

**Abstract**

Cocaine addiction is increasingly considered to stem from the development of maladaptive, stimulus bound, drug seeking habits that both contribute to the maintenance of drug use despite aversive consequences, and also to high rates of relapse. However because relapse by definition occurs only after a period of abstinence, the relative contribution of habits and pharmacological withdrawal from the drug to relapse is unknown. In this study we demonstrate that preventing rats from expressing their drug seeking habits after forced abstinence results in aberrant, compulsive drug seeking behaviour at relapse. Thus, Lister-Hooded rats were trained under a fixed-interval (FI) 15-min schedule or a FI 15 (FR10:S) second order schedule of reinforcement, the latter having been shown to recruit stimulus bound, dorsolateral striatum-dependent, maladaptive habits. Indeed, in this procedure every ten active lever presses produces the presentation of a 1s (CS) so that rats respond more vigorously for the drug in the presence, than in the absence, of the drug CS. The results showed that a 3-day forced abstinence period increased cocaine seeking responses only in the group trained under second-order schedule of reinforcement, while cocaine abstinence had no effect in the FI 15 group who responded for cocaine but without earned drug cue presentations. In order to test if this increase in responding depended on the motivational effect of pharmacological withdrawal from cocaine, rats then received non contingent cocaine injections while being prevented from responding for the drug for a 3-day “instrumental seeking abstinence” period. The results showed that despite receiving the same amount of cocaine as during the self-administration sessions, only the rats with a history of CS-dependent cocaine seeking habits displayed the robust increase in cocaine seeking after abstinence. These results strongly suggests that the expression of maladaptive seeking habits, rather than pharmacological drug withdrawal itself, contribute to addiction by invigorating drug seeking behaviour in individuals under abstinence, indicating a core psychological component of the addiction cycle.

**Speaker 3: Sabine Vollstädt-Klein, Germany**

**Title:** Neural cue-reactivity in addiction: association with consumption patterns and treatment response  
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**Abstract**

**Background:** The primary motivation for substance use shifts during the development of addiction. Everitt and Robbins (1) posit that habitual or automated substance consumption plays a prominent role in later stages of addiction. While this hypothesis was mainly examined for stimulant and opioid addictions, its implication for the understanding of alcohol use disorders and their treatments is largely unexplored.

**Methods:** To examine the association between consumption patterns and neural cue-reactivity, we tested social drinkers and alcohol-dependent patients using a cue-reactivity task using functional Magnetic Resonance Imaging (fMRI). Additionally we assessed automated alcohol consumption (2) and obsessive-compulsive craving (3). Furthermore, we examined the association between neural cue-reactivity and treatment outcome in recently detoxified alcohol-dependent patients.

**Results:** In social drinkers, increased obsessive-compulsive craving was associated with higher activation in the dorsal and

lower activation in the ventral striatum (4). Alcohol-dependent patients, who reported uncontrolled alcohol consumption and consumption without awareness, showed reduced neural cue-reactivity in the insula, the occipital cortex, fusiform gyrus, medial frontal cortex as well as in limbic areas. In contrast, automated craving related to unawareness and loss of control, were positively associated with brain activation in the thalamus, the red nucleus and the putamen. Besides this, high neural cue-reactivity in the ventral striatum and orbitofrontal cortex of alcohol-dependent patients was associated with early relapse (5).

**Discussion:** Our results emphasize the importance of habitual and automated substance consumption in later stages of addiction. In these stages the initial hedonic effects decrease. This may be indicated by lower neural cue-reactivity in the insula and reward-related brain areas. Patients with automated or obsessive-compulsive alcohol consumption might no longer be attracted to appetitive external alcohol-associated stimuli. Instead, processing of alcohol-cues might be similar to habit-processing in these patients. The association between high neural cue-reactivity and poor treatment outcome indicates that patients with high cue-reactivity might benefit from treatment aiming to reduce responses to alcohol-associated cues. In contrast, patients with low neural cue-reactivity and automated consumption patterns might be candidates for cognitive behavioral treatment, where patients learn how to experience craving consciously and avoid the automated initiation of alcohol consumption.

**References**

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**Speaker 4: Marco Leyton, Canada**

**Title:** Changes in Drug Cue-Induced Dopamine Release in the Development of Stimulant Addictions in Humans

**Abstract**

Progressive changes to mesocorticolimbic circuit function have long been implicated in the development of substance use disorders. However, direct evidence of sequential changes in humans has been lacking. Here, we describe recent studies using functional neuroimaging and methods for manipulating