INPLASY

HLA and microRNAs as key orchestrators of mild cognitive impairment and Alzheimer's disease

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ADMINISTRATIVE INFORMATION

Support - No external funding.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 July 2024 and was last updated on 11 July 2024.

INTRODUCTION

Review question / Objective We aimed to analyze the discriminative value of HLA variants and miRNAs in MCI, AD and controls; to evaluate the protective or causative effect of HLA in cognitive decline; to establish the role of miRNAs as biomarkers for the early detection of AD; and to find a possible link between miRNAs and HLA.

Rationale To establish the involvement of HLA and microRNAs in mild cognitive impairment and Alzheimer Disease.

Condition being studied The concept of MCI or pre-dementia stage is highly significant in the field of aging, since MCI is regarded as a borderline condition between normal aging and very early dementia. Individuals with MCI have a high risk of developing dementia and higher mortality rates compared to cognitively normal people . Depending on the cause, patients with MCI remain stable, return to normal, do not develop AD, or develop AD. Due to the scarcity of disease-modifying treatments for dementia, the importance of diagnosing and initiating early treatment during the MCI stage has been widely recognized as a key strategy for the effective management of this condition, early intervention offering the potential for improved long-term outcomes.

METHODS

Search strategy For the systematic review, PubMed and Web of Science were searched for case control and cohort studies published in English using the following keywords: Alzheimer's disease, mild cognitive impairment and HLA, diagnostic, biomarker, haplotype.

Participant or population Patients with Mild cognitive impairment, Alzheimer" s disease and normal controls.

Intervention The selected studies included human patients with AD validated by magnetic resonance

imaging (MRI) or the Mini Mental State Examination (MMSE).

Comparator Mini Mental State Examination (MMSE) and magnetic resonance imaging (MRI).

Study designs to be included For the systematic review, PubMed and Web of Science were searched for casecontrol and cohort studies published in English between January 2015 and June 2024,using the following keywords: Alzheimer's disease, mild cognitive impairment and HLA,diagnostic, biomarker, haplotype. Abstracts, reviews and studies with incomplete datawere excluded.

Eligibility criteria The reference list of relevant systematic reviews was examined for relevant studies and possible data sources. Reviews and abstracts were excluded. The selected articles included cohort and case control studies of human participants with AD, diagnosed with validated neuropsychological instruments (e.g., Mini Mental State Examination). In these included studies, AD patients were tested for the expression of HLA avriants.

Information sources International databases, using the above mentioned search terms, all relevant citations were identified by two independent researchers. In the next phase, based on the assumed inclusion criteria, the full text of relevant studies was reviewed. The data were extracted from studies that met all eligibility criteria and entered into a database.

Main outcome(s) For the systematic review, we identified 184 potentially relevant studies based on an electronic search in PubMed and Web of Science. After thoroughly analyzing all these studies, we selected 32 studies that presented the link between cognitive ability and HLA class I and II.

Data management The reference list of relevant systematic reviews was examined for relevant studies and possible data sources. Reviews and abstracts were excluded. The selected articles included cohort and case control studies of human participants with AD, diagnosed with validated neuropsychological instruments (e.g., Mini Mental State Examination).

Quality assessment / Risk of bias analysis Using the above mentioned search terms, all relevant citations were identified by two independent researchers. In the next phase, based on the assumed inclusion criteria, the full text of relevant studies was reviewed. The data were extracted from studies that met all eligibility criteria and entered into a database. All disagreements were resolved by discussion between reviewers.

Strategy of data synthesis Using the above mentioned search terms, all relevant citations were identified by two independent researchers. In the next phase, based on the assumed inclusion criteria, the full text of relevant studies was reviewed. The data were extracted from studies that met all eligibility criteria and entered into a database. All disagreements were resolved by discussion between reviewers.

Subgroup analysis Heterogeneity analysis proved a significant heterogeneity of the results.

Sensitivity analysis Another conclusion based on these results is that it is difficult to reliably identify at a meta-analytical level the discriminative value of each HLA as long as there are very few HLA that are replicated from one study to another.

Language restriction English.

Country(ies) involved Romania.

Keywords Alzheimer's disease; mild cognitive impairment; human leukocyte antigens; microRNAs, biomarkers, neuroinflammation.

Contributions of each author

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