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Blockage of system xc- improves cocaine addiction in cocaine-dependence mice

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The cystine-glutamate antiporter or system x_c^- is a membrane-bound Na+-independent amino acid transporter which exchanges intracellular glutamate for extracellular cysteine. Previous studies have shown that activation of system x_c^- by its activator N-acetylcysteine (NAC) inhibits reinstated cocaine or nicotine seeking behaviors. In addition, the expression of system x_c^- subunit xCT in brain was up-regulated in cocaine dependence mice, but down-regulated in cocaine withdrawal mice, suggesting a dynamic change in xCT expression and its activity during addiction. Unfortunately, system x_c^- is not the only target for NAC and all pharmacological inhibitors commonly used to study system x_c^- activity have off-target effects. These issues raise the uncertain role of system x_c^- in addiction. In this study, we tested xCT knockout (xCT-/-) mice for dependence-induced drinking using the chronic intermittent cocaine-two bottle choice drinking protocol. There was significant inhibition in daily cocaine consumption in xCT-/- mice during free-choice drinking as compared to wild type (WT) mice, indicating genetic deficiency of system x_c^- blocked cocaine dependence. Moreover, sulfasalazine (SAS), the US Food and Drug Administration (FDA) that blocks system x_c^-, significantly attenuated the daily cocaine consumption during free-choice drinking in cocaine-dependence mice as compared to control vehicle (DMSO). Taken together, these findings show blockage of system x_c^- improves cocaine addiction in cocaine dependence-mice. Inhibition of system x_c^- represents a new class of therapeutics against cocaine addiction.

Biography

Vivian Hsu is currently obtaining her Master's Degree at China Medical University. She opts to apply for Doctorate studies in the future. She is a student of Professor Chia-Hung Hsieh who has published more than 10 research papers in notable journals. He is currently researching on therapeutics for cocaine addictions with a plan to go into clinical trials.

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