

Maintaining brain health: Overlapping pathophysiology for multiple disorders?

Associate Professor Lis Evered

Principal Research Fellow, University of Melbourne and Head of Research, St Vincents Hospital

The first few slides of this presentation will cover my time in New York at Weill Cornell Medicine where I commenced on 1st January 2020. This will centre around the impact of the pandemic on an unprepared epicentre.

Perioperative Neurocognitive Disorders (PND) is a term which encompasses the preoperative and postoperative cognitive and functional impairment/decline temporally associated with anaesthesia and surgery, including frailty and any known or unknown vulnerabilities brought to the operating room by the patient. Vulnerabilities associated with older individuals including preoperative cognitive impairment (often subtle and undiagnosed) and frailty, which increase the risk of PND. Higher frailty scores preoperatively are associated with an increased risk of PND at 12 months postoperatively. Additionally, an assortment of co-morbidities is likely to burden older individuals presenting for elective surgery putting them at further risk. An important factor to consider is that cognitive impairment does not occur in isolation but is associated with functional disability over the longer-term, increased risk of dementia, institutionalisation and death.

I will focus briefly on postoperative delirium, one of the perioperative neurocognitive disorders. I will define the two types of delirium (hyperactive and hypoactive) and the current non-pharmacological recommendations to try to prevent an episode of POD and therefore prevent the long-term sequelae. In addition, I will present some recent work demonstrating long-term psychosocial effects of delirium following cardiac surgery following a recent qualitative analysis of interviews with patients 3 years post-surgery. These long-term themes include depression, trauma, loneliness and awareness of cognitive and functional decline.

Possible anaesthesia effects will be briefly covered revealing little evidence of a contribution to PND by anaesthetic agents. Our current neuroinflammatory / neuronal damage hypothesis will be presented and discussed in terms of PND and other inflammatory injury/disease that may overlap pathophysiological pathways, such as COVID-19 and acute traumatic brain injury. This work suggests surgery may play a more critical role than anaesthetic agents in the development of PND.

To date, with the assistance of biomarkers and with the elimination of other factors, the most supported hypothesis suggests that peripheral inflammation leading to neuroinflammation followed by downstream neuronal damage is the most likely pathophysiology underlying these cognitive and functional changes.

Multi-component interventions for the prevention of PND will be discussed in the context of routine care pathways as part of promoting 'Brain ERAS' to be part of every surgical care pathway. The PROTECT trial is a NHMRC funded non-pharmacological multi-component trial investigating strategies from preoperatively to 12 months postoperatively to prevent PND and will be briefly outlined. Resources for preventing delirium will be identified.

PND will be discussed in the context of COVID-19 'long-haulers' and what we can learn from the overlap between these and other disorders. The overlap between long-term symptoms will be addressed and suggests a possible common pathway. This may offer insights and opportunities for further research and preventive strategies. Biomarkers may hold the key to insight in this regard, and further biomarker research, particularly over the long-term is critical to preventing the long-term poor outcomes of both PND and inflammatory diseases such as COVID-19.

In summary, this presentation will discuss PND including delirium and associated poor outcomes; current evidence for mechanisms and possible overlap with other inflammatory disorders such as COVID-19 'long-haulers' with overlapping risk factors.

