How does early-life stress lead to increased vulnerability to develop cognitive and metabolic dysfunction? A synergistic action of stress, inflammation and nutrition

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Early-life stress (ES) is associated with increased vulnerability to cognitive impairments as well as metabolic disorders like obesity later in life. We investigate the role of a synergistic effect of stress, metabolic factors, nutrition and the neuroimmune system in this early-life induced programming.

We use an established model of chronic ES and expose mice to limited nesting and bedding material during first postnatal week and study the central and peripheral systems under basal and challenged conditions (i.e. LPS, amyloid accumulation, western style diet (WSD) and exercise) to gain further insight in the functionality of brain plasticity, neurogenesis microglia and adipose tissue. In addition, given the high nutritional demand during development, we propose that early nutrition is critical for programming of brain and body. We focus on essential micronutrients and fatty acids and propose that an early dietary intervention with a diet enriched with these nutrients might protect against ES-induced functional deficits.

We show that ES leads to cognitive impairments associated with reduced hippocampal neurogenesis at basal conditions as well as in response to exercise, primed microglia with exaggerated response to LPS or amyloid accumulation. Metabolically, ES mice exhibit a leaner phenotype but they accumulate more fat in response to WSD. Finally, with an early dietary intervention with micronutrient or fatty acid we were able to (at least partly) prevent ES-induced cognitive decline, likely mediated by modulation of microglia, without however affecting the ES-induced metabolic profile. These studies give new insights for the development of targeted dietary interventions for vulnerable populations.