Microelectrode Array Electrophysiological Recording of Neuronal Network Activity during a Short-Term Microgravity Phase

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During spaceflight, humans are subjected to a variety of environmental factors which deviate from Earth conditions. Especially the lack of gravity poses a big challenge to the human body and has been identified as a major trigger of many detrimental effects observed in returning astronauts but also in participants of spaceflight-analog studies. Structural alterations within the brain as well as declines in cognitive performance have been reported, which has brought the topic of brain health under microgravity into the focus of space research. However, the physiological mechanisms underlying these observations remain elusive.

Every aspect of human cognition, behavior and psychomotor function is processed by the brain based on electro-chemical signals of billions of neurons, which relay information *via* neuronal networks throughout the body. Alterations in neuronal activity are the main cause of a variety of mental disorders and changed neuronal transmission may also lead to diminished human performance in space. Thus, understanding the functioning of these fundamental processes under the influence of altered gravity conditions on a cellular level is of high importance for any manned space mission. Previous electrophysiological experiments using patch clamp have shown that propagation velocity of action potentials (APs) is dependent on gravity.

With this project, we aim to advance the electrophysiological approach from a single-cell level to a complex network level by employing Microelectrode array (MEA) technology. MEAs feature the advantage of real-time electrophysiological recording of a complex and mature neuronal network *in vitro*, without the need for invasive patch clamp insertion into cells. Using a custom-built pressure chamber, we were able to integrate and conduct our experiment on the ZARM Drop Tower platform, exposing the entire system to 4.7 s of high-quality microgravity (10^{-6} to 10^{-5} x g_0). With this setup we were able to evaluate the functional activity patterns of iPSC-derived neuronal networks subjected to microgravity, while keeping them under controlled and stable temperature and pressure conditions.

Activity data was acquired constantly - immediately before the drop, during the free-fall (microgravity) phase and during a subsequent post-drop recording phase. For neuronal activity analysis the action potential frequency in each experiment phase was calculated for the single electrodes. We found that during the 4.7 s lasting microgravity phase the mean action potential frequency across the neuronal networks was significantly elevated. Additionally, electrical activity readapted back to baseline level within 10 minutes of post-drop recordings. Our preliminary data shows that real-time, electrophysiological recording of neuronal network activity based on MEA technology is possible under altered gravity conditions and that differences in activity can be detected already in very short time frames in the second range. Furthermore, the observation that microgravity has an effect on the electrophysiological activity of neuronal networks is in line with previously published findings in single neurons and poses further questions with regards to astronaut brain health on manned space missions.

The MEA payload system was approved for autonomous recording of redundant cellular electrophysiological data in the Drop Tower. It will be applied on other microgravity platforms such as sounding rockets and parabolic flights and thus increased experimental time. Apart from neurons, various other electrically active cellular systems such as myocytes or myotubes could be examined using this hardware.