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Barbash, S, Soreq H. 2012.

Abstract:

End-stage Alzheimer's disease (AD) involves drastic modifications in neuronal molecular and cellular processes, but little is known about the dynamics of these modifications during disease initiation and progression. Here, we report meta-analysis of 100 publicly available Microarray datasets using threshold-independent analysis. We found that different patients react to AD progression by variable single transcript alterations which however lead to similar changes in functional gene groups. Stratification by patients' cognitive deterioration presented hippocampal-specific mRNA alterations which involved progressively changed gene categories and indicate changes in epigenetic state and microRNA profiles. In addition, datasets from laser-captured neurofibrillary tangles-free hippocampal neurons and transcript classification by cell types identified many of these changes in neurons. Intriguingly, we discovered that early-onset decline in alternative splicing, protein folding and transport transcripts occur concurrently with decreases in synaptic transmission, whereas at later stages these changes progressed into enhanced oxidative stress and inflammation. Our findings open new venues for identifying novel targets for intervention with AD progression.

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