



Doctoral Dissertation Defense Announcement

“Investigation of the necessity, sufficiency, and specificity of the dmPFC cocaine seeking ensemble”



Shuai Liu

Candidate for Doctor of Philosophy

IDP / Pharmacology & Toxicology

School of Graduate Studies

Medical College of Wisconsin

Committee in Charge:

Christopher Olsen, PhD (Mentor)

Cecilia Hillard, PhD

John Mantsch, PhD

Qing-song Liu, PhD

Kajana Satkunendrarajah, PhD

Date: Monday, April 8, 2024

Time: 9:00 AM (CST)

Defense Location: HUB A5520/5628

Graduate Studies:

Biochemistry of the cell

Techniques of molecular and cell biology

Molecular and cellular biology

Mechanism of cellular signaling

Classical and molecular genetics

Ethics and integrity in science

Modern Drug Discovery & Development

Research Ethics Discussion Series

Fundamental of Neuroscience

Survey or Principle of Drug Action

Ion Channels & Signal Transduction

Seminars

Reading and Research

Doctoral Dissertation

Dissertation

“Investigation of necessity, sufficiency, and specificity of the dmPFC cocaine seeking ensemble”

Cocaine use disorder is a chronic and relapsing neuropsychiatric disorder characterized by a strong propensity for relapse upon re-exposure to a previously drug-associated environment. The dorsal medial prefrontal cortex (dmPFC) is a critical node in the mesocorticolimbic system related to cocaine seeking. There is evidence that learned associations between drug cues and drug seeking behavior are encoded by a specific ensemble of neurons sparsely scattered throughout the dmPFC. We hypothesized that inhibition of dmPFC cocaine seeking ensembles inhibits cocaine seeking memory retrieval, and these ensembles are not involved in fear conditioning memory retrieval, which is also mediated by the dmPFC. We tested this hypothesis by co-injection of viruses expressing TRE-Cre and a cre-dependent inhibitory PSAM-GlyR into the dmPFC of male and female cfos-tTA mice to enable “tagging” of ensemble neurons with an inhibitory chemogenetic receptor. Mice then underwent cocaine self-administration (0.5 mg/kg, 14 days) and fear conditioning. In Experiment 1, a dmPFC cocaine seeking ensemble was tagged, while in Experiment 2, a dmPFC ensemble for fear recall was tagged. In both experiments, subsequent cocaine seeking and fear recall were tested during inhibition of the tagged dmPFC ensemble (0.3 mg/kg uPSEM792s, 30 min prior to sessions). In both sexes, inhibition of the cocaine seeking ensemble suppressed cocaine seeking, but not recall of fear memory, while inhibition of the fear ensemble reduced conditioned freezing but not cocaine seeking. These data demonstrate that cocaine and fear recall ensembles in the dmPFC are stable, but mutually exclusive from one another.

Shuai Liu
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EDUCATION

Medical College of Wisconsin Graduate School 2018- present

Interdisciplinary Doctoral Program in Biomedical Sciences

Department of Pharmacology and Toxicology

Neuroscience Research center

Beijing Institute of Basic Medical Science 2013- 2016

Master of Science, May 2016

Major: Pharmacology

Wuhan Institute of Technology

Bachelor of Science, May 2012

School of Chemistry Engineering & Pharmacy

Major: Applied Chemistry

RESEARCH EXPERIENCE

Ph.D candidate, August 2018- Present

Medical College of Wisconsin

Dr. Christopher Olsen Lab, Department of Pharmacology and Toxicology

- Investigation of the neuronal ensemble mechanisms underlying cocaine seeking in the medial prefrontal cortex (mPFC)

Visiting scholar, August 2017- May 2018

Medical College of Wisconsin

Dr. Qing-song Liu Lab, Department of Pharmacology and Toxicology

- Investigation of the roles of Zona Incerta (ZI) and medial habenula (MHb) in drug addiction

Master, August 2013 - May 2016

Beijing Institute of Basic Medical Science

Dr. Zheng Yang Lab

- Pharmacokinetics studies of Chinese herbs – Tetrahydropprotoberberines (THPBs) and their metabolites l-Corydalmine (l-CDL) and l-Tetrahydroberberrubine (l-THR)

SKILLS

Electrophysiology patch-clamp; Stereotaxic surgery; Jugular catheterization surgery; Optogenetics; Chemogenetics; Western blot; RNAscope; Immunohistochemistry, CLARITY.

