Neurosciences & Brain Imaging

Open Access Commentary

HuD Levels Were Found to be Significantly Lower in a Neurodegenerative Disease Characterized by Progressive Loss of Memory and Cognitive Function

Shirin Hosseini*

Department of Cellular Neurobiology, Zoological Institute, Braunschweig, Germany

DESCRIPTION

The involvement of HuD in learning and memory formation paved the way for research into its impairment in Alzheimer's disease, which was associated with an increase in Amyloid (A) aggregates in postmortem hippocampal tissues of AD patients. They found higher levels of the 42-residue pathogenic peptide A (A1-42) compared to the shorter physiological form (A1-40). This could be partially due to impaired ADAM10 mRNA stabilization due to lower HuD levels. ADAM10 encodes one of the most important secretes involved in the cleavage of APP to form soluble and non-pathogenic APP. The presence of an ARE region in the ADAM10 3'UTR suggested that HuD may be involved in post-transcriptional regulation. ADAM10 mRNA is a target of HuD, according to immunoprecipitation analysis. In addition, protein kinase C can promote the binding of HuD to the ADAM10 ARE (PKC). PKC, which is reduced in postmortem Alzheimer's brain tissues, is directly involved in the activation of ADAM10-secretase, leading to increased production of soluble APP at the expense of A fragments. In addition, PKC promotes the export of HuD from the nucleus as well as its cytoplasmic and cytoskeletal localization, which has important implications for the up-regulation of HuD targets. In contrast to an earlier study that found decreased levels of HuD in the hippocampus, other authors later reported increased levels of HuD in postmortem samples from Alzheimer's patients. Increased levels of HuD were found in the superior temporal gyrus and frontal cortex, possibly due to increased thyroid activation. Regarding the underlying pathological mechanisms, the researchers investigated the relationship between the HuD, secretase BACE1 and the long non-coding RNA (lncRNA) BACE1AS. B-secretase enzymes are essential for A production and may be therapeutic targets for the treatment of AD. Due to its sequence complementarity to BACE1 mRNA, BACE1AS acts as an enhancer of BACE1 expression. Binding of HuD to BACE1AS increases its levels, thereby indirectly promoting BACE1 stabilization and translation. Consequently, increased levels of HuD in AD brains were mirrored by increased levels of BACE1AS and BACE1 mRNA. In addition, HuD overexpressing mice had higher levels of A, APP, BACE1, and BACE1AS in the hippocampus, cortex, and cerebellum. These findings add to the evidence that HuD plays a role in controlling APP cleavage during AD progression. Transcript levels of another HuD target, neuroserpin, are elevated in Alzheimer's disease brains. Neuroserpin is a tissue plasminogen activator inhibitor. Inhibition of tPA significantly reduces the activity of plasmin protease, which regulates and degrades amyloid plaques to maintain brain homeostasis. Thus, increased HuD activity in the brains of Alzheimer's patients may lead to an abnormal rise in neuroserpin protein levels. In a recent study, the effects of loss and gain of HuD function were investigated in an iPSC-based model of AD. Overexpression of HuD attenuated the AD associated phenotype by increasing the expression of specific splice isoforms of APP and decreasing the A1-42/ A1-40 ratio. The authors found a significant increase in the APP695 splicing isoform, which is down regulated in Alzheimer's disease, at the expense of the APP751 and APP770 isoforms. In addition, cortical neurons overexpressing HuD had lower levels of A1-42 than the amyloid-protecting A1-40 counterpart. HuD regulates several cellular pathways according to transcriptomic and proteomic analysis of overexpressing neurons. Of particular note is exogenesis

Received:	01-March-2023	**Manuscript No:**	IPNBI-22-15258
Editor assigned:	03-March-2023	**PreQC No:**	IPNBI-22-15258 (PQ)
Reviewed:	17-March-2023	**QC No:**	IPNBI-22-15258
Revised:	22-March-2023	**Manuscript No:**	IPNBI-22-15258 (R)
Published:	29-March-2023	**DOI:**	10.36648/ipnbi.7.1.001

Corresponding author: Shirin Hosseini, Department of Cellular Neurobiology, Zoological Institute, Braunschweig, Germany; E-mail: s.hosseini@tu-braunschweig.de

Citation: Hosseini S (2023) HuD Levels Were Found to be Significantly Lower in a Neurodegenerative Disease Characterized by Progressive Loss of Memory and Cognitive Function. J Neurosci Brain Imag. 7:001.

signaling, which involves axonal guidance and regulation of synaptogenesis. In addition, abnormal DNA damage, cell cycle re-entry and mitochondrial pathways were impaired under HuD knock-down and AD conditions.