Acute hypoxia induced an imbalanced M1/M2 activation of microglia through NF-κB signaling in Alzheimer's disease mice and wild-type littermates

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Alzheimer's disease (AD) is the most common neurodegenerative disease mainly caused by abnormal tau phosphorylation, amyloid β (Aβ) deposition and neuroinflammation. As an important environmental factor, hypoxia has been reported to aggravate AD via exacerbating Aβ and tau pathologies. However, the link between hypoxia and neuroinflammation, especially the changes of pro-inflammatory M1 or anti-inflammation M2 microglia phenotypes in AD, is still far from being clearly investigated. Here, we evaluated the activation of microglia in the brains of APPswe/PS1dE9 transgenic (Tg) mice and their wild type (Wt) littermates, after a single episode of acute hypoxia (24 h) exposure. We found that acute hypoxia activated M1 microglia in both Tg and Wt mice as evidenced by the elevated M1 markers including cluster of differentiation 86 (CD86), tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), C-C motif chemokine ligand 2 (CCL2) and CCL3. In addition, the markers of M2 microglia phenotype (arginase-1 (Arg-1), CD206, IL-4 and IL-10) were decreased after acute hypoxia exposure, suggesting an attenuated M2 phenotype of microglia. Moreover, the activation of microglia and the release of cytokines and chemokines were associated with Nuclear factor-κB (NF-κB) induction through toll-like receptor 4 (TLR4). In summary, our findings revealed that acute hypoxia modulated microglia M1/M2 subgroup profile, indicating the pathological role of hypoxia in the neuroinflammation of AD.