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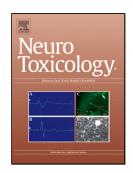
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### ACCEPTED MANUSCRIPT

# Identification of risk factors associated with onset and progression of amyotrophic lateral sclerosis using systematic review and meta-analysis

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#### **ABSTRACT**

Although amyotrophic lateral sclerosis (ALS) was identified as a neurological condition 150 years ago, risk factors related to the onset and progression of ALS remain largely unknown. Monogenic mutations in over 30 genes are associated with about 10% of ALS cases. The age at onset of ALS and disease types have been found to influence ALS progression. The present study was designed to identify additional putative risk factors associated with the onset and progression of ALS using systematic review and meta-analysis of observational studies. Risk factors that may be associated with ALS include: 1) genetic mutations, including the intermediate CAG repeat expansion in *ATXN2*; 2) previous exposure to heavy metals such as lead and mercury; 3) previous exposure to organic chemicals, such as pesticides and solvents; 4) history of electric shock; 5) history of physical trauma/injury (including head

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