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Acupuncture reduces the expression of ΔfosB Expression after chronic exposure to Amphetamine in mice

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Changes in gene expression have been proposed to be an integral part of behavioral adaptation in humans exposed to drug of addiction. One such change is the elevation of alternative splicing of immediate early genes (FosB) to deltaFosB. The study aims to qualitatively and quantitatively validate the effect of electro acupunc-ture (EA) on both in vivo mRNA and protein expression of ΔFosB in the amphetamine sensitized live mice using gene transcript–targeted MRI (tMRI) and immunohistochemistry (ICH). A total of n = 16 mice received D-amphetamine (4 mg/kg, sc) every other day for a total seven doses (sensitization), then half of the mice received EA or mock EA treatment during the period of withdrawal. EA was applied bilaterally on 36S for 20 min (2Hz/1mA) every other day for two weeks, while the other half of the animals received puncture but no electric stimulation. On the day of the MRI, we delivered SPION-ΔFosB (T2 constrast agent targeting ΔfosB mRNA) via intracerebroventricular (icv) infusion; all animals received either amphetamine (4mg/kg, i.p.) four hours later. We acquired T2, T2* three hours later; R2* values were calculated from T2* (R2* =1/T2*X1000, 1/sec). We compared R2* values to evaluate ΔFosB mRNA expression. We also obtained brain tissue samples to compare ΔFosB protein expression by ICH. Power analysis (p = 80%, $\alpha = 0.05$) determined the numbers of mice to be treated in each group. AMPH induced hyper-activities in mice. AMPH exposed mice showed lelvation of ΔFosB mRNA levels in the medial prefrontal cortex (mPFC) and nucleus accumbens (NAc) by MRI. We found that EA treatment significantly reduced AMPH-induced ΔFosB mRNA level in the medial prefrontal cortex (mPFC) and nucleus accumbens (NAc). ICH confirms the reduction in ΔFosB protein in the NAc. The studies demonstrate that acupuncture can decrease ΔFosB both at the gene transcript and protein level in drug abuse models. We validated the MRI and histological findings for ΔFosB mRNA as a biomarker. In light of AMPH induces hyperthermia and BBB leakage, we currently focused on non-invasive delivery of SPION-ΔfosB for potential translational approach.

Biography

Dr. Ren has completed his MD and Ph.D from China Medical University and Kyushu University (Japan) and postdoctoral studies from Harvard Medical School. of Medicine. He is a instructor of MGH and Harvard Medical School. He has published more than 35 papers in reputed journals.

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