

Subject: Neurogenetics

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Background and Aim: Introduction: Amyotrophic Lateral Sclerosis (ALS) is the most common motor neuron disease. ALS usually appears sporadic (SALS), but 1%-13% of cases are familial (FALS). Approximately 21 loci and 20 ALS-causing genes are known, and mutations in most are very rare. Based on functions of the genes, oxidative stress, axonal transport, vesicular transport, protein aggregation, and RNA metabolism are relevant to ALS pathology. Importantly, mutations in various ALS genes have also been observed in other neurodegenerative diseases including frontotemporal dementia, Alzheimer, Parkinson, hereditary spastic paraplegia, Charcot-Marie-Tooth diseases. It is thought that understanding the pathology of ALS will contribute to understandings of other neurodegenerative disorders.

Methods: Methods: We for the first time studied the genetic basis of ALS in 107 Iranian patients. Initially, linkage analysis in four families using high density SNP microarrays was performed and a candidate gene in the linked region was sequenced in the patients. Subsequently, SOD1, the hexanucleotide repeat expansion (RE) mutation in the newly discovered C9ORF72 gene, and TARDBP were screened in all patients.

Results: Results: Linkage analysis led to identification of a locus that included the well-known SOD1 gene in three of the families. Mutation screening identified the common p.Asp90Ala mutation in SOD1 in the three families. Subsequently, screening of SOD1 in all patients revealed it is causative in approximately 12% of the cohort, and in 40% of the FALS cases. The RE in C9ORF72 was observed in only two patients. For TARDBP, we observed a mutation in one FALS, but no mutations were found in SALS patients. Therefore, TARDBP mutations were found in <1% of the entire cohort.

Conclusion: Conclusions: Our finding suggests that SOD1 mutations contribute significantly to ALS among Iranians. The RE in C9ORF72 is not a major cause of ALS among Iranian patients. The contribution of the RE to ALS in patients of the Far East is also low, whereas the expansion is the most common cause of ALS in most Western populations. Finally, it appears that mutations in TARDBP are very rare and the frequency of Iranian ALS patients who harbor mutations in TARDBP is similar to frequencies reported for other populations.

Keywords: ALS, Linkage analysis, SOD1, C9ORF72, TARDBP

A New Model of Pain Sensation in Spinal Cord for Instantaneous Inhibition of Pain Stimuli

Subject: Computational Neuroscience, and Cognitive Modeling

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Background and Aim: The Gate Control Theory (GCT) proposed by Melzack can interpret different cases of acute and chronic pain according to which, the Substantia Gelatinosa of spinal cord plays a role of gating across the information transfer to brain. Mathematical models have shown the efficacy of the GCT already. However, the abrupt and instantaneous painless states in case such as sudden accident is not consistent with the GCT theory. A person may not feel any pain at all immediately after accident despite large pain stimuli (nociceptors C fibres) whereas no cognitive feedback has been established yet. In this paper, a new structure of pain system in the spinal cord has been presented and simulated.

Methods: We have proposed a modified pain system in the spinal cord which in this model, two new categories of synapses are considered in addition to previous works. activating synapses of small diameter fibres with inhibitory cells and deactivating synapses of inhibitory cells to excitatory cells. Adding these synapses, two extra terms appear in the previous mathematical model (Britton et al.). The proposed mathematical model has been simulated regarding different paradigms of pain sensation in the spinal cord.

Results: The proposed model has been mathematically simulated using three different cell population in the spinal cord: T-cells (lamina V), inhibitory and excitatory cells of Laminae I-IV. According to simulation, painless state may occur even in the presence of nociceptor signals, before any cognitive or midbrain modulating signal affecting the synapses with spinal cord cells (T-cells).

Conclusion: We have proposed a modified pain system in the spinal cord which can interpret immediate suppression of pain in the presence of small-diameter stimuli.

Keywords: instantaneous inhibition, Spinal cord, mathematical modeling

SCAP: An Initiative for Cognitive Neuroscience in Iran

Subject: Neuropsychiatry and Neuropsychology

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Background and Aim: New era of Brain research induces dreams of several applications from those of war through those for peace. Space, Criminology, (fine) Arts, and Psychiatry (abbreviated as SCAP) constitute a peaceful quartet of an initiative proposed in this paper for the very first time. Hereby, we will