



DENTATE GYRUS MOLECULAR LAYER MICROGLIA CHANGES, IL-1 β AND BEHAVIOR IN MOUSE VALPROIC ACID MODEL OF AUTISM SPECTRUM DISORDERS



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To assess the exploratory and locomotor activities of mature BALB/c mice exposed *in utero* to valproic acid (VPA), count the number of microglia in the molecular layer of dentate gyrus using stereology, and measure plasmatic pro-inflammatory cytokines level. Valproic acid mouse model of autism spectrum disorders has been largely used to investigate social abnormal behavior in association with cellular and molecular changes, but no reports explored potential correlations between hippocampal-dependent cognitive deficits in correlation with inflammatory microglial response in the molecular layer of dentate gyrus and peripheral proinflammatory cytokines in adult female mice. Pregnant females on day 12.5 of pregnancy received either VPA diluted in saline (600 mg/kg body weight) or saline. Their offspring were housed in standard laboratory cages from 21st postnatal day onwards. At adulthood (5 months) female mice were submitted to behavioral tests, peripheral blood collection for cytokines analysis (IFN- γ , IL-1 β , IL-6 and TNF- α), and had their brains processed for microglial selective marker (IBA-1 antibody). In the open field (travelled distance, immobility, crossed lines, and periphery vs. center index) and elevated plus-maze (travelled distance, immobility, closed vs. open arm index) tests, cytokines analysis (IL1- β) and stereological unbiased microglial counts showed significant differences between VPA and control groups, (two-tail t-tests, $p < 0.05$). We suggest that both peripheral and central inflammation may be associated with abnormal hippocampal-dependent task performances in the valproic acid female mouse model of autism spectrum disorders.

