex, treatment-resistant neuropsychiatric conditions, childhood dementias, mucopolysaccharidoses, Rett syndrome, septo-optic dysplasia; acquired brain injury, and serious psychotropic-induced side-effects. Both teams collaborate extensively and develop research questions arising from clinical issues and quick transfer from lab to clinical practice because of joint and cross-working between the teams. The CIPPRD was the winner of 2015 RCPsych Award for Children & Adolescents Psychiatric Team of the Year and Professor Paramala Santosh won the MQ: Transforming Mental Health & NIHR CRN Service User Involvement in Research Award in 2016.

The CPMRS is an exemplar of the joint working between IoPPN and SLaM as the grant obtained specifically provides for both clinical care as well as for research into Rett syndrome. The clinical trials are conducted in collaboration and we have led and completed the first clinical trial in Rett syndrome within the UK, ensuring NHS patients can access new treatments, and have obtained commercial research grants for further Rett clinical trials.

Our translational clinical research agenda places the needs of complex treatment-resistant patients and those with rare disorders at its centre, especially those with autonomic dysregulation. We have developed artificial intelligence algorithms using clinical data to help risk stratification and personalize treatment. Collaborative working between the clinical and research teams have improved service delivery and helped deliver on clinical trials.

The CIPPRD, CPMRS and CIPPRT have pioneered the use of digital health technology through using the HealthTracker™-based symptom and side-effect monitoring, and multi-sensor based physiological monitoring in routine clinical care. This has helped our personalised medicine approach using artificial intelligence strategies, leading to improved, cost-effective care and has reduced the time taken to get optimal clinical outcomes. It has especially helped improve care in those with limited communication ability by using real-time psychophysiological data to make useful clinical inferences.

Data collected using sensor-based psychophysiology and web-based HealthTracker™ has allowed us to develop artificial intelligence algorithms to risk-stratify patients and provide effective personalized

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care. We are also focussing on objective measures of EBAD, that will allow us to develop specific treatment protocols depending on type of physiological abnormality.

The CIPPRT will continue to develop patient reported outcomes such as the Transition Readiness Assessment Measure (TRAM), which identifies areas that need to be targeted to get optimal transition outcomes when moving to adult services; and Transition Related Outcome Measure (TROM), which helps measures transition-related outcomes; Suicidality Assessment Scale (SAS); Profile Of Neuropsychiatric Symptoms (PONS); Profile of Medication Side-effects (POMS); and the HealthTrackerTM-based Structured Medication Review (HT-MRS) (Sheehan et al, 2019). Such developments will significantly help NHS improve clinical care across the UK.

We will continue to conduct pioneering clinical trials in rare disorders such as Rett syndrome, with a view to developing the ground for implementing transformative clinical trials such as gene therapy when it becomes available.

Key Publications

- Singh J, Lanzarini E, **Santosh P**. Autonomic Dysfunction and Sudden Death in Patients with Rett Syndrome: A Systematic Review. *Journal of Psychiatry and Neuroscience*. 2019 Nov 8;45(1):190033. doi: 10.1503/jpn.190033
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- Singh J, **Santosh P**. Key issues in Rett syndrome: emotional, behavioural and autonomic dysregulation (EBAD) - a target for clinical trials. *Orphanet J Rare Dis*. 2018 Jul 31;13(1):128. doi: 10.1186/s13023-018-0873-8. Review.

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