Cocaine addiction is a global public health issue with more than 1.5 million users in the United States\(^1\). Cocaine has a high rate of relapse and there are no FDA-approved pharmacotherapies to treat cocaine addiction\(^5\). Thus, it is vital to discover and develop innovative pharmacological treatments for this brain disorder.

Glucagon-like Peptide-1 (GLP-1) is an incretin hormone produced both peripherally and centrally\(^6\). Endogenous GLP-1 stimulates insulin secretion, reduces blood glucose levels, and controls normal food intake\(^2\). GLP-1 receptors are expressed widely throughout the brain including the VTA and nucleus accumbens, two brain regions known to mediate the reinforcing effects of both drugs of abuse and natural rewards\(^1\). Importantly, GLP-1 receptor agonists are FDA-approved for treating type II diabetes and obesity\(^2\). Recent studies suggest that peripheral administration of a GLP-1 receptor agonist reduces cocaine self-administration and cocaine-induced conditioned place preference (CPP)\(^2,5,6\). However, the role of these receptors in the reinstatement of cocaine-seeking behavior, an animal model of relapse, remains unclear.

Since GLP-1 regulates addiction-like behaviors\(^6\), we hypothesized that peripheral administration of a GLP-1 receptor agonist would attenuate reinstatement of cocaine seeking in rats.

### METHODS

#### Self-administration

- Extinction
- Reinstatement

21 days

5 – 7 days

0.25mg/infusion

### RESULTS

**Figure 1:** Systematic administration of a GLP-1 receptor agonist reduces cocaine seeking during reinstatement test sessions. (a) Peripheral administration of Fluoro-Exendin-4 (0.25 µg/kg, i.p.) prior a cocaine priming injection reduces active lever responses during reinstatement test sessions (n=15). (b) Peripheral administration of Fluoro-Exendin-4 reduces active lever responses dose-dependently (n=9). There was no effect on inactive lever presses. Statistical analysis was performed using a Two-way ANOVA test. *p < 0.05 compared to vehicle (Tukey’s HSD).

**Colocalization of Fluoro-Exendin-4 with neurons and astrocytes in the VTA and nucleus accumbens**

**Figure 2:** Systematic administration Fluoro-Exendin-4 penetrates the brain and colocalized with neurons and astrocytes in the VTA and nucleus accumbens. (a, c, d) Fluoro-Exendin-4 stained in green, GFAP stained in red; NeuN stained in magenta and DAPI stained in blue. (b) Fluoro-Exendin-4 stained in green, TH stained in red.

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### REFERENCES

1. 2014 National Survey on Drug Use and Health

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