Investigating Sterol Carrier Protein-2 Inhibition to Prevent Endocannabinoid Uptake: A Novel Treatment of Anxiety

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Anxiety is the most common mental disorder in the United States, affecting some 40 million adults each year. During anxiety attacks, neurons release excessive amounts of adrenaline, causing hyperventilation and convulsing. Current treatments involve the use of benzodiazepines, an addictive family of drugs that drastically lower breathing rates to frequently cause fatal overdoses. CB1 is a receptor protein capable of reinstating a balance of neurotransmitters without lowering breathing rates. The purpose of this study was to identify a drug that increases the prevalence of CB1 agonists as a safer treatment for anxiety. The process by which CB1 agonists are broken down was not previously understood, but this study provides novel evidence that Sterol Carrier Protein-2 (SCP-2) initiates this process. AM404 is a metabolite of Acetaminophen (Tylenol) that has been shown to relieve anxiety in Wild Type mice, but the drug pathway was not understood. To test the hypothesis that AM404 acts as an inhibitor of SCP-2, SCP-2 knockout mice were given doses of AM404 and their anxiety was quantified using the Elevated Plus Maze assay. AM404 did not produce anxiety relief in SCP-2 knockout mice, suggesting that it must interact with SCP-2 to relieve anxiety. Having provided novel In-Vivo evidence that SCP-2 inhibition can reduce anxiety without a dangerously sedating side effect, computational software was used to begin searching for other inhibitors of SCP-2. Mutagenesis revealed that negatively charged coenzymes have the potential to inhibit SCP-2, providing the basis for drug design and ultimately an unprecedented treatment of anxiety that may minimize the risk of overdoses and addiction.

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