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5-HT_{2A} Receptor Activation Normalizes Exaggerated Fear Behavior in *p*-Chlorophenylalanine (PCPA)-Treated Rats

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ABSTRACT

Deficits in serotonin (5-hydroxytryptamine, 5-HT) neurotransmission are implicated in abnormal emotional behaviors such as aggression, anxiety, and depression. However, the specific 5-HT receptor mechanisms involved are not well understood. The role of 5-HT2 receptors in fear potentiated startle, (FPS) was examined in rats chronically treated with pchlorophenylalanine (PCPA) to reduce brain 5-HT. PCPA-treated rats show an enhanced magnitude of FPS. Systemic administration of the 5-HT2 receptor agonist (±)-2,5-Dimethoxy-4-iodoamphetamine hydrochloride (DOI) reduced FPS in both PCPA-treated and saline (SAL)-treated control animals, normalizing the exaggerated fear response in PCPA-treated rats. In both SAL- and PCPA-treated animals, the DOI-induced reduction of learned fear was reversed by the 5-HT2 antagonist ketanserin, but not by the 5-HT2B/2C antagonist SB 206553. Together, these findings suggest 5-HT_{2A} receptors are critical regulators of learned fear, and that 5-HT_{2A} receptors may be an important pharmacological target to normalize exaggerated learned fear resulting from chronic 5-HT-ergic disruption.

KEYWORDS

Fear Conditioning; Startle Reflex; 5-HT2; DOI; Ketanserin; SB 206553

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