Silent synapses in alcohol addiction

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Alcohol addiction, defined as a state of compulsive alcohol consumption, could be conceptualized as a pathological, extremely durable form of memory. One potential mechanism underlying addiction is alcohol-induced adaptations at glutamatergic synapses within the brain reward circuitry. In this study we used a mouse model of alcohol addiction, where mice living in the IntelliCages had a long-term free access to alcohol, followed by 1 week of withdrawal and cue relapse. Focusing on synaptic plasticity in the dentate gyrus (DG) of the hippocampus – an emerging player in reward-driven behaviour, we discovered that long-term alcohol exposure alters AMPA receptors-mediated synaptic transmission by triggering the appearance of silent synapses – immature synaptic connections that function as substrates for increased learning. These silent connections are reversed by withdrawal but reappear after presentation of alcohol-associated cue. Chemogenetic inhibition of DG prevents the reappearance of silent synapses during relapse and affects alcohol seeking and drinking. These results suggest that synaptic plasticity in DG contributes to development of addiction-related behaviors.