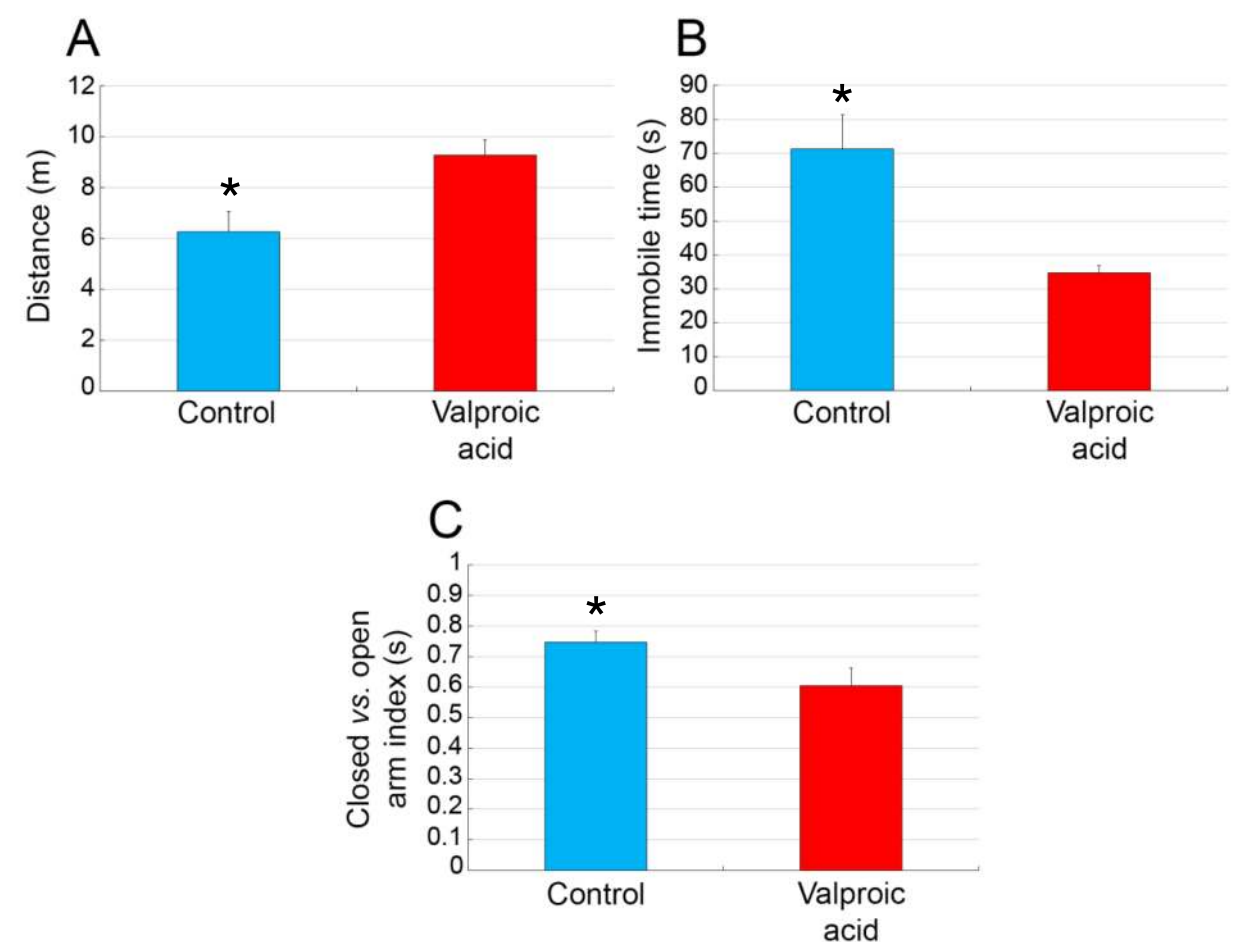


Figure 02 - Elevated plus-maze Test. (A) Distance Traveled; (B): Immobile Time; (C) Closed vs. Open Arm Index

