



SYSTEMATIC REVIEW

Is Semantic Memory a clue to distinguish Alzheimer's disease from late-life depression ?

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Introduction

Late life depression (LLD) and Alzheimer's disease (AD) are difficult to distinguish

- ✓ They share similar cognitive impairment¹ in memory, executive functions and attention².
- ✓ The depressive symptoms (**DS**) are present in 20-30% of early AD.
- ✓ LLD can be part of prodrome or risk factor of AD.

Question 1:
Does the presence of DS predict
→ conversion to AD
→ incidence of AD

AD has specific deficit of Semantic Memory

Present 5 years before the clinical diagnosis, it is linked to early atrophy of hippocampal complex in AD³.
This deficit is not supposed to be present in LLD.

Question 2.1 :
Is there an association between DS and performances at semantic tasks ?

Question 2.2. :
Is Semantic Memory differently affected by LLD and AD or mild cognitive impairment (MCI)?

Method

PRISMA guidelines for systematic review⁴ - Quality Assessment for quantitative studies⁵.

KEY WORDS IN MOTOR RESEARCH

Motor research : Proquest, PubMed, Science Direct
Key words : Depression / MCI / Alzheimer / Semantic Memory / Test / Prodrome / Prodromal / Longitudinal / Aging / Ageing / Late-life / Geriatrics

N= 1355

SCREENING

Exclusion of 1278 articles that were not relevant based on title and abstract

N= 77

FULL ARTICLE ASSESSMENT

Exclusion of :
Review or meta-analysis (N=3);
Validation of assessment tools (N=6);
Neurophysiological evidences-based (N=12);
Population under 50 years old (N=4);
Did not apply the key questions (N=11).

N= 41

ANALYSE OF DATA IN 41 REMAINING ARTICLES

Authors – year of publication – independent variables – dependent variables – length and rhythm of follow-up – diagnosis criteria for LLD, MCI, AD – assessment tools for DS, semantic performances – statistical method – results – p value.

Results

Question 1: Does the presence of Depressive Symptoms (DS) predict conversion to, or incidence of AD ?

The presence of **DS is not a risk factor** of conversion to AD for individuals who, in baseline have :

- Normal cognition** (Jessen, 2011)
- MCI** : Mild Cognitive Impairment (Belleville, 2014, Dexler, 2013, Richard, 2013)
- Amnesic MCI** (Summers, 2012)
- Non amnesic MCI** (Kida, 2016, Summers 2012)

The presence of **DS can be a risk factor** of cognitive decline, or conversion to AD, according to their :

SEVERITY

High severity of DS are predictive of conversion for :
Normal cognition (Ezzati, 2019, Gracia Garcia, 2015, Mirza, 2016)
MCI (Defrancesco, 2017, Donovan, 2014)
Amnesic MCI (Kida, 2016)

ONSET

When **the first onset** of depression happens in **late life**, DS are predictive of conversion from LLD to AD (Barnes, 2012, Hesser, 2013, Tapiainen, 2017, Gracia Garcia, 2015, Dillon, 2014).

SUBDOMAIN

Specific **thymic subdomains** are predictive of conversion :
*High score of « depression » domain at the NPI Q is predictive of cognitive decline in AD (Santacruz Escudero, 2019)
*Depressive profil with high cognitive concern, withdrawal and hopelessness, and lower worry can predict AD in confront of other type of dementia (Shdo, 2020)

Question 2.1

Is there an association between DS and performances at semantic tasks ?

	SEMANTIC FLUENCY	PHONEMIC FLUENCY	NAMING
Research with non-demented elderly showed a significant effect of DS over the decline of performances at :	Elderkin Thompson, 2011 Klojcnik, 2017 Rajtar-Zembati, 2017 Dillon, 2011 Mougias, 2019 Barhanullah, 2020 Turners, 2015	Elderkin Thompson, 2011 Dillon, 2011 Mougias, 2019 Turners, 2015	Dillon, 2011 Turner, 2015
Associated with DS, impaired performances to this tasks were predictive of conversion to AD :	Pantzar, 2016; Singh-Manoux, 2010	Potter, 2013, Singh-Manoux, 2010	
Higher level of DS were associated to lower score to this tasks for different groups :	MCI De Paula, 2016 Gonzales, 2017 Lang, 2019	MCI & AD De Paula, 2016	MCI, AD De Paula, 2016 MCI, Dementia Lang, 2019
	aMCI Seo, 2015		
	AD De Paula, 2016 Gonzales, 2017		
	Dementia Lang, 2019		

Results to other tests assessing semantic memory :

- More **semantic intrusions** in AD (>LLD) (Croisile, 2011) ;
- Worst results at **Famous persons test** for aMCI+DS (<LLD & aMCI) (Callahan, 2015) ;
- Impaired results at **Vocabulary** (Pantzar, 2016) and **Mill Hill** (Singh-Manoux, 2010) predicted **conversion from LLD to AD** ;
- Impairment results at **wide achievement test** were associated with **DS** for **non-demented elderly** (Turners, 2015) ;
- Lower number of **verbal strategies** in a recall task were associated with **DS** for **non-demented elderly** (Morimoto, 2011).

Question 2.2. Is Semantic Memory differently affected by LLD and AD or MCI ?

Research showing significant (*) differences between groups at performances to semantic tasks.

	SEMANTIC FLUENCY	PHONEMIC FLUENCY	NAMING
Beck, 2014	AD <* MCI = LLD	AD <* MCI = LLD	AD <* MCI = LLD
Brunet, 2011	aMCI <* LLD & aMCI+DS aMCI+DS <* LLD & aMCI	aMCI <* LLD & aMCI+DS	aMCI <* LLD & aMCI+DS
Callahan, 2015	aMCI <* LLD & aMCI+DS aMCI+DS <* LLD & aMCI	aMCI+DS <* LLD & aMCI	
Lehfeld, 2019			Dementia <* LLD & MCI
Chamberlain, 2011	AD <* LLD	AD <* LLD	AD <* LLD

DISCUSSION

First, the results collected in this systematic review show that there is indeed a link to be determined between the different forms of LLD (according to their severity, their onset and their domain) and their impact on cognitive decline, or even on conversion to a neurodegenerative process.

Secondly, these data indicate that tasks which measure semantic memory give very mixed results on the comparison of LLD and AD (or MCI).

However, these tasks require not only the integrity of the content of the semantic memory, but also the integrity of the executive processes involved.

In order to make a true distinction between the effects of LLD and AD on semantic memory, it seems essential to use protocols that allow the underlying processes to be distinguished. This aspect does not appear to have been covered yet in the literature.

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