

Tuberous Sclerosis Complex is a genetic disease that manifests by tumours, epilepsy and neuropsychiatric disorders, such as autism spectrum disorder, anxiety, and intellectual disability. Neuropsychiatric disorders are present in some patients with Tuberous Sclerosis Complex, and in some not. Even patients carrying the same mutation may express different neuropsychiatric symptoms. This is called variable expressivity. The variable expressivity of neuropsychiatric symptoms in Tuberous Sclerosis Complex suggests that environmental factors play a role in their pathogenesis. Our data indicates that white matter and long-distance inter-hemispheric connections regulate anxiety-like behaviour in the zebrafish model of Tuberous Sclerosis Complex. Also in the Tuberous Sclerosis Complex patients with diagnosed autism spectrum disorder, connectivity of white matter fibres across multiple regions was impaired within the first two years of life. **It indicates that environmental factors may influence development of white matter fibres to produce neuropsychiatric disorders like anxiety or autism spectrum disorder.** The existing research on environmental influence on neuropsychiatric symptoms is mainly correlative (human studies) or lacks a population-like scale (rodent models) which hinders research on highly variable neuropsychiatric symptoms. Zebrafish having external development and small size is useful for high-throughput studies that are needed for highly variable phenotypes. Moreover, understanding the aetiology of neuropsychiatric disorders requires knowledge of the developmental and cellular contexts in which the differences between healthy and affected brains arise. Zebrafish allows integration of research on multiple levels including behavioural level, cellular level in the context of the whole brain, and molecular level. Several environmental factors have been proposed in the pathogenesis of neuropsychiatric disorders and this project focuses on factors related to maternal infection during pregnancy, such as maternal immune system activation, repeated or prolonged fever during pregnancy, or maternal stress (maternal-fetal cortisol transfer). **How these environmental insults interact with changes caused by genetic mutation and how these interactions shape connectivity development and brain function to regulate specific behaviours related to neuropsychiatric disorders in the offspring remains unknown.** This project aims at elucidating influence of prenatal maternal infection on aberrations in early development of the brain circuits that are responsible for neuropsychiatric symptoms and is based on an unbiased and comprehensive approach to link specific behaviours to specific brain circuits and gene expression profiles on a population-like scale. The neuropsychiatric disorders affect more and more people worldwide and are still incurable, so is Tuberous Sclerosis Complex. Unravelling the developmental mechanisms that lead to autism spectrum disorder or intellectual disability has a high impact for Tuberous Sclerosis Complex patients giving possibility to find therapies or improve patients' quality of life. Brain connectivity development and neuropsychiatric disorders are hard to study in mammals *in vivo*, therefore zebrafish models seem more convenient for developmental research as high-resolution live imaging from very early embryonic stage is possible. Moreover, zebrafish presents a possibility for high-throughput screening of chemical compounds if proper disease-related phenotypes are deeply characterized and reproduce the disease symptoms. The project will contribute new insights into signalling pathways that orchestrate the brain connectivity development in Tuberous Sclerosis Complex and may bring novel therapeutic strategies for neuropsychiatric disorders.