Exploring the Relationship Between Social Cognition Deficits and Neurodegenerative Dementia: Protocol for a Systematic Review

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Protocol

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Abstract

Background: Due to demographic evolution and the progressive aging of the population, the incidence of dementia has increased worldwide. Many questions about this syndrome have not been resolved yet, such as the relationship between dementia and deficits on social cognition.Therefore, the present review aims to explore this relationship and to establish the possible differential patterns of social cognition deficits in diverse types of neurodegenerative dementias.

Methods: The literature searchwas conducted in several electronic databases, including MEDLINE database via Pubmed, Cochrane Library, Lilacs, Web of Science (WoS) and PsycINFO.In order to avoid possible bias during the data extraction, all citations, abstracts information and full-text articles will be independently screen by two reviewers. Themethodological quality of thestudies will be appraised using the Joanna Briggs Institute Critical Evaluation Checklists. All studies published in English or Spanish between October 2009 and October 2019 will be taken into account.

Discussion: This systematic review will summarize the evidence provided during the last 10 years regarding the relationship between neurodegenerative dementia and social cognition deficits. This could provide a useful reference to clinicians, since properly defining social cognition profile of each type of neurodegenerative dementia would improve detection and diagnosis, which would undoubtedly guarantee better interventions.

Systematic review registration: PROSPERO, ID: 152562

1. Background

Dementia is a clinical syndrome characterized by cognitive deterioration that causes a decline in intellectual functions(previously acquired), with preservation of the vigilance level, and that also significantly interferes in the performance of activities of daily living. All epidemiological studies have confirmed that age is the main risk factor for the development of dementia, so demographic evolution and the progressive aging of the population have led to an increase in cases(1, 2).According to the World Health Organization, there are around 50 million people with dementia and every year there are 10 million new cases (3).

Social Cognition (SC), in general terms, refers to the set of mental operations that underlie social interactions (4, 5) and necessarily involves processes related to the interpretation and development of responses to the intentions and behaviours of others (6). The MATRICS project, developed under the sponsorship of the National Institute of Mental Health, reached a consensus that SC includes several areas of interest: theory of mind, emotional processing, social perception, and attribution bias (7).

There is an extensive literature on SC deficits among psychiatric illness such as schizophrenia (8) or bipolar disorder (9), as well as on neurodevelopmental conditions such as autism spectrum disorders (10). There are studies that have also detected these deficits in patients with dementia, mainly in

frontotemporal dementia (FTD), specifically in its behavioural variant (bvFTD) (11, 12).However, these studies are less frequentlyfound in other types of neurodegenerative dementias (ND).

Although the progressive increase in dementias prevalence is clear, many questions have not been answered yet, such as the importance of SC deficits on thesyndrome onset. To date, different reviews have been published in which the relationships between SC and ND have been studied. Christidi et al. (13) pointed out that some deficits in SC may represent central diagnostic criteria in bvFTD, while in others, such as Alzheimer-type dementia (AD), these deficits may arise during the course of the disease as critical aspects. Strikwerda-Brown et al. (14) limited their review to the relationship between theory of mind and neurodegenerative disorders, but did not consider other aspects of SC. These and other published reviews (13-15)about the relationships between SC and neurodegenerative disorders were not performed systematically and did not describe the methodology used. Thus, we consider that the present work, in addition to fill in the gaps of the previous reviews, will provide strength to the results obtained, since it is a systematic review. In our opinion, enriching knowledge about the relationship between SC and ND could benefit clinical practice. Establishing the correct relationship between SC components and the different types of ND could help physicians to perform a more accurate assessment to reach the diagnosis.

Therefore, all the information available in articles published in the last 10 years related to SC and ND will be compiled and organized, with the main objective to explore if there is a relationship between the two. A second objective will be to establish possible relationships between the different SC components and the different ND.

2. Methods

This protocol is being reported in accordance with the reporting guidance provided in the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) 2015 statement(16), and the checklist can be found in the additional **File 1**. This protocol will guide the review. If there is any modification of the protocol during the review, it will be informed and reasoned in the final manuscript. The review has been registered in the International Prospective Registry of Systematic Reviews (PROSPERO) with registration number 152562 (awaiting for publication).

2.1. Eligibility criteria

All studies that meet the following inclusion criteria will be included in the review: a) studies with adult population that present some type of ND in which dementia is the main symptom (Alzheimer's disease, frontotemporal dementia, body Lewydementia); b) studies that evaluate SC in any of its dimensions (theory of mind, emotional processing, social perception or attribution bias); c) observational studies, including cross-sectional, case-control and cohort studies; d) studies published in English or Spanish; and e) studies published in the last 10 years (October 2009-October 2019).

It should be noted that we will include all FTD types. This coversbvFTD and primary progressive aphasia (PPA), in its three variants: (i) non-fluent variant PPA (nfvPPA); (ii) semantic variant PPA (svPPA) (also called dementia semantic); and (iii) logopenic variant PPA (lvPPA)(17).

The following studies will be excluded from the review: a) those studies on populations with degenerative disorders in which dementia syndrome is not the main manifestation of the disorder (e.g.,dementia in Parkinson's disease, dementia in Huntington's disease, dementia in Wilson's disease ...); b) review or meta-analysis articles; c) single case studies, comments, books, conference papers, letters, editorials, theses and all those not peer-reviewed (grey literature).

2.2. Search strategies and data source.

To establish the search strategy necessary to identify all relevant articles, an expert librarian from the Marqués de Valdecilla University Hospital (Santander, Spain) was consulted. The systematic search was carried out in the following databases: MEDLINE database via Pubmed, Cochrane Library, Lilacs, Web of Science (WoS) and PsycINFO. Appropriate search terms were used, that is, MeSH terms and when this was not possible.Free text was considered using keywords related to dementia and SC. The detailed search strategy can be found in Additional **File 2**. A manual search of reference lists of articles identified as eligible will be performed. All studies published in English or Spanish between October 2009 and October 2019 will be taken into account.

