

Commentary: Comment on the Effect of Endocannabinoid System on Rat Behavior



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I read the recently published article in Vol 6 (3) of Basic and Clinical Neuroscience entitled “Study the Effect of Endocannabinoid System on Rat Behavior in Elevated Plus-Maze” by Komaki et al. (2015). In this valuable article, the authors uncovered the effects of AM251 as a CB₁ receptor antagonist on anxiety-like behaviors of rats using elevated plus-maze. However, I have a few comments on this article:

In the discussion section, the anxiogenic-like effect of AM251 in rats was completely attributed to blockade of CB₁ receptors. However, based on the following argument, I believe the authors have ignored the role of GPR55 receptors in this process.

GPR55 receptors are a class of G protein-coupled receptors suggested as the third member of cannabinoid receptors family (Ryberg et al., 2007; Lauckner et al., 2008). Previous studies show that both 2-arachidonoylglycerol and anandamide (enhanced by URB597) are endogenous ligands for GPR55 receptors (Ryberg et al., 2007; Lauckner et al., 2008). Furthermore, AM251 is a potent GPR55 receptor agonist (Ryberg et al., 2007; Henstridge et al., 2010). On the other hand, CB₁ and GPR55 receptors influence each other's signaling pathways (Sharir et al., 2012; Kargl et al., 2012). The potential role of GPR55 receptors in anxiety has been evaluated recently (Rahimi, Hajizadeh Moghaddam, & Roohbakhsh, 2015). Accordingly, the intracerebroventricular administration of O-1602 and ML193 as GPR55 receptor agonist and antagonist produce anxiolytic- and anxiogenic-like effects in rats, respectively. Taken together, considering GPR55 receptors in the reported effects of AM251 and URB597 in the discussion, will improve our knowledge about the effects of these drugs on anxiety. One more comment, the researchers should be cautious in employing such drugs in future studies.

*** Corresponding Author:**

Ali Roohbakhsh, PhD

Address: Pharmaceutical Research Center, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran.

Tel: +98 (51) 38823255

E-mail: roohbakhsha@mums.ac.ir

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