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Gene Expressions Of C9orf72 And Rab7ain Human Tissues Derived From The Central Nervous System (Cns) In Amyotrophic Lateral Sclerosis (Als), Frontotemporal Dementia (Ftd) And Alzheimer's Disease (Ad)

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ABSTRACT

The non-coding hexanucleotide repeat expansions (HRE) in intron 1 of the C9ORF72 gene have been identified as the most frequent genetic cause of familial ALS and familial frontotemporal degeneration (FTD). In this report, we studied the effect of C9ORF72 HRE in C9ORF72 and RAB7A (Rab7)expressions using human postmortemtissues derived from the spinal cord of sporadic ALS and the motor cortex of other frontotemporal dementia (FTD) with or without C9ORF72 HRE and Alzheimer's disease (AD).To investigate the pathogenic effects of C9ORF72 HRE in these diseases, the gene expression approach was applied through RNA extraction, cDNA synthesis and quantitative PCR.Here, we compared the C9ORF72 isoforms a and b mRNA levels in the spinal cord from sporadic ALS cases compared to controls and there was no difference in both of C9ORF72 isoforms mRNA levels. We found that in frontal and temporal cortex, there was no difference in the C9ORF72 isoform a mRNA level in frontal and temporal cortex samples between frontotemporal (FTD) individuals in the presence or absence of C9ORF72 HRE and Alzheimer's disease (AD) compared to healthy controls. Interestingly, in frontal cortex, there was a significant upregulation in C9ORF72 isoform b mRNA expression in FTD without C9ORF72 HRE and AD cases whilst in temporal cortex, there was a significant upregulation in C9ORF72 isoform b mRNA level in FTD individuals with C9ORF72 HRE. We also observed that in Alzheimer's disease cases, Rab7 mRNA was significantly downregulated in frontal cortex whilst in temporal cortex Rab7 mRNA was significantly upregulated. C9ORF72 expression have been well established in ALS but less so in frontotemporal dementia and Alzheimer's disease. Further, the C9ORF72 HRE expressions have been investigated mainly in cerebellum and cervical spinal cord whilst our study focusing in lumbar spinal cord and motor cortex. Our results suggested that different C9ORF72 isoforms may play different roles in the pathogenesis of ALS and Alzheimer's disease (AD).