The molecular neuropathology of amyotrophic lateral sclerosis: protocol for systematic review and meta-analysis

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ABSTRACT

A significant body of neuropathological research examining the molecular heterogeneity across ALS phenotypes exists and an up to date formal review of these studies is now required. Through conducting a systematic review and meta-analysis of the existing ALS human neuropathology literature we aim to outline the current pathological molecular profile of ALS.

A search will be conducted without language or publication date restrictions across three databases; 1. PubMed, 2. MEDLINE, 3. EMBASE. Studies comparing human ALS or ALS-FTD brain and/or spinal cord samples to controls will be selected. The primary outcome measure will be molecular species quantification followed by an assessment of study heterogeneity as a secondary outcome measure. The Systematic Review Facility online screening tool (app.syrf.org.uk) will be used by two independent authors to screen the titles and abstracts based on predefined criteria. Data will be extracted by one reviewer and an assessment of study quality will be conducted against the CAMARADES' study quality checklist (adapted). Additional study quality assessment and data extraction will be carried out by an independent reviewer for 10% of the selected studies. Where appropriate, standardised mean differences (SMD) will be used to describe outcome measures to enable inter-study comparison.

Advances in transcriptional profiling technology have generated a variety of high throughput platforms, ranging from microarray gene chips with a specific range of oligonucleotide probes through to sequencing at a whole genome level. Human pathological studies to date have revolutionised our understanding of the ALS disease aetiology. Here we aim to review the outcomes of these studies across the field as a whole and to consider the impact of methodological heterogeneity on the results presented.

ATTACHMENTS

neuropathology_systematic_review.pdf

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KEYWORDS

ALS, FTD, neuropathology, systematic review, meta-analysis

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