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**MEETING ABSTRACT**

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**Dopamine synthesis during neuroinflammation: a focus on tetrahydrobiopterin**

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A growing body of evidence suggests that neuroinflammation, especially through cytokines, acts on the dopaminergic system and related behaviours. In particular, pro-inflammatory cytokines have been shown to induce dopamine synthesis impairment. The pathway that mediates protein synthesis is pretty well-known, involving three major enzymes: phenylalanine hydroxylase (PAH), tyrosine hydroxylase (TH) and DOPA-decarboxylase. Even though it has been less studied, tetrahydrobiopterin (BH4) is also an essential component of this pathway. Indeed, BH4 is a mandatory co-factor for PAH and TH activity and therefore essential for dopamine synthesis. Inhibition of BH4 production in the brain leads to dramatic decrease in dopamine levels. Interestingly, inflammation can influence BH4 availability by acting on its synthesis and degradation. Despite its importance, the effects of BH4 on dopamine synthesis and the potential effect of neuroinflammation on BH4 have been poorly characterized.

Here, we used lipopolysaccharide (LPS) to model acute inflammation in mice and evaluated the effects on BH4 and dopamine levels by HPLC and electrochemical detection. We also tested whether administration of BH4 could reverse inflammation-induced alterations of dopamine levels. The related protein levels in mesolimbic dopaminergic system were evaluated by western blots. Dopamine release in nucleus accumbens in response to palatable food and amphetamine injection using *in vivo* microdialysis after LPS and BH4 injections was also evaluated.

We show that LPS injection induces a strong neuroinflammation in the dorsal striatum, nucleus accumbens and ventral tegmental area. Only enzymes involved in BH4 synthesis are affected by neuroinflammation, contrary to TH and PAH which are not affected by LPS injection. Preliminary data show that BH4 administration induces a slight increase in basal dopamine levels and an important increase after amphetamine injection compared to control mice. Moreover LPS seems to decrease dopamine release after amphetamine injection.

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