



Review Article

Lifestyle and neurodegeneration in midlife as expressed on functional magnetic resonance imaging: A systematic review

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Abstract

Introduction: Lifestyle factors may influence brain health in midlife. Functional magnetic resonance imaging is a widely used tool to investigate early changes in brain health, including neurodegeneration. In this systematic review, we evaluate the relationship between lifestyle factors and neurodegeneration in midlife, as expressed using functional magnetic resonance imaging.

Methods: We searched MEDLINE, EMBASE, and PsycINFO combining subject headings and free text terms adapted for each database. Articles were screened, and their quality was assessed independently by two reviewers before final inclusion in the review.

Results: We screened 4116 studies and included 29 in the review. Seven lifestyle factors, such as alcohol, cognitive training, excessive internet use, fasting, physical training, smoking, and substance misuse, were identified in this review.

Discussion: Cognitive and physical trainings appear to be associated with a neuroprotective effect, whereas alcohol misuse, smoking, and substance misuse appear to be associated with neurodegeneration. Further research is required into the effects of excessive internet use and fasting.

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Keywords:

Neurodegeneration; Neuroprotection; Magnetic resonance imaging; Life Style; Middle aged

1. Background

There is increasing recognition that neurodegenerative diseases, which manifest clinically as dementia in later life, have their origins in midlife, or even earlier [1]. Recent research on cognitive, neuroimaging, and biological markers suggest that changes in several parameters may well precede overt clinical symptoms by not just many years, but decades [2]. Functional magnetic resonance imaging (fMRI) offers considerable promise as a marker for neurodegenerative disease. It could also be of value in monitoring disease progres-

sion and response to interventions [3] such as lifestyle modification. In midlife, lifestyle modification could potentially alter neurodegenerative disease progression and thereby reduce an individual's risk of dementia in later life [4]. If this were the case, it is critical to identify which potentially modifiable lifestyle factors are associated with neurodegeneration in midlife. Therefore, in the absence of any previous systematic reviews, we evaluate the relationship between lifestyle factors and neurodegeneration in midlife as expressed on fMRI in the published literature.

2. Methods**2.1. Identification of studies**

MEDLINE, EMBASE, and PsycINFO were searched via the OVID platform on 5th December 2016. MEDLINE was

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searched from 1946 to November 2016, EMBASE from 1980 to November 2016, PsycINFO from 1806 to November 2016. There were no limits on language or publication dates. A specific search was constructed for each database using subject headings and free text terms, and these can be found in the [Supplementary Material](#). The search terms covered the areas of neuroimaging, lifestyle, and regional changes in cerebral metabolism or blood flow, blood volume, or oxygenation.

The systematic review aimed to include all published studies that assessed the relationship between lifestyle factors and neurodegeneration, neuroprotection, or both as expressed on fMRI in midlife. A study was defined as having assessed individuals in midlife if it included individuals aged 40–59 years or if two standard deviations around the mean fell within the 40–59 years age range. Neurodegeneration was defined as any pathological condition primarily affecting neurons [5]. Neuroprotection was considered to be an effect that may result in salvage, recovery, or regeneration of the nervous system, its cells, structure, and function [6]. The exposure in the review was lifestyle factors, as defined by the World Health Organization: “Lifestyle is a way of living based on identifiable patterns of behavior, which are determined by the interplay between an individual’s personal characteristics, social interactions, and socio-economic and environmental living conditions” [7]. The outcome in the systematic review was the numerical outcome measures derived from the fMRI scan. fMRI is a brain imaging technique to capture regional changes in cerebral metabolism or in blood flow, volume, or oxygenation in response to task activation or during rest [8]. The systematic review aimed to include studies using both resting-state and task-based fMRI experimental protocols and studies assessing the general population and those conducted in a general medical setting. There were no limits by language or publication date.

2.2. Eligibility

The inclusion/exclusion criteria for the systematic were as follows:

Inclusion criteria

- i. Original human research study.
- ii. Population includes a lifestyle factor in midlife.
- iii. Study includes an fMRI outcome in midlife.

Exclusion criteria

- i. Not an original human research study.
- ii. Study population has a diagnosis of dementia either in general or based on specific subtypes classified using standard diagnostic criteria, for example, the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer’s Disease and Related Disorders Association [9].
- iii. Study population does not include a lifestyle factor in midlife.

- iv. Study population does not include individuals in midlife.
- v. The aim of the study is not to look at the effect of a lifestyle factor on fMRI outcome.
- vi. fMRI outcome is not a proxy for neurodegeneration or neuroprotection.

2.3. Study selection and data collection

The titles and abstracts of all articles identified by the search were screened independently by two reviewers against the inclusion and exclusion criteria with any disagreements in the final lists of included studies resolved by discussion. Potentially relevant articles were then retrieved and examined against the inclusion and exclusion criteria. Differences between reviewers’ selections were again resolved by discussion. Data were extracted from included articles by one reviewer on the number of study participants, mean age, standard deviation and age range of participants, study methodology and design, and the key findings from the study related to this systematic review.

2.4. Quality of evidence

The quality of studies was assessed using a modified version of the Effective Public Health Practice Project Quality Assessment Tool [10] tailored to the literature being assessed in this review. This tool has been judged suitable for use in a systematic review [11] and forms a global quality rating for a paper based on six assessment criteria: selection bias, study design, confounders, blinding, data collection method, and withdrawals and dropouts.

2.5. Protocol and registration

The systematic review protocol was registered on the PROSPERO International Prospective Register of Systematic Reviews, registration number CRD42016045237 (<https://www.crd.york.ac.uk/PROSPERO/>).

3. Results

The PRISMA diagram (Fig. 1) for the screening and selection of studies shows that 4116 records were identified through database searches. Following de-duplication and title and abstract screening, 255 full-text articles were assessed for eligibility. After excluding 226 articles for the reasons outlined in Fig. 1, a total of 29 articles were included in the systematic review. Table 1 gives a summary overview of the 29 articles included in the systematic review, arranged by lifestyle factors. Table 2 then summarizes the key findings from the 29 individual articles.

3.1. Alcohol

Of the six studies looking at the effect of alcohol as expressed on fMRI, three used a task-based fMRI protocol, and three studies used a resting-state protocol. Of the

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