2.3. Study Selection

All the references found in the different databases that responded to the search criteria were imported into the EndNote (software) program (Clarivate Analytics, Philadelphia, USA), which eliminated duplicate citations. The work team made up of four reviewers (ESS, NMG, MSR and GAF) will independently evaluate each of the selected titles and abstracts according to the eligibility criteria. The full texts of potentially relevant articles will be retrieved and revised again. Each study will be reviewed by at least two reviewers. The final decision regarding the inclusion of studies will be made based on a thorough review of the full articles by two reviewers. In case of discrepancies, these will be evaluated by the entire team, as well as by a senior researcher (RAA). The result of the selection process will be reported in a PRISMA flow diagram (18).

2.4. Assessment of risk of bias of primary studies

Reviewers will perform the risk of bias assessment of each selected article. Each study will be evaluated by at least two reviewers independently and discrepancies will be resolved by the full review team. The evaluation process will be carried out using the Joanna Briggs Institute (JBI) Critical Evaluation Checklists(19). Because the type and propensity for bias of the different studies varies depending on the

design of each one, the following checklists will be used: a) JBI critical appraisal checklist for analytical cross-sectional studies; b) JBI critical appraisal checklist for case-control studies; and c) JBI critical appraisal checklist for cohort studies. A summary of the assessment of risk of bias of the studies will be provided through tables.

2.5. Data extraction

A registry has been designed for data extraction among all members of the review team. The following information will be extracted from all included studies: author, year of publication, location, N, population (type of ND), type of study, mean age, domain of SC evaluated, summary of results, follow-up period (if corresponds), and data from the healthy control group (if applicable). The data extraction task will be carried out among the team members and each article will be reviewed by at least two reviewers independently. If necessary, the authors of the articles will be contacted to collect data that are not available in the manuscript.

During the data extraction process, the consensus of the entire team will also be used in case of discrepancies before reaching a final decision.

2.6. Data synthesis

A narrative synthesis of all the studies included in the review will be carried out and the relevant data from the studies will be presented in a table. The data will be grouped according to the different types and subtypes of ND, and within these groups we will try to synthesize the results attending to the different domains of the SC, as far as possible.

3. Discussion

This systematic review will summarize the evidence provided during the last 10 years regarding the relationship between ND andSC deficits. Paying special attention to the different profiles in what refers to SC, of the different types of ND.

Recently, the increase of aging population has turned into a growing concern for those responsible for health. The study of dementias has become a new challenge due to the increase in life expectancy. Reaching a good comprehension implies knowing and understanding all the factors associated with these syndromes, among which are deficits on SC.

In the last years, studies regarding the association between ND and SC areas have proliferated. Some studies have pointed out that alterations in SC represent the earliest and core symptoms of bvFTD(20), so the detection of deficits in SC could signal the diagnosis of this syndrome instead of other dementias. In fact, the integration of SC tests into clinical practice in cases of suspected bvFTD has been suggested to improve diagnosis (21, 22).

Recent reviews have also focused on the study of the relationship between specific areas of SC and some ND. In the review by Fittipaldi et al.(23), the relationship between primary progressive aphasia (PPA), FTD subtype, and deficits in areas and sub-areas of SC such as the theory of mind, emotion recognition or empathy cannot be precisely assert for PPA as a whole; instead, specific links are recognized for each variant. On the other hand, Torres Mendonça De MeloFádel et al.(24),studied the relationship between emotional recognition and Alzheimer's disease, without a consistent conclusion.

The present review could provide a useful reference to clinicians, since properly defining the SC profile of each type of ND would improve detection and diagnosis, which would undoubtedly guarantee better interventions.

Strengths and limitations: To the best of our knowledge,this is the first study that will address the relationship between the different components ofSC (theory of mind, emotional processing, social perception and attribution of bias) and the different types of ND (Alzheimer's disease, frontotemporal dementia and Lewy body dementia) and will integrate the results, so that the differences among the types of ND in terms of SC can be outlined. However, we are aware that we will find issues that will pose limitations in our review. Mainly, we refer to the great heterogeneity that we envisage to discover relative to the denominations and definitions of the SC areas in the different studies, as well as we expect to find a wide range of tools to evaluate these areas.

Abbreviations

WoS: Web of Science; SC:Social Cognition; FTD:Frontotemporal Dementia; bvFTD: Frontotemporal Dementiabehavioural variant; ND: Neurodegenerative Dementia; AD:Alzheimer-type dementia; PRISMA-P:Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols; PROSPERO:Prospective Registry of Systematic Reviews; PPA:Primary Progressive Aphasia;nfvPPA:non-fluent variant PPA; svPPA: semantic variant PPA; lvPPA:logopenic variant PPA; JBI: Joanna Briggs Institute.

Declarations

Acknowledgements

Not applicable.

Authors’ contributions

ESS, DRG and RAA conceived and designed the study.

ESS and DRG developed the search strategy.

ESS, NMG, MSR and GAFreview and select candidate studies.

ESS prepared the initial draft of the protocol.

RAA revised the protocol.

All authors read and approved the final protocol.

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Availability of data and materials

Both systematic search strategy and the checklist can be found in the additional files 1 and 2

Ethics approval and consent to participate

Due to the character of this study, ethics approval and informed consent are not applicable.

Consent for publication

The final manuscript has been seen and approved by all authors.

Competing interests

The authors declare that they have no competing interests.

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