

TITLE: Neonatal Pain and Inflammation Impairs Hippocampal-Dependent Memory in Middle-Aged Rats

AUTHORS: Nivedita Nagar, Yoko Ogawa, Nicole C. Victoria, Anne Z. Murphy, and Marise B. Parent

FACULTY SPONSOR: Marise B. Parent, Ph.D., Associate Professor, Neuroscience Institute and Department of Psychology

In the United States, one out of every eight infants is born prematurely each year. They are typically hospitalized into the Neonatal Intensive Care Unit (NICU) where they receive multiple painful and inflammatory procedures without the presence of any analgesics. Painful experiences are associated with an increase in stress responses. This is critical because stress impacts the brain negatively, especially the hippocampus, a brain region that is important for learning and memory. Previous studies showed that neonatal stress induced by a decrease in maternal care disrupts hippocampal morphology and synaptic plasticity, resulting in hippocampal-dependent memory deficits in middle-aged rats, but this was not observed when they were adults. Based on these findings, we hypothesized that neonatal pain impairs hippocampal-dependent memory in middle-aged, but not in adult rats. To test this, on the day of birth, male Sprague-Dawley rats were either handled or injected with the inflammatory agent carrageenan (1%) to the right hindpaw, which causes approximately 72 hr of pain and inflammation. In adulthood and middle age, we tested their learning and memory using hippocampal-dependent spatial water maze. We found that there were no effects of neonatal pain on spatial learning in both adult and middle-aged rats. However, middle-aged rats (postnatal days 424-439) that were injured on the day of birth showed memory impairments, but they did not when they were younger (postnatal day 144-158). These results suggest that premature male infants that undergo painful procedures around the time of birth have a high risk of developing memory deficits later in life. Future experiments need to examine how the injury affects the hippocampus and how aging is involved in these neonatal injury-induced memory deficits.

KEYWORDS: Neonatal Stress, Pain, Inflammation, Hippocampus, Memory, and Aging