



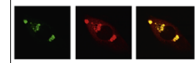
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Review

Synaptic changes in the hippocampus of adolescent female rodents associated with resilience to anxiety and suppression of food restriction-evoked hyperactivity in an animal model for anorexia nervosa

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ABSTRACT

Anorexia nervosa is a mental illness that emerges primarily during early adolescence, with mortality rate that is 200 times higher than that of suicide. The illness is characterized by intense fear of gaining weight, heightened anxiety, obstinate food restriction, often accompanied by excessive exercise, in spite of mounting hunger. The illness affects females nine times more often than males, suggesting an endocrine role in its etiology. Its relapse rate exceeds 25%, yet there are no accepted pharmacological treatments to prevent this. Here, I summarize studies from this laboratory that have used adolescent female rodents in activity-based anorexia (ABA), an animal model of anorexia nervosa, with the goal of identifying neurobiological underpinnings of this disease. We put forth a hypothesis that a GABAergic mechanism within the hippocampus is central to regulating an individual's anxiety which, in turn, strongly influences the individual's resilience/vulnerability to ABA. In particular, we propose that ionotropic GABA_A receptors containing the subunits alpha4 and delta, are at play for exerting shunting inhibition upon hippocampal pyramidal neurons that become more excitable during ABA. Since these receptors confer insensitivity to benzodiazepines, this pharmacological profile of ABA fits with lack of report indicating efficacy of benzodiazepines in reducing the anxiety experienced by individuals with anorexia nervosa. The idea that the GABAergic system of the hippocampus regulates resilience/vulnerability to anorexia nervosa complements current opinions about the important roles of the prefrontal cortex, amygdala, striatum, gustatory pathways and feeding centers of the hypothalamus and of the neuromodulators, serotonin and dopamine, in the etiology of the disease.

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Abbreviations: ABA, activity-based anorexia; AN, anorexia nervosa; CON, control; EX, exercise; FR, food restriction; GABA, gamma-aminobutyric acid; GAD, glutamic acid decarboxylase; LTP, long-term potentiation; MWM, Morris water maze; Rm, membrane resistance; SR, stratum radiatum; SLM, stratum lacunosum-moleculare; THP, 3 α ,5 α [β]-tetrahydroprogesterone; Rs, receptors; Vm, membrane potential
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