ALCOHOL CONSUMPTION DURING PREGNANCY INDUCES ALTERED TRANSCRIPTIONAL REGULATION IN MOTHERS AND OFFSPRING PARTIALLY COUNTERACTED BY ENVIRONMENT ENRICHMENT

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Introduction: Alcohol use by mother during pregnancy is a phenomenon ever more increasing, reaching 75% of world population. It was already shown that alcohol use during pregnancy may lead not only to mental or physical problems for the newborn, but also to an increased risk of alcohol use for the offspring. Not to be underestimated, the problems may involve not only the offspring but also the mothers themselves, possibly increasing the risk of alcohol use due to heightened stress. All these factors seem to suggest an epigenetic action, indicating a possible epigenetic regulation of genes transcription. Using an animal model of prenatal ethanol exposure, we here studied in mothers postpartum and in their offspring the effects of brain transcriptional regulation of target genes and how environmental enrichment might modulate possible alterations.

Materials and methods: The dams were given one daily intragastrically administration of 0.015ml/g of a 16.8% v/v ethanol solution or a similar volume of vehicle (gestational days 17-20). After delivery litters were randomly divided in two groups to distinguish infancy from adolescence and randomly placed to an enriched (standard cages with wheels, tubes and boxes added) or not enriched environment. Mothers were also divided in two groups and assigned to an enriched/not-enriched environment. Starting from PD14in both infants and adolescents were evaluated anxiety-like behavior and exploratory activity together with risk-taking behavior in the light-dark box and in the concentric square field test respectively. Mothers were sacrificed 21days after delivery by decapitation, offspring were sacrificed one day after the behavioral tests (PD32), brain dissected and nucleic acids extracted for genes expression studies and genes promoter evaluation of DNA methylation/hydroxymethylation.

Results: Our findings so far show selective altered expression for BDNF (brain derived neurotrophic factor) and prodynorphin genes in the VTA (ventral tegmental area) of adolescent rats prenatally exposed to alcohol and of dams exposed to alcohol during pregnancy, whereas environmental enrichment partially reverted these changes at least in adolescent offspring. Moreover, altered methylation at specific CpG sites at both gene promoters was observed consistently with the changes in genes transcription.

Discussion: These data, even if preliminary, might be promising in order to understand the protective role of environmental switch on the effects evoked by alcohol also suggesting molecular mechanisms accounting for it. Furthermore, by managing to modulate these regulatory mechanisms through a simple environmental change, new pharmacological therapies could be designed to stop the development of disorders like alcoholism during the early stages of the disease, managing to act before the disorder is completely established in the subject.