Exploring the role of sphingolipid metabolism in the vulnerability and resilience to stress-induced anhedonia in the CMS model of depression

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Stress has been identified as a main environmental risk factor for the onset or exacerbation of major depressive disorder (MDD). However, the impact of stress varies considerably, with the majority of stressed individuals demonstrating resilience and a capacity for positive coping mechanisms while a smaller are susceptible to stress-related psychopathologies, necessitating pharmacological interventions [1]. Despite the elusiveness of the molecular mechanisms underlying resilience and vulnerability, their identification is imperative for the development of more efficacious therapeutic strategies. Recently, significant attention has been directed towards the relevance of the ASM/Cer system in the context of MDD [2]. Acid sphingomyelinase (ASM) is a lysosomal glycoprotein that catalyses the hydrolysis of sphingomyelin into the bioactive sphingolipid ceramide (Cer), a major regulator of sphingolipid metabolism. On these bases, we explore the involvement of several mediators of the ASM/Cer system in the development of stress-induced anhedonia, by measuring their expression in the brain of rats exposed to the chronic mild stress paradigm, a well-known model of MDD [3]. Our data, although preliminary, suggest that resilience may be associated with an increased ability to modulate sphingolipid metabolism by favouring the production of substances with a beneficial impact on the structure/function of the nerve cell to the detriment of those (like ceramide) that can damage it.

Keywords: Stress, depression, rat brain, sphingolipid

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