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## Varenicline reduced DNA damage and tau mislocalization to prevent cognitive impairment induced by laparotomy in aged mice

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Postoperative cognitive dysfunction (POCD) occurs more frequently in the elderly and has characteristics in common with other neurodegenerative diseases such as Alzheimer's Disease (AD), such as neuroinflammation and abnormal tau protein phosphorylation or mislocation. Cholinergic system manipulation has been considered a potential strategy in the treatment of this disease. This study investigates the contribution of surgical trauma and the effect of the cholinergic agonist varenicline on the development of POCD. Aged male wild type C57BL/6N mice (18-month-old) were divided into control (CON), sevoflurane only (SEVO) and laparotomy (LAP) groups, with all three groups either treated with vehicle (normal saline) or varenicline, which was orally administrated daily from one day before treatment continuously for 13 days. Cognitive function was assessed by Novel Object Recognition (NOR) and Y-maze tests, and locomotor activity by the Open Field test (OFT), motor function by Rota rod test on postoperative day 14. Hepatic mRNA levels of IL-1 $\beta$ , TNF- $\alpha$ , IL-6 and MCP-1 were significantly increased in LAP compared with SEVO. In the hippocampus, IL-1 $\beta$ , IL-6 and MCP-1 were significantly elevated in LAP. Cognitive impairment was observed in LAP, indicating by increase in latency and error number in the Y-maze test, and a lower discrimination index in NOR. Persistent glia activation was observed by using immunofluorescent staining with GFAP (astrocyte) and Iba-1 (microglia) in LAP in the hippocampus at 14 days postoperatively. Simultaneously, there was significant aberrant high level of tau protein phosphorylation (AT8) in both cytosol and nucleus in LAP, which was attenuated by varenicline intervention. Neuroinflammation and tau protein phosphorylation may play role in the development of cognitive dysfunction induced by laparotomy and varenicline improved cognition by reversing these changes.

### Biography

Chunxia Huang is pursuing her PhD under the supervision of Gordon Wong in the Department of Anaesthesiology, Faculty of Medicine, The University of Hong Kong and is scheduled to complete her studies in September 2017. She has already published 2 papers related to the contributory role of anesthetics on the development of Post Operative Cognitive Dysfunction.

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