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## A novel martial arts-based virtuality reality intervention modulates pain and the pain neuromatrix in patients with opioid use disorder

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**Abstract Title:**

A novel martial arts-based virtuality reality intervention modulates pain and the pain neuromatrix in patients with opioid use disorder

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**Keywords:** methadone; martial arts; fMRI; pain neuromatrix; postcentral gyrus; craving; cortisol

**Background:** Standard-of-care for opioid use disorder (OUD) includes medication and counseling. However, there is an unmet need for complementary approaches to treat OUD patients coping with pain; furthermore, few studies have probed neurobiological features of pain or its management during OUD treatment. This preliminary study examines neurobiological and behavioral effects of a martial arts-based intervention in patients undergoing methadone maintenance treatment (MMT).

**Methods:** Fifteen (11 female) MMT patients completed a virtual reality, therapist-guided martial arts intervention that included breathing and relaxation exercises; sessions were scheduled twice weekly. Assessments included functional magnetic resonance imaging (fMRI) of pain neuromatrix activation and connectivity (pre- and post-intervention), saliva cortisol and C-reactive protein (CRP) at baseline and weeks 4, 8 and 12; and self-reported pain and affective symptoms before and after each intervention session.

**Results:** After each intervention session (relative to pre-session), ratings of pain, opioid craving, anxiety and depression (but not anger) decreased. Saliva cortisol (but not CRP) levels decreased from pre- to post-session. From pre- to post-intervention fMRI assessments, pain task-related left postcentral gyrus (PCG) activation decreased. Higher baseline cortisol levels were associated with greater post-intervention pain task-related insular activation. At baseline, PCG showed positive connectivity with other regions of the pain neuromatrix, but this pattern changed post-intervention.

**Conclusions:** These preliminary findings demonstrate feasibility, therapeutic promise, and brain basis of a martial arts-based intervention for OUD patients undergoing MMT.