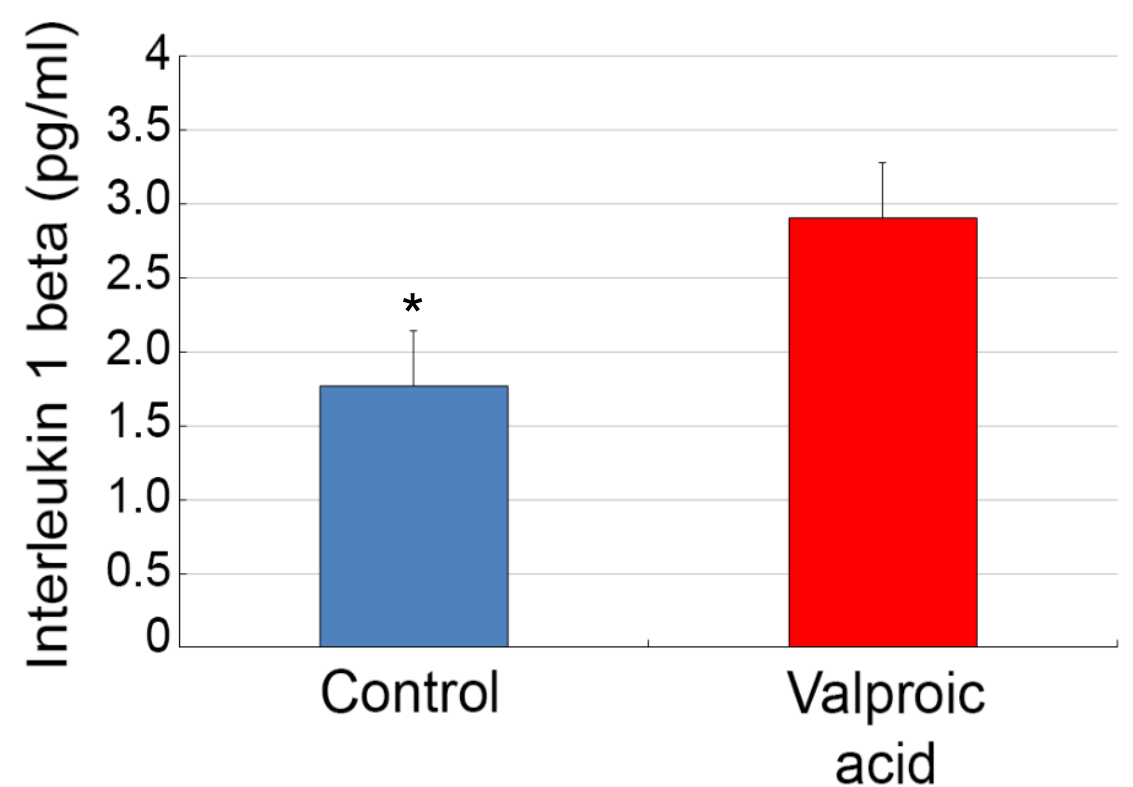


Figure 03 - Cytokines analysis. Peripheral interleukin 1 beta (IL1- β) levels.

