

## **ETHANOL-CONDITIONED WITHDRAWAL SYNDROME**

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The withdrawal syndrome is closely related to the concepts of tolerance and physical dependence. The chronic consumption of a drug is believed to induce adaptive changes that are designed to oppose the acute effects of the drug. Such adaptive changes increase the tolerance to acute drug effects but lead to physical dependence, which is revealed by withdrawal symptoms when the drug is cleared from the body. However, another form of adaptive response to repeated drug consumption has been identified. This adaptive response appears after the intermittent repeated administration of a drug in association with the same set of environmental stimuli. After several associations, these environmental stimuli become able to induce a conditioned adaptive response. Such response leads to the phenomenon of “environment-dependent tolerance” that was observed with many drugs of abuse. However, if the drug is not administered, the conditioned stimuli alone may induce a “conditioned withdrawal syndrome”. Although less studied than the classical withdrawal syndrome, this conditioned withdrawal syndrome may be of importance for the development of drug dependence. In our experiments, we have studied the development of a conditioned withdrawal syndrome after repeated associations of a specific set of environmental stimuli with ethanol injections in Wistar rats. After repeated administrations of ethanol, the rats showed a clear environmental-dependent tolerance to ethanol. Furthermore, these conditioned stimuli induced behavioral (hyperexcitation) and neurochemical (increase glutamate release) responses similar to those observed after chronic alcohol withdrawal.