Département de psychiatrie

Centre de Neurosciences Psychiatriques

CNP SEMINARS

ANNOUNCEMENT

Friday, August 20 2021, 11:00 – 12:00

Autism and "Astro"logy: *New insights from recordings in human brain cells*

Professor Sumantra Chattarji, PhD
Centre for Brain Development and Repair, Institute of Stem Cell Biology and Regenerative Medicine,
National Centre for Biological Sciences, Bangalore, India

Important insights into the pathophysiology of Fragile X Syndrome (FXS), a common monogenic cause of autism spectrum disorder, have emerged from analyses of rodent models. However, these findings have been less effective in developing therapeutic interventions, thereby highlighting the need for model systems of human origin. Moreover, earlier studies focused on neurons, and the role of glia remains largely unexplored in FXS. Here, we used human induced pluripotent stem cells to examine the potential role of astrocytes in physiological abnormalities in FXS neurons. Whole-cell recordings from FXS cortical neurons, co-cultured with FXS astrocytes, revealed spontaneous bursts of action potentials that are more frequent, but shorter in duration, compared to control neurons co-cultured with control astrocytes. However, the same FXS neurons, when co-cultured with control astrocytes, fire like controls. Conversely, control neurons exhibit aberrant firing in the presence of FXS astrocytes. Thus, the genotype of astrocytes determines the physiological phenotype of neurons. Strikingly, even astrocytic conditioned medium by itself is capable of eliciting the same effects. Next we examined the mechanisms through which the astrocytic secretome mediates these effects in neurons. We found higher levels of the astroglial-derived protein, S100b, in FXS astrocytes and its conditioned medium. And high levels of S100b, in turn, trigger aberrant neuronal firing. A lower level of S100b, in contrast, restores normal firing by reversing the suppression of a persistent sodium current in FXS neurons. Together, these results reveal an important non-cell-autonomous contribution of astrocytes in correcting aberrant electrical activity in human FXS neurons, thereby suggesting a framework for exploring new therapeutic strategies aimed at neuron-glia interactions.

Invited by Ron Stoopo
ron.stoop@chuv.ch

Related publications

1. *Yasmin F, Colangeli R, Morena M, Filipski S, van der Stelt M, Pittman QJ, Hillard CJ, Teskey GC, McEwen BS, Hill MN, Chattarji S. Stress-induced modulation of endocannabinoid signaling leads to delayed strengthening of synaptic connectivity in the amygdala. Proc Natl Acad Sci U S A. 2020 Jan 7;117(1):650-655. doi: 10.1073/pnas.1910322116. Epub 2019 Dec 16.*
2. *Chattarji, S., Tomar, A., Suvrathan, A., Ghosh, S., and Rahman, M. M. (2015) Neighborhood matters: divergent patterns of stress-induced plasticity across the brain. Nature Neuroscience 18, 1364–1375. doi:10.1038/nn.4115.*
3. *Ghosh S, Chattarji S. Neuronal encoding of the switch from specific to generalized fear. Nat Neurosci. 2015 Jan;18(1):112-20. doi: 10.1038/nn.3888. Epub 2014 Dec 1.*

This event will take place on a virtual space on **Friday, August 20 2021 at 14:00** through the link:

https://chuv.webex.com/chuv/j.php?MTID=mbfc1067529840cd0ac0547cddb06fe1d

Meeting number (access code): 1375 22 8570 Meeting password: 2enWBaqxf87

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