PUBLICATIONS

Liu, S., Nawarawong, N., Liu, X., Liu, Q.S., and Olsen, C.M., 2023. Dissociable dorsal medial prefrontal cortex ensembles are necessary for cocaine seeking and fear conditioning in mice. (Under review of Biological Psychiatry)

Sarka, B.C., **Liu, S.**, Banerjee, A., Stucky, C.L., Liu, Q.S. and Olsen, C.M., 2023. Neuropathic pain has sex-specific effects on oxycodone seeking and drug-seeking ensembles in the dorsomedial prefrontal cortex. *bioRxiv*, pp.2023-07.

Mu, L., Liu, X., Yu, H., Vickstrom, C.R., Friedman, V., Kelly, T.J., Hu, Y., Su, W., **Liu, S.**, Mantsch, J.R. and Liu, Q.S., 2023. cAMP-mediated upregulation of HCN channels in VTA dopamine neurons promotes cocaine reinforcement. *Molecular Psychiatry*, pp.1-13.

He, Y., Madeo, G., Liang, Y., Zhang, C., Hempel, B., Liu, X., Mu, L., **Liu, S.**, Bi, G.H., Galaj, E. and Zhang, H.Y., 2022. A red nucleus–VTA glutamate pathway underlies exercise reward and the therapeutic effect of exercise on cocaine use. *Science Advances*, 8(35), peabo1440.

Liu, X., Vickstrom, C.R., Yu, H., **Liu, S.**, Snarrenberg, S.T., Friedman, V., Mu, L., Chen, B., Kelly, T.J., Baker, D.A. and Liu, Q.S., 2022. Epac2 in midbrain dopamine neurons contributes to cocaine reinforcement via facilitation of dopamine release. *Elife*, 11, p.e80747.

Jessen, K., Slaker Bennett, M.L., **Liu, S.** and Olsen, C.M., 2022. Comparison of prefrontal cortex sucrose seeking ensembles engaged in multiple seeking sessions: Context is key. *Journal of Neuroscience Research*, 100(4), pp.1008-1029.

Vickstrom, C.R., Liu, X., **Liu, S.**, Hu, M.M., Mu, L., Hu, Y., Yu, H., Love, S.L., Hillard, C.J. and Liu, Q.S., 2021. Role of endocannabinoid signaling in a septohabenular pathway in the regulation of anxiety- and depressive-like behavior. *Molecular psychiatry*, 26(7), pp.3178-3191.

Mi, G., Gao, Y., Yan, H., Jin, X., Ye, E., **Liu, S.**, Gong, Z., Yang, H. and Yang, Z., 2016. l-Scoulerine attenuates behavioural changes induced by methamphetamine in zebrafish and mice. *Behavioural brain research*, 298, pp.97-104.

Mi, G., Gao, Y., **Liu, S.**, Ye, E., Li, Y., Jin, X., Yang, H. and Yang, Z., 2016. Cyclin-dependent kinase inhibitor flavopiridol promotes remyelination in a cuprizone induced demyelination model. *Cell Cycle*, 15(20), pp.2780-2791.

Mi, G., **Liu, S.**, Zhang, J., Liang, H., Gao, Y., Li, N., Yu, B., Yang, H. and Yang, Z., 2017. Levo-tetrahydroberberrubine produces anxiolytic-like effects in mice through the 5-HT 1A receptor. *Plos one*, 12(1), p.e0168964.

CONFERENCES AND PRESENTATIONS

Winter Conference on Brain Research — Poster presentation, January 2023

MCW GSA 6th Annual symposium — Poster presentation, May 2023

Society for Neuroscience — Poster presentation, November 2022

MCW GSA 5th Annual symposium — Poster presentation, August 2022

Pavlovian Society — Poster presentation, January 2022

Society for Neuroscience — Poster presentation, November 2021

MCW GSA 4th Annual Symposium, April 2020

Society for Neuroscience, October 2020

MCW GSA 3rd Annual Symposium, March 2019