NFKB TRANSCRIPTION FACTOR MODULATES MICROGLIAL RESPONSES IN APP/PS1 TRANSGENIC MICE

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Introduction: Nuclear factor kappa-B (NFκB) is known to be an important regulator of immune and inflammatory responses in both acute and chronic conditions.

Aims: We set out to determine the functional role of NFκB p50 subunit in acute inflammatory conditions in Alzheimer neuropathology. For this purpose, we crossed APPswe/PS1dE9 (APdE9) transgenic mice with NFκB p50⁻/⁻ mice and established a mouse line carrying mutated APP and PS1 transgenes on NFκB p50 null background.

Methods: Under surgical anesthesia, saline and LPS were stereotactically injected into left and right hippocampi of female mice, respectively. One week after the injection brains were processed for immunohistochemistry. Hippocampal Aβ burden was quantified by pan-Aβ and microglial activation by Iba-1 immunoreactivity, respectively.

Results: APdE9 x p50⁻/⁻ mice had normal general health. As expected, in ApdE9 mice intrahippocampal LPS injection caused significant increase in microglial activation with concomitant decrease in hippocampal Aβ burden. Interestingly, LPS caused similar reduction in hippocampal Aβ load in both ApdE9 and APdE9 x p50⁻/⁻ mice, however, APdE9 x p50⁻/⁻ mice showed significantly lower microglial response compared to ApdE9 mice.

Conclusions: APdE9 X p50⁻/⁻ female mice show decreased microglial activity in response to acute inflammatory stimuli caused by intrahippocampal LPS injection. Lack of functional p50 in these mice does not however prevent the reduction of hippocampal Aβ load.