INPLASY PROTOCOL

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Review Stage at time of this submission: **Piloting of the study selection process.**

Conflicts of interest:
The authors report no competing interests.

Cerebrospinal fluid and blood levels of neurofilament light chain in Parkinson's disease: a protocol for systematic review and meta-analysis

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Review question / Objective: **Whether patients with PD exhibit alterations of cerebrospinal fluid and blood levels of neurofilament light chain relative to healthy controls.**
Condition being studied: **Parkinson's disease (PD) is a common neurodegenerative disorder. Biomarkers for the early diagnosis, disease monitoring, and prognostic evaluation of PD are under investigation. Neurofilament light chain (NfL) is a neuronal cytoskeletal protein that plays pivotal roles in axonal and dendritic branching and growth. Increased NfL levels in the cerebrospinal fluid (CSF) and blood are increasingly recognized as a promising biomarker of axonal damage of the central nervous system in multiple neurological disorders, including PD. However, the results are not consistent across studies in PD. Therefore, performing a meta-analysis could increase statistical power and provide quantitative evidence of CSF and blood NfL levels in patients with PD.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 07 June 2020 and was last updated on 07 June 2020 (registration number INPLASY202060025).

INTRODUCTION

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METHODS

Participant or population: The participants were idiopathic PD patients according to the United Kingdom Parkinson Disease Society Brain Bank clinical diagnostic criteria or Movement Disorder Society Clinical Diagnostic Criteria for Parkinson's disease.

Intervention: Evaluation of CSF and blood NfL levels.

Comparator: Healthy controls.

Study designs to be included: Case-controlled studies.

Eligibility criteria: Inclusion criteria: (1) original and peer-reviewed article; (2) established diagnostic criteria for idiopathic PD; (3) case-control studies with the evaluation of NfL differences in the CSF or blood between idiopathic PD patients and healthy controls Exclusion criteria: (1) studies without healthy controls; (2) studies with missing data to estimate the mean levels and standard deviation of CSF or blood NfL; (3) non-human studies; 4) the patient sample in one study was overlapped with those with a larger sample size in another study.

Information sources: The online databases PubMed, EMBASE, and Web of Science were systematically searched from the earliest available date to June 7th, 2020. Additional eligible studies will be obtained through cross-checking cited references. No language or publication period restriction was set.

Main outcome(s): Differences in cerebrospinal fluid and blood levels of neurofilament light chain between PD patients and controls.

Additional outcome(s): Contributions of demographic, clinical, and methodological factors to heterogeneity across studies.

Data management: The author's surname, year of publication, age, sex (male percentage), PD severity (UPDRS- III score), disease duration (years), H&Y stage, LEDD (mg/day), MMSE score, the mean and standard deviation of CSF NfL and blood NfL in PD patients and healthy controls.

Quality assessment / Risk of bias analysis: The methodological quality of studies was assessed according to the New Castle-Ottawa scale (NOS).

Strategy of data synthesis: Stata 12.0 software will be used to perform the final data combination and meta-analysis. We also conducted several complementary analyses, such as subgroup analyses, meta-regressions, publication bias, and sensitivity analyses to assess the robustness of the results.

Subgroup analysis: Subgroup meta-analyses were conducted in PD patients with dementia and those patients without dementia regarding differences in cerebrospinal fluid and blood levels of neurofilament light chain.

Sensibility analysis: Sensitivity analysis will be conducted to assess the robustness of the results.

Language: No limits.

Country(ies) involved: China.

Keywords: Parkinson's disease; neurofilament light chain; meta-analysis; cerebrospinal fluid; blood.

Contributions of each author:
Author 1 - HongZhou Wang - Author 1 drafted the manuscript.

Author 2 - WanHua Wang - The author provided statistical expertise.
Author 3 - HaiCun Shi - The author contributed to the development of the selection criteria and the risk of the bias assessment strategy.
Author 4 - LiJian Han - The author read, provided feedback, and approved the final manuscript.
Author 5 - PingLei Pan - The author read, provided feedback, and approved the final manuscript.