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03.016 **Lack of Involvement of the 5-HT2A Receptor in the Effect of Ayahuasca on Fear Memory Reconsolidation.** Daneluz DM[1], Silveira GO[2], Yonamine M[2], Stern CAJ[1]. [1]UFPR, Dept of Pharmacology; [2]FCF-USP

Introduction: Post-traumatic stress disorder (PTSD) develops from trauma exposure, creating a resistant type of memory. Treatment of PTSD is limited, with no drugs targeting traumatic memories. Evidence suggests that psychedelics may alleviate PTSD symptoms by interfering with memory processing. Previous work of our group showed that a low dose of Ayahuasca impaired fear memory reconsolidation, producing a lasting reduction of fear expression. Ayahuasca (AYA) is an Amazonian psychedelic brew rich in DMT (dimethyltryptamine) and b-carbolines, compounds with affinity for serotoninergic receptors and monoamine oxidase, respectively. Considering the involvement of 5-$HT_{2A/2C}$ receptors on the mechanism of action of psychedelics, we aimed to investigate the involvement of 5-HT_{2A} receptor located in the dorsal hippocampus (DH) in the effects of AYA on fear memory reconsolidation. **Methods:** Adult male Wistar rats with bilateral guide-cannulas aimed at the CA1 region of the DH were conditioned to Context A (3 foot shocks of 0.8 mA/3 s, 30 s intervals). To induce reconsolidation, 24 h after conditioning, animals were exposed to Context A for 3 minutes (Retrieval), without foot shock presentation. Independent groups received ketanserin (KET; 10 nmol/0.5 ul; antagonist of 5-HT_{2A} receptor) or vehicle (saline 0.9% plus Tween 0.2%) in a volume of 0.5 µL/side into the CA1 region. Immediately after, rats received 60 mg/kg of AYA or H_2O (AYA vehicle) by gavage (o.g.). Treatments were delivered 20 min before retrieval. On the day after retrieval, animals were re-exposed to Context A (Test A), and on the next day, to a neutral Context B (Test B) to analysis of fear generalization. Composition of AYA was analyzed through liquid chromatography-tandem mass spectrometry (DMT: 0.43 mg/mL; Tetrahydroharmaline: 0.75 mg/mL; Harmaline: 0.11 mg/mL; and Harmine: 0.70 mg/mL). Freezing time was assessed as a fear memory index. Data are expressed as mean ± S.E.M and were analyzed by two-way repeated-measures ANOVA followed by Newman-Keuls post-hoc. All procedures were approved by the UFPR ethics committee (CEUA 1572). **Results:** During retrieval, no significant differences were observed among H_2O-VEH (55.44±3.04), AYA-VEH (52.65±4.14) and H_2O-KET (54.5±10.05) groups. However, KET-AYA group presented significantly less freezing (16.87±5.56; $p<0.05$) compared to all other groups. During Test A, AYA-VEH group (39.4±3.8; $p<0.05$) significantly reduced freezing behavior compared to control H_2O-VEH (64.62±5.2), suggesting a reconsolidation impairing effect. Of note, AYA-KET group (39.72±6.11; $p<0.05$) presented significantly less freezing than groups H_2O-VEH (64.62±5.2) and H_2O-KET (64.65±7.34), but a similar freezing compared to AYA-VEH (39.4±3.8), suggesting a lack of involvement of 5-HT_{2A} receptor on the reconsolidation impairing effect of AYA. No significant differences were found in Test B. **Conclusion**: Together, our results suggest that the 5-HT_{2A} receptor in the CA1 region of the DH is not involved in the impairing effect of AYA during the early phase of memory reconsolidation. However, the 5-HT_{2A} receptor might be involved in the control of fear memory expression. **Financial Support:** CAPES and CNPq.