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Ionic imaging and bio-energetic analysis of club drug-induced cognitive deficiency by time-of-flight secondary ion mass spectrometry (TOF-SIMS)

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Motivation and Aim: Excessive exposure to club drug gamma-hydroxybutyric acid (GHB) would cause cognitive dysfunction in which impaired hippocampal Ca^{2+}-mediated neuroplasticity may correlate with this deficiency. However, the potential changes of *in vivo* Ca^{2+} together with molecular machinery engaged in GHB-induced cognitive dysfunction have never been reported. This study aims to determine these changes in bio-energetic level through ionic imaging, spectrometric, biochemical, morphological, as well as behavioral approaches.

Methods and Algorithms: Adolescent rats subjected to GHB were processed for TOF-SIMS, immunohistochemistry, biochemical assay, together with Morris water maze to detect the ionic, molecular, neurochemical, and behavioral changes of GHB-induced cognitive dysfunction, respectively. Extent of oxidative stress and bioenergetics were assessed by levels of lipid peroxidation, Na^+/K^+ ATPase, cytochrome oxidase, and [^{14}C]-2-deoxyglucose activity.

Results: The study indicated that in GHB intoxicated rats, decreased Ca^{2+} imaging and reduced NMDAR1, nNOS, and p-CREB reactivities were detected in hippocampus. Depressed Ca^{2+}-mediated signaling corresponded well with intense oxidative stress, diminished Na^+/K^+ ATPase, reduced COX, and decreased 2-DG activity, which all contributes to the development of cognitive deficiency. As impaired Ca^{2+}-mediated signaling and oxidative stress significantly contribute to GHBinduced cognitive dysfunction, delivering agent(s) that improves hippocampal bio-energetics may thus serve as a promising strategy to counteract the club drug-induced cognitive dysfunction emerging in our society nowadays.

Conclusion: In summary, with the assistance of advanced spectrometric, ionic imaging, biochemical, morphological as well as behavioral approaches, the present study addressed for the first time that chronic and excessive exposure to GHB would cause cognitive dysfunction in which impaired hippocampal bio-energetics may contribute to the pathogenesis of this deficiency.

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