Neurotoxicity in Older Brains -

Does Anaesthesia trigger Delirium, Dementia or Alzheimer's Dementia?

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Much emphasis of anaesthetic agents and their effects on the brain has been on neuroprotective mechanisms, including GABA potentiating effects of the volatile[1] and intravenous agents[2], α-2 blocking effects[3], antioxidant effects[4] apoptosis prevention[5] and preconditioning[6].

How then does one relate these theoretical advantages of anaesthetic agents to the common development of postoperative delirium (PD) in some patients[7]? The long-term effects of PD may include prolonged hospital stay, premature rest home placement, increased risk of death [8] and increased functional decline into dementia [9-12]. Whilst the likely role of central cholinergic deficiency remains a likely common pathway in delirium[13], it remain difficult to link the role of anaesthetic agents and intra-operative factors[14] to increased risk for delirium.

Persistent postoperative cognitive decline (POCD), experienced by patients as memory impairment, decreased executive function, early retirement and increased mortality risk[15] can occur in 10% of patients older than 60 undergoing non-cardiac surgery[16]; with a higher incidence in cardiac surgical patients[17]. No single mechanism explains this phenomenon. What is becoming clear is that anaesthetic agents may exert lasting effects on memory[18] and gene expression[19] that persist long after initial recovery from the anaesthetic.

A mechanism of neurotoxicity in older brains that has been suggested is that of anaesthetic agents inducing accumulation of hyperphosphorylated tau proteins [20], as well as enhancing oligomerisation of amyloid beta-precursor protein [21]. These cover two of the biochemical pathway hypotheses of Alzheimer's dementia[22]. These processes have been demonstrated in neural cell cultures, models of cell stress including Alzheimer's and Huntington's disease, as well as animal models[23]. Inhaled anaesthetic agents all appear to interact with neurodegeneration pathways that lead to cellular stress and neuronal apoptosis. [24]

This presentation will explore and review the current evidence for anaesthetic neurotoxicity in older patients, and whether these can be linked to cognitive decline, later neurological disease or indeed any post-operative outcome.