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## Effect of increasing doses of anandamide in the hypothalamus on panic-like behavior evoked during threatening situations: Role of CB1 and TRPV1 receptors

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The endocannabinoid system plays an important role in the organization of panic like defensive behavior. Threatening situations recruit some brain areas like dorsomedial hypothalamus (DMH). Behavioral evidences indicate that cannabinoid receptors endogenous ligand anandamide can modulate these responses. However, there is a lack of studies addressing the hypothalamus. Thus, the aim of this work was to investigate which mechanisms provide the anandamide mediated responses and determine the localization of cannabinoid receptor type 1 (CB1) and transient receptor potential vanilloid type-1 channel (TRPV1) in DMH. To confirm the hypothesis that the anandamide provide panicolytic like effects, male C57/BL6 mice were treated with intra-DMH microinjections of increasing doses of anandamide (0.5, 5 and 50 pmol/100 nL) and then confronted with South American rainbow Boidae snakes in a polygonal arena for five minutes. DMH-anandamide treated-group showed a bell-shaped dose response curve with no effect of low and high doses and significant panic like responses inhibition for intermediated dose. In addition, this panicolytic like effect was prevented through the pre-treatment of the DMH with the CB1 receptor antagonist AM251. In other hand, the pre-treatment of the DMH with the TRPV1 receptor antagonist 6-I-CPS restored the panicolytic-like effect of the highest dose of anandamide. Immunofluorescence assay showed that CB1 receptors were identified mainly on axonal fibers, and TRPV1 receptors were found almost exclusively surrounding perikarya. The present results suggest a panicolytic like effect played by anandamide on DMH by recruiting CB1 receptors and the TRPV1 receptors is involved in the lack of effect of the highest dose of the anandamide.

### Biography

Tayllon dos Anjos Garcia is a Bachelor of Pharmacy (2011), has completed his MSc in Pharmacology (2013) and is currently a PhD student (2017) at the Department of Pharmacology, Ribeirão Preto Medical School of the University of São Paulo. He has experience in Neuropsychopharmacology focused on animal models of anxiety and panic. He is interested in understanding the neural control of defensive behavior and currently, he has been studying the role of endocannabinoid signaling in the hypothalamus nuclei.

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