**Electrophysiological characterization of the mesolimbic circuit in wild mice**

L. Andreoli1, J. W. R. de Freitas1, E. Morya1, R. C. Moioli1, M. F. de Araújo1

1Neuroengineering Postgraduate Program, Edmond and Lily Safra International Neuroscience Institute, Macaiba (RN), Brazil

**Introduction:** Currently about 450 million people are affected by mental disorders. The underlying neurophysiology of these disorders is not fully understood, but many studies suggest that dopaminergic pathways are related to the pathophysiology of these diseases. Mesolimbic pathway dysfunction changes anxiety and hyperactivity levels, which are symptoms of many psychiatric disorders. This study aimed at characterizing the electrophysiological activity of the mesolimbic circuit of wild mice in an experimental paradigm designed to assess exploratory activity and anxiety levels.

**Materials and Methods:** All procedures were performed according to approved protocols by AASDAP Ethics Committee under no. 02/2013. A 32-channel microelectrode array (tungsten 30µm coated wire) recorded local field potentials (LFP) of eight wild mice freely behaving in an elevated plus-maze task testing anxiety. The microelectrode array recorded simultaneously four areas of the mesolimbic pathway in both hemispheres with four electrodes in each area: ventral tegmental area (VTA), nucleus accumbens (Nac), basolateral amygdala (BLA) and prelimbic cortex (PrL). LFPs were acquired with the MAP system (2 kHz, Plexon Inc, USA), videos were recorded with the Cineplex software (80 Hz, Plexon Inc, USA) and data were analyzed with the Chronux Toolbox [1] for Matlab (MathWorks, Natick, MA).

**Results:** We found differences in time (F = 23.62, p<.05), distance (F = 20.77, p<.05) and speed (F = 25.7, p<.05) of mice on the closed arms of the maze in comparison to the open arms. For the electrophysiological results, power spectra and coherence at the open and closed arms of the elevated plus-maze were compared to that when the mice were in the nesting box. At the open arms of the maze, there was an increase (p<.05) in the power spectrum between 10 and 16 Hz in the right Nac and between 8 and 12 Hz in the left Nac; at the closed arms, we found a significant increase between 10 and 16 Hz in both Nac and between 70 and 100 Hz in the right Nac. Coherence of oscillations increased in the 8 – 12 Hz band between left VTA and PrL and in the 35 – 40 Hz band between left Nac and VTA when animals were at the open arm; at the closed arms, coherence increased in the 8 – 12 Hz band between VTA e PrL.

**Discussion:** Our results with the elevated plus-maze were similar to those found in the zero-maze [2]. We observed synchrony in the 35 - 40 Hz band between Nac and VTA, which might relate to anxiety behavior at the open arms of the plus-maze. This supports the hypothesis that changes in Nac-VTA synchrony reflect neurophysiological circuit changes underlying the expression of anxiety-related behaviors. In addition to previous work [2], we also observed a change in synchrony between VTA and PrL in the 8 - 12 Hz band when animals were in the nesting box or in the maze. Since both areas connect with Nac, an area with an important role in anxiety-related behaviors, this could explain the synchrony modulations found in the experiment.

**Conclusion:** Our findings corroborate with the hypothesis that changes in Nac-VTA synchrony reflect neurophysiological circuit changes underpinning anxiety-related behavior and reinforces the role of mesolimbic pathway structures in anxiety and other mental disorders symptoms.

**References:** [1] Bokil H et al., Journal of neuroscience methods 192(1): 146-151, 2010; [2] Dzirasa K et al., Journal of neuroscience 31(17): 6449-6456, 2011.

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