RIT1 is required for IGF1-mediated Neurogenesis

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The formation of new neurons (neurogenesis) persists in the postnatal and adult mammalian hippocampus dues to the existence of neural stem cells (NSCs). As with other somatic stem cells, adult NSCs are found within specialized niches that are organized to facilitate stem cell self- renewal and differentiation, under the control of extracellular growth factor signaling. While circulating insulin-like growth factor I (IGF1) is known to promote neurogenesis, its mechanisms of action remain incompletely characterized. Here, we identify the RIT1 GTPases as playing a central role in IGF-1R dependent hippocampal neurogenesis. Using a genetic strategy to express activated RIT1 in the dentate gyrus (DG), we observed robust stem cell proliferation and neurogenesis in the adult dentate gyrus. In vitro studies using cultured hippocampal neuronal precursor cells (HNPCs) demonstrate that IGF-1 promotes a RIT1-dependent increase in Sox2 transcription factor activity, resulting in pro-neural gene expression and increased neurogenesis. When compared to wild -type NPCs, knockdown of Rit impairs IGF-1-dependent Akt signaling, and neuronal differentiation. Collectively, these data provide new insight into mechanisms that enable IGF-1 signaling and in stem-cell maintenance, embryogenesis and development, and suggest that activation of RIT1 has broad therapeutic potential in the setting of traumatic brain injury and for the treatment of a range of neurological disorders.

An examination of corticomotor plasticity in individuals with and without chronic ankle instability

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Context: Previous literature has found decreased excitability within the corticospinal pathway of the fibularis longus(FL) muscle using Transcranial Magnetic Stimulation(TMS) assessment in patients with chronic ankle instability(CAI), indicating a potential reorganization in the supraspinal sensorimotor system. Mapping of the motor cortex may further quantify this potential reorganization by identifying shifting and/or expansion of the area of the motor cortex associated with selected muscle.

Objective: Compare differences of the corticomotor map output for the FL muscle in patients with and without CAI.

Design: Single-blinded case control study.

Setting: Research laboratory. Patient or Other Participants: Seventeen CAI patients (23.5±3.7years,179.17±7.3cm,73.19±11.5kg) and 16 Healthy-controls(HC) (21.1±2.2years,168.6±10.4cm,66.5±10.2kg) volunteered.

Interventions: Peripheral nerve stimulation was applied over the superficial peroneal nerve to determine the average of three maximum muscle response (Mmax) of the FL. The average of three motor evoked potentials(MEP) at Active Motor Threshold(AMT) intensity was recorded for each scalp site and was then normalized to Mmax.

Main Outcome Measures: Corticomotor plasticity was determined through 1) size of the corticomotor map area and 2) volume of the corticomotor map. The map area is expressed as the mean number of sites from which normalized MEPs were evoked. The map volume was calculated as the sum of normalized MEP amplitude across scalp sites. Independent T-tests were used to assess group differences and Cohen's d effect sizes along with 95% confidence intervals(CI) were calculated.

Results: CAI patients exhibited less map volume (P=0.018,CAI:8.3±3.3vs.HC:11.3±3.8,d=0.85,CI:0.12,1.54) and map area (P=0.046, CAI:12.8±6.0vs.HC:17.37±6.8, d=0.70,CI:0.02,1.38) compared to HC

Conclusions: The smaller map area and volume suggest a more concentrated area of motor cortical cells associated with the FL muscle in patients with CAI. This may explain altered movement strategies that lead to ankle re-injury.