Alpha-amyrin disrupts prepulse inhibition of startle in rats: a cannabinoid mechanism.

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\textbf{Key Words:} alpha-amyrin; PPI; cannabinoid.

\textbf{Introduction:} Alpha-amyrin (aAMY) is a bioactive terpene extract from the resin of \textit{Protium sp.}, plants used in folk medicine to treat inflammatory diseases, among other purposes. Simão da Silva \textit{et al.} (Pain, 152, 1872, 2011) reported that anti-inflammatory effects of a,b-AMY are related to cannabinoid mechanisms. Psychotomimetic drugs, such as cannabinoid agonists, reduce prepulse inhibition of startle (PPI) in laboratory animals, which indicates a compromise of circuitry that filters input information. This study aims to evaluate the effect of aAMY on sensorimotor gating and the involvement of cannabinoid mechanism in such response.

\textbf{Experimental Procedure:} Male \textit{Wistar} rats (n=7-9, 250-350 g) were habituated to chamber (5 min of 65 dB background noise) and stimuli, with 10 pulse alone trials (P, 120 dB, for 50ms, inter-trial interval of 20s). PPI was tested via 60 trials with an inter-trial interval of 20 s: 20 P trials, 10 prepulse alone trials (75 dB for 20 ms, 3000 Hz), 20 prepulse+pulse trials (PP, with 20 ms interval) and 10 no stimuli trials. PPI was measured by %PPI=100-[(100xPP/P)]. All drugs were dissolved in vehicle (VHC, 1:2:7 Tween80:DMSO:PBS) and injected 1 μL/rat icv (stereotaxic surgery performed a week before experiment). In the first test, the rats were treated with VHC or aAMY 0.1, 1.0 or 10.0 μg/μL before the PPI test. For the second test, rats received VHC or AM251 1.0 μg/μL, 5 min later VHC or AMY 0.1 μg/μL and then placed into PPI chamber. Statistics were performed with ANOVA followed by Newman-Keuls post hoc test.

\textbf{Results/Discussion:} All aAMY doses caused PPI deficit in rats [F(3,21)=7.50, p=0.001] and this effect was prevented by the CB1R inverse agonist [F(1,29)=5.50, p=0.026], suggesting a cannabinoid mechanism for aAMY result on PPI. AM251 had no effect on PPI \textit{per se} (p=0.575).

\textbf{Conclusion:} These data suggest that a plant used in traditional medicine in Brazil has a component (aAMY) with action on information processing disruption probably by means of cannabinoid effect.

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\begin{figure}[h]
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\includegraphics[width=\textwidth]{Figure1.png}
\caption{A) Effect of aAMY0.1, 1.0 and 10.0 μg/μL on PPI.ANOVA/NK, n=7-8. B) Influence of cannabinoid inverse agonist, AM251, on the effect of aAMY. Two-Way ANOVA/NK, n=8-9. Data express the mean ± SEM, *p<0.05 compared with control (VHC).}
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