α-Tocopherol Restriction Exacerbated Lipopolysaccharide-Induced Inflammatory Response in α-Tocopherol Transfer Protein-Null Mice

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Objectives: The α-tocopherol transfer protein-null (*Ttpa*$^{-/-}$) mouse model is a valuable tool for studying the molecular and functional consequences of vitamin E (α-tocopherol, αT) deficiency. Our objective was to assess how dietary αT restriction, followed by lipopolysaccharide (LPS) exposure affected the inflammatory response in *Ttpa*$^{-/-}$ and wild-type (*Ttpa*$^{+/+}$) mice.

Methods: After weaning (3 weeks of age), male *Ttpa*$^{+/+}$ and *Ttpa*$^{-/-}$ littermates (n = 36/genotype) were fed an αT deficient diet *ad libitum* for 4 weeks. At 7 weeks of age, mice were injected with LPS (1 or 10 μg/mouse) or saline (control) intraperitoneally and sacrificed 4 hours post-injection. Brain and heart IL-6 levels, a marker of inflammatory response, and serum and tissue αT concentrations were measured via ELISA and HPLC-PDA, respectively. Hippocampal *Il6*, *Tnf*, and *Gpx1* expression, markers of inflammatory and oxidative stress response, were measured via RT-qPCR, and blood immune cell profiles were measured via a hematology analyzer.

Results: αT concentrations in serum and most analyzed tissues were below the limit of detection in *Ttpa*$^{-/-}$ mice but not *Ttpa*$^{+/+}$ mice. Circulating white blood cell levels, particularly lymphocytes, were lower in all LPS groups compared to controls ($P < 0.01$). The 10 μg LPS groups had elevated IL-6 in the cerebellum and heart compared to controls, confirming an acute inflammatory response ($P < 0.01$). Hippocampal *Il6* and *Tnf* expression were significantly increased in *Ttpa*$^{-/-}$ mice that received 10 μg LPS compared to those that received saline (∼20- and ∼3-fold higher, respectively) ($P < 0.01$). Comparing expression patterns by genotype, the 10 μg LPS-*Ttpa*$^{-/-}$ mice had ∼2-fold lower *Gpx1* and ∼2-fold higher *Il6* expression than the 10 μg LPS-*Ttpa*$^{+/+}$ mice. Hippocampal *Il6* expression was increased by LPS in a dose-dependent manner ($P < 0.05$).

Conclusions: LPS, especially at the higher dose, altered inflammatory markers in the brain, heart, and serum. αT restriction further exacerbated the expression of select hippocampal genes.

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