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Alcohol induced alterations in protein-protein interactions of transcription factors associated with proliferation changes in fasd and alcoholism.

Excessive alcohol consumption, during pregnancy (Fetal Alcohol Spectrum Disorders, FASD) or in adult alcoholism, induces significant developmental and neurological alterations that effect neuronal development or brain plasticity respectively. It has been shown that alcohol exposure leads to alterations in neuronal stem cell proliferation, apoptosis and cell migration. Our interest was to begin delineation of the mechanism(s) associated with altered growth patterns of neuronal stem cells associated with FASD and alcoholism. Recent studies on protein expression demonstrate alcohol induced increases in expression of cell cycle proteins that effect the G1/S phase transition and likely DNA replication. These include the E2F1 family of transcription factors that regulate transcription of S-phase specific genes at the start of DNA replication. In addition, alcohol is shown to induce overexpression of the E2F1 dimerization partner(s) DP1 family and the retinoblastoma protein (RB), both of which demonstrate importance in regulation of transcription from E2F1 consensus sites. However, the mechanism of altered E2F1 activity is poorly understood. We examined E2F1 interactions with both DP1 and RB by Co-immunoprecipitation of E2F1 and western blotting. We used cortical neuronal stems cells from a rat in cell culture with a moderate (400mg/dl for 8 hr.) alcohol exposure. We examined protein interaction changes for both DP family isoforms as well as the RB protein. Our antibody capture of E2F facilitated all 8 isoforms. We suggest that alterations in RB binding to E2F1 alter transcription of S-phase specific genes and increases transcription of S-phase specific genes in a premature fashion.