Identifying functional changes in central cardiovascular control in epilepsy

Research:

When one thinks of epilepsy, seizures immediately come to mind. And while not all epileptic episodes are associated with these events, it is known that seizures result in cardiovascular and respiratory consequences that, in some individuals may lead to death. Indeed, Sudden Unexplained Death in Epilepsy (SUDEP) is one of the most poorly understood consequences of epilepsy. By definition, the mechanisms leading to SUDEP are unknown. But given that cessation of breathing and cardiac events are the terminal events, this suggests that changes in the brainstem networks responsible for maintaining respiration and cardiovascular control must precipitate SUDEP. But how do epileptic foci, which are mostly located in cortical areas far removed from the brainstem, lead to these changes?

Our research aims to explore this in detail, using the state-of-the-art brain imaging protocol developed by Vaughan Macefield and Luke Henderson. By using a tungsten microelectrode inserted into a peripheral nerve in awake participants, we can tap into the bursts of muscle sympathetic nerve activity (MSNA) that originate in the brain. These bursts lead to the constriction of blood vessels in muscles throughout the body and significantly impact the control of blood pressure. Individuals with high blood pressure (hypertension) and heart failure have greatly elevated MSNA, and high MSNA is a known cardiovascular risk factor. By recording MSNA at the same time as performing functional magnetic resonance imaging (fMRI) of the brain we have been able to identify areas of the brain responsible for the generation of MSNA. Indeed, this test has allowed us to identify the cortical and subcortical regions that comprise the sympathetic connectome involved in the control of blood pressure in unprecedented detail, and we are the only group in the world using this approach.

Now, having established a productive collaboration with Terry O'Brien and his team in Melbourne, we are extending our research to understand how functional and structural changes in the brain lead to increased cardiovascular risk in drug-resistant epilepsy.

Outcome

Although we have undertaken some successful recordings in people with epilepsy using this approach, recruitment of suitable participants has been slow – and then COVID hit. Nevertheless, we predict that will be able to identify disturbances in the operation of the sympathetic connectome in certain people with epilepsy, just as we have in those with hypertension. In addition to these invasive studies, we have been assessing the changes in heart rate variability (HRV) in video-documented cases of SUDEP and non-SUDEP controls. HRV provides a non-invasive tool for examining autonomic control of the heart. Already, we have identified differences in HRV metrics in those individuals who succumbed to SUDEP.By assessing baseline HRV as well as MSNA we anticipate being able to identify changes in the brain associated with epilepsy that increase the probability of SUDEP in certain individuals. By documenting changes in areas of the brain involved in cardiovascular control we hope to be able to identify individuals at risk of SUDEP, ultimately preventing sudden death in epilepsy from occurring.

Research Team:

Chief Investigator - Prof Vaughan Macefield, Baker Heart and Diabetes Institute, Melbourne

Co-Investigator - Prof Terence O'Brien, Department of Neuroscience, Central Clinical School, Monash University, Melbourne

Co-Investigator - Prof Luke Henderson, Brain and Mind Centre, University of Sydney