**Unveiling the alcohol-dependent alterations of local translation in the prefrontal cortex during adolescence**

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Alcohol use disorder (AUD) is a devastating relapsing disease which represents the fourth leading cause of preventable death worldwide. AUD has mainly been considered as a pathological condition in adults, but recent evidence suggests that the roots of alcohol addiction begin to grow during adolescence. Adolescence is a critical developmental period characterized by significant changes in brain architecture and behaviors. Brain maturation begins in posterior regions and progresses towards anterior higher-order regions, including the prefrontal cortex (PFC). The PFC is implicated in executive functions and its immaturity in adolescents is associated with lack of inhibitory control over behavior, increased impulsivity and desire of risk-taking. It is widely believed that the enhanced ability of the adolescent PFC to undergo experience-dependent changes is associated with heightened vulnerability to exogenous agents, including alcohol. Adolescent Alcohol Exposure (AAE) may interfere with the ongoing maturation of frontal brain circuits, leading to profound long-lasting consequences on PFC structure and function. In addition, AAE is related to serious psychological problems, comorbid psychopathology and detrimental neurocognitive consequences, and clinical studies have shown that AAE significantly increases the risk of developing psychiatric and behavioral disorders later in life, including addiction. However, the precise cellular mechanisms underlying the alcohol-induced cognitive and behavioral impairments, the molecular mechanisms underlying defects in PFC maturation, and possible sex differences are still poorly understood.

Alcohol addiction is considered as a maladaptive form of learning and memory. Indeed, alcohol is thought to “usurp” the molecular mechanisms underlying those processes, including synaptic plasticity, which depends on the local translation of mRNAs at synaptic sites. It has been shown in adult mice that excessive alcohol consumption modifies synaptic protein composition in brain regions associated with the mesocorticolimbic pathway, promoting the development and maintenance of addiction. Here we use a mouse model of voluntary adolescent binge drinking to study the alcohol-dependent structural and functional defects in the PFC as well as the behavioral consequences. We report that excessive alcohol consumption during adolescence leads to long-lasting behavioral impairments in adulthood, such as increased anxiety and alcohol intake as well as reduced cognitive performances, both in males and females.

Our preliminary results also suggest that AAE modulates the activity of local translation regulators in the PFC, such as mTORC1 and eIF2α. By using transgenic mouse lines and Ribotag profiling, we will then compare the synaptic translatome of specific neuronal populations in the PFC (i.e. glutamatergic neurons and interneurons) in order to identify candidate synaptic mRNAs whose translation levels are modified by AAE.