**Please nominate 1 category that best fits your submitted abstract:**

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| Paediatric and/or congenital diseases  Maternal and/or prenatal health  Cardiometabolic diseases  Chronic diseases  Healthy aging  Cancer  Neurodegenerative diseases  Public health  Other |

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**Anti-inflammatory effect of butyrate and lauric acid on Alzheimer’s disease**

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**Background and Aims:**

Alzheimer's disease (AD) manifests pathologically as senile plaques comprising beta-amyloid aggregates, phosphorylated tau protein-mediated neurofibrillary tangles, neuronal loss, neuroinflammation and brain atrophy. Astrocytes are key regulators of neuroinflammation in AD and can be activated by Aβ and tau proteins. Recently, the roles of short-chain fatty acids (SCFAs), the main metabolites generated by fermentation of dietary fiber by gut microbiota, in the pathogenesis of AD have attracted considerable interest. SCFAs specially butyrate could reduce neuroinflammation and amyloid protein toxicity. However, the mechanism of how SCFAs supress or activate microglia and astrocytes, which are important for neuroinflammation is still unclear. Medium chain fatty acids (MCFAs), especially lauric acid is another fatty acid which has anti-inflammatory and antioxidant properties. Studies indicate that lauric acid, may have the ability to improve mitochondrial function and reduce neuronal hyperactivity, which is often seen in AD. However, the effects of MCFAs on Aβ mediated activation of microglia and astrocytes, the primary mediators of neuroinflammation in AD, are still unclear. Further, SCFAs and MCFAs have not been studied extensively for their independent and synergistic effects on AD pathology. Importantly, very little is known about the synergistic effects of SCFAs and MCFAs on the activation of astrocytes and microglia in AD.

**Methods:** Butyrate and lauric acid were administered independently and in combination to astrocytes derived from induced pluripotent stem cells (iPSCs) obtained from healthy control subjects. The objective of this investigation was to examine the impact of these substances on the inflammatory responses of astrocytes, which were exposed to synthetic amyloid beta.

**Results:** Cytotoxicity assay revealed no statistically significant difference in treated astrocytes, indicating the absence of plasma membrane damage within the cell population (p > 0.05).

**Conclusions and Significance/Impact:** The findings demonstrate butyrate and lauric acid are not toxic to astrocytes and Alzheimer’s induced astrocytes. While further analysis on cytokine activity is required

(300 words max.)

**Lay Title: Anti-inflammatory effect of butyrate and lauric acid on Alzheimer’s disease**

(100 characters max.)

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**Lay Summary:** Alzheimer's disease is a complex condition characterized by brain changes like amyloid beta plaques and inflammation. Astrocytes, can become activated in response to these changes in the brain. Short-chain fatty acids like butyrate, produced by gut bacteria, have shown promise in reducing brain inflammation, while medium-chain fatty acids like lauric acid have potential benefits for AD. In this study, we tested butyrate and lauric acid on astrocytes exposed to amyloid beta, a key player in AD. Fortunately, we found that neither substance harmed the astrocytes. More research is needed to understand their effects on inflammation in AD.

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