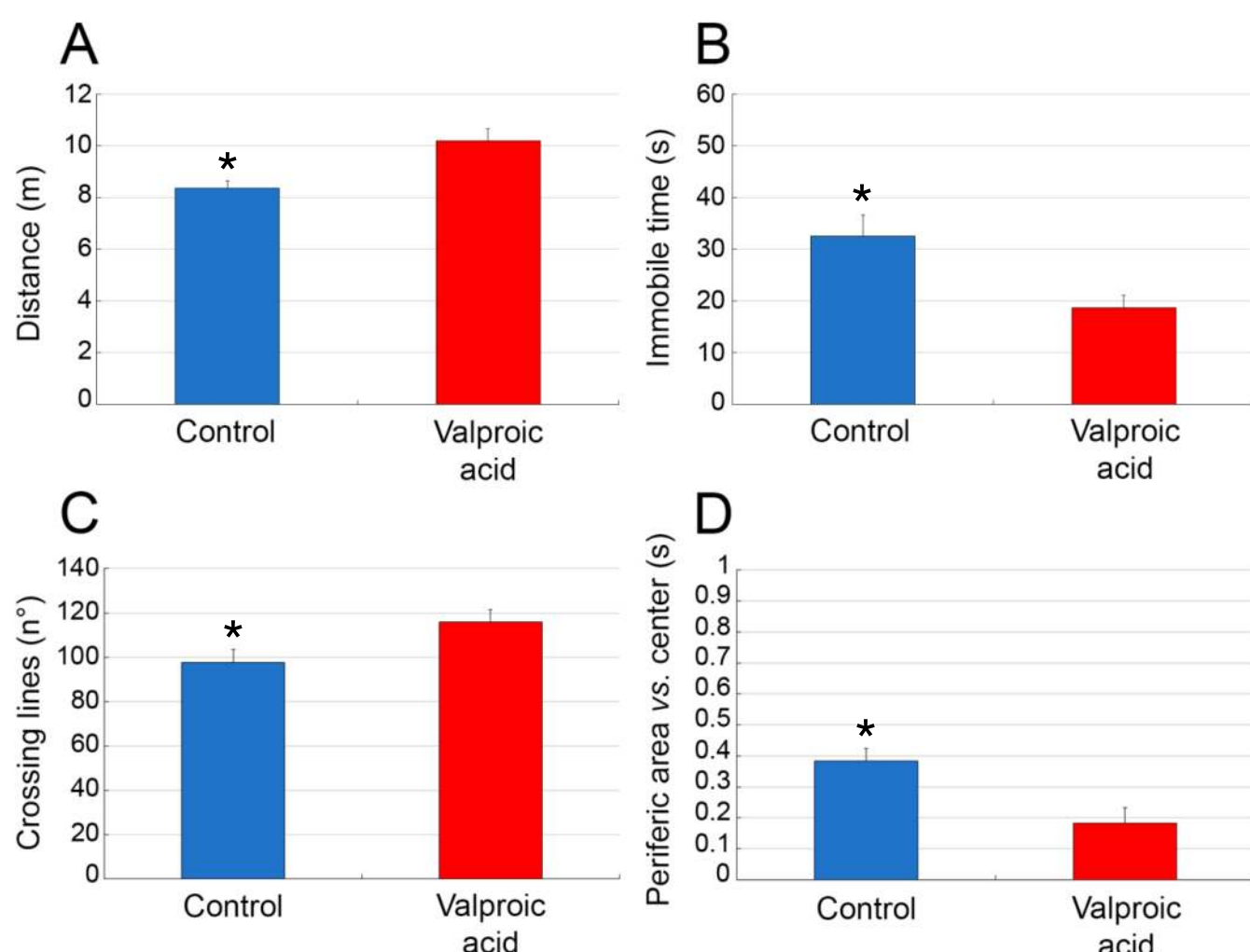


Figure 01 - Open Field Test. (A) Distance Traveled; (B): Immobile Time; (C) Crossed-line; (D) Periphery vs. Center

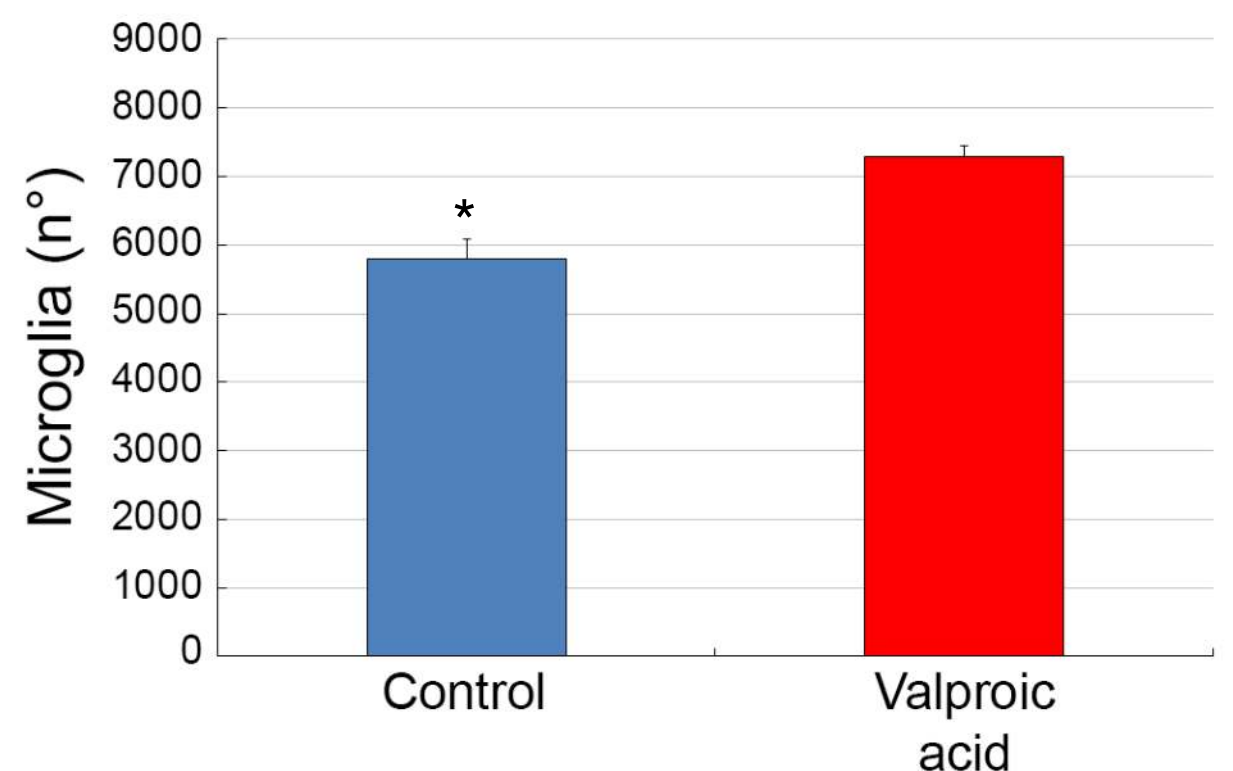


Figure 04 - Total estimation of microglia in the molecular layer of the dentate gyrus using an optical fractionator technique.