## Brain responses to drug-related cues in former drug addicts: An fMRI study

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## **ABSTRACT**

Introduction: Despite the various treatments and rehabilitation services provided for managing drug addiction, drug relapse rates continue to skyrocket in Malaysia. One prominent factor that may have contributed to this increasing relapse rate is the exposure of former drug addicts (FDAs) to drug-related cues following their release into the community after serving time in rehabilitation centres. Emerging studies reported that exposure to drug-related cues may increase activations in the brain regions associated with drug cravings, and that heightened activations in these regions are linked to drug relapse. However, these studies focused mainly on active drug abusers, thus less is known about the FDAs. Therefore, this study investigates whether drug-related cues significantly evoke the brain regions associated with drug cravings in the FDAs. Materials and Methods: A total of 24 male FDAs were recruited from community-based rehabilitation centres operated by the National Anti-Drugs Agency (NADA) for this cross-sectional study. Four participants were excluded as they did not meet the eligibility criteria. The remaining 20 participants underwent a task-based functional MRI (fMRI) experiment. During the experiment, participants viewed a series of drug-related and neutral cues presented in a block-design manner. A total of 96 functional volumes were acquired during the 16-minute fMRI scan. The functional data underwent slice-timing correction, realignment, co-registration, segmentation, normalisation, and smoothing. Individual data were analysed using the fixed effect analysis (FFX). Individual brain activation maps were next generated for the following contrasts: i) drug > baseline, ii) neutral > baseline, and iii) drug > neutral. Within-group brain activation maps were then generated using the random fixed effect analysis (RFX). Data preprocessing and analyses were performed using Statistical Parametric Mapping 12 (SPM12) operating in MATLAB version 9.14 -R2023a. The statistical threshold was set at PFWE < 0.05. Results: When viewing drug-related cues, participants showed significant brain activations in the inferior occipital gyrus (IOG), inferior temporal gyrus (ITG), occipital fusiform gyrus (OFuG), middle occipital gyrus (MOG), occipital pole (OCP), left fusiform gyrus (FuG), and left calcarine cortex (Calc). On the other hand, when they viewed neutral cues, they showed significant brain activations in bilateral IOG, bilateral MOG, and bilateral OCP, left FuG, left OFug, left Calc, right ITG, and right thalamus proper. However, the results did not reveal any significant brain activations when participants viewed drug-related cues compared to neutral cues. These findings indicate that the drug-related cues did not significantly evoke greater brain response in the brain regions associated with drug cravings. A plausible reason is that the FDAs may have recovered from drug addiction and were no longer entited by drug-related cues. Conclusion: The study has provided evidence that the brains of the FDAs do not significantly respond to drug-related cues. This finding suggests that the treatment and rehabilitation services may have inhibited the activations in the brain regions associated with drug cravings of the FDAs. Future works are warranted to explore other factors that may have contributed to the high relapse rates in Malaysia.