New analysis of gene regulation may help in detecting the early events that occur in Alzheimer’s disease.

**Threshold-independent meta-analysis of Alzheimer’s disease transcriptomes shows progressive changes in hippocampal functions, epigenetics and microRNA regulation**

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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. We analyzed 100 publicly available Microarray datasets using a method that detects continuous changes in gene groups and found that different patients react to AD progression by variable single transcript alterations that however lead to similar changes in functional gene groups. Several distinct molecular levels have shown a progressive change with disease progression. This enabled us to point at the molecular events that are altered in the beginning of the disease and distinguish them from those that are altered late. Detecting the early events that occur in AD is of significant importance to early diagnosis and effectiveness of treatment of the disease.
Figure: Stratifying patients by their cognitive deterioration dictates gradual changes in functional and cell specific gene groups
(a) Number of changed biological processes for different significance thresholds in hippocampal RNA extracted using whole tissue dissection (left side, plain) from incipient, moderate and severe AD patients, and from hippocampal neurons extracted from non-demented controls and severe AD patients using Laser Capture Microscopy (right side, dotted). (b) Three example biological processes showing gradually increased change along disease progression. (c) Mean and Standard Error of the Mean of log2 values of fold change between each of the three patient groups and that of control, for cell type-specific transcripts. Tissues were as in (a). One or two asterisks indicate post-hoc Tukey test (after ANOVA) P-values of P<0.05 or P<0.01, respectively. # symbols represent crossing the threshold for detection. (d) Specific neuronal sub-cellular compartments are colored by the shift (KS P-value) they undergo in each of the three disease stages. Tissues were as in (a).

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