Morphine addiction comorbid depressive behaviors in behavioral and neural mechanisms in rats

Tsai Yu Tung, and Andrew Chih Wei Huang

佛光大學 Fo Guang University

Department of Psychology, Fo Guang University, No. 160, Linwei Rood, Jiaosi Shiang,Yi-Lan 26247, Taiwan

Abstract :

Clinical studies indicate that patients with Opioid Use Disorder (OUD) frequently exhibit significant depressive symptoms. However, animal models capable of simultaneously reflecting the addiction process and depressive-like behaviors remain scarce, hindering the clarification of neural mechanisms and the advancement of preclinical research.

This study utilizes morphine as a model to investigate whether depressive-like behaviors are induced following the formation of addiction-related positive reward (Conditioned Place Preference, CPP) and negative aversion (Conditioned Taste Aversion, CTA), thereby establishing an animal model for morphine addiction comorbid with depression.

Model Validation: To establish and validate a rat model of morphine addiction comorbid with depressive-like behavior.

Neural Mapping: To utilize **c-Fos immunohistochemistry** to identify activation patterns in key brain regions, including:

- Medial Prefrontal Cortex (mPFC)
- Amygdala
- Hippocampus
- Raphe Nucleus
- Ventral Tegmental Area (VTA)
- Nucleus Accumbens (NAc)

Serotonergic System Analysis: To examine changes in **Tryptophan Hydroxylase (TPH)** expression within these regions to evaluate the role of the serotonergic system in modulating comorbid behaviors.

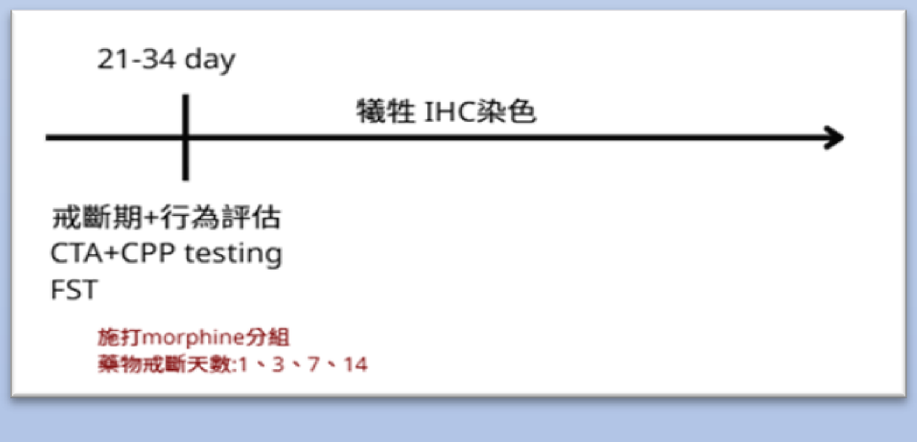
Dual-Labeling: To employ **double-labeling immunofluorescence** to analyze the co-expression of neural activity markers and serotonergic signaling in specific brain nuclei.

Expected Contributions

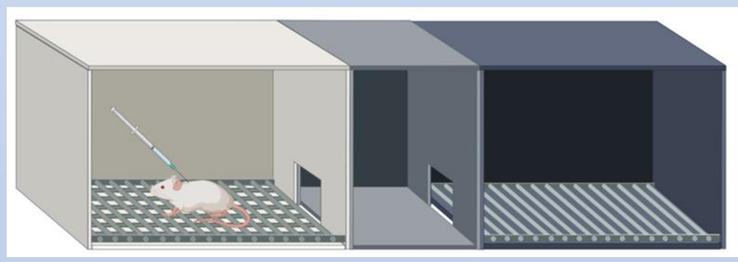
This study expects to establish a reliable and valid animal model for opioid addiction comorbid with depression. By elucidating the underlying regional brain activity and serotonergic regulatory mechanisms, this research provides a critical experimental foundation for preclinical studies and offers substantial insights into the neurobiological mechanisms of OUD and its depressive comorbidities.

Material and Method :

Animals:
C57BL/6



Apparatus:



(Leung, Chan, et al., 2022)

Group:

戒斷期/組別	1d	3d	7d	14d
saline	g1			
morphine	g2	g3	g4	g5

Expected Outcomes:

study investigates the induction of depressive-like behaviors following the establishment of morphine addiction.
The expected outcomes are as follows:

1. Establishment of the Comorbid Animal Model

Outcome: Successful development of a reliable rat model for morphine addiction comorbid with depressive-like behavior.
Key Finding: Identification of the precise **withdrawal window**
(the specific number of days post-morphine cessation) required to consistently trigger depressive-like phenotypes, establishing a standardized protocol for this behavioral model.

2. Characterization of Neural Activation Patterns

Outcome: Identification of regional neural activation during withdrawal via **c-Fos** immunohistochemical mapping.
Key Finding: Anticipated involvement and altered c-Fos expression across a specific network of brain regions mediating this comorbidity,