Postmortem Human Brain Physiology

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Research question and background

Electrophysiological recordings from neuronal tissue allow for direct and real-time investigation of the functional state of neuronal networks and for the characterization of individual neuronal types within the network. With the majority of recordings deriving from rodent tissue, although extremely valuable, there remains a significant translational gap. Our department, in collaboration with the VUMC, has been successful in providing pristine quality recordings from surgically resected human brain tissue, from drug resistant epileptic patients. However, substantial limitations still remain with this approach. Namely, the tissue is neither from healthy controls nor from patients with specific neuropsychological disorders, it is restricted mainly to temporal cortex and patient age range is limited to 18-65 years. Taken together, these constraints limit the questions that can be addressed. Therefore, the ability to perform electrophysiological recordings from individual neurons in post-mortem tissue provides an exceptional opportunity to overcome these limitations. This approach will permit for recordings from a variety of brain areas, allowing for across brain comparisons but also for experiments targeted at specific brain regions - inaccessible with the current approach. Furthermore, given the diversity of donor tissue present in the BrainBank database, studies addressing age-related changes in fundamental properties of neurons in the human brain would be feasible. Additionally, data from syndromic brain tissue will allow for disease specific hypotheses to be tested, and for direct assessment of the validity of syndromic animal models - providing fundamental insights currently lacking from literature.

Methods and tissues used

Presently, prefrontal and temporal cortical areas are resected and assessed for their potential to provide viable recordings from individual neurons, through evaluation of their physiological and morphological properties. Furthermore, several different solutions for tissue transfer, slicing, and incubation, are currently being tested to evaluate the most optimal protocol for acquiring functional recordings.

Results and conclusion

Acquiring electrophysiological recordings from post-mortem tissue presents a unique opportunity to address fundamental questions about human brain function and pathophysiology. We have successfully acquired preliminary viable recordings from individual neurons within post-mortem brain tissue from cortical regions of adult human donors. However, success rate is limited and strongly dependent upon post-mortem delay. We are now further refining our approach, adapting protocols used for adult rodent brain preparations and for tissue obtained from adult surgical patients. Using these modified protocols, the quality of the tissue and success rate of recordings has dramatically improved, and we anticipate increased tissue viability and success, leading to a documented method upon which to built and test future experimental hypotheses.