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# Evaluating the Role of Microglia in the PFC on Fentanyl Escalation Using PLX 3997 in Sprague-Dawley Rats

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In people with opioid use disorder (OUD), chronic drug use causes microglial reactivity and subsequent release of proinflammatory cytokines leading to inflammation, potentially weakening one's executive control over drug taking and ultimately leading to greater use. Previous research in our laboratory pointed to a positive correlation between Treml1 expression in the PFC and mean infusions on the last 3 days of fentanyl self-administration ($p < 0.05$). Thus, it is our hypothesis that depletion of microglia using PLX 3397 will result in a reduction in escalation of fentanyl intake, and a reduction of inflammatory signaling, compared to controls. Male and female Sprague-Dawley rats underwent daily 1h acquisition sessions for i.v. fentanyl self-administration (2.5 µg/kg; FR1) for 7 days. Starting experimental day 8, rats received once daily injections of PLX 3397 (25 mg/kg, s.c.) until the end of the study. On experimental days 15-35, rats underwent daily 6h escalation sessions. Approximately 20h after the last self-administration session, acute symptoms of fentanyl-withdrawal were assessed, blood plasma was collected to assess peripheral cytokine and chemokines, and tissue from prefrontal cortex was collected for immunohistochemistry (IHC) and qPCR. Using IHC, IBA1 was evaluated to verify knockdown of microglia. Rats that received PLX 3397 and vehicle showed similar rates of fentanyl SA during acquisition and escalation sessions, and mRNA transcripts of inflammatory targets within the PFC were assessed. Ongoing investigations including greater statistical power will continue to assess the inflammatory markers that may drive fentanyl escalation.

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