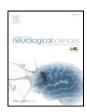
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Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns



Information about medications may cause misunderstanding in older adults with cognitive impairment

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ARTICLE INFO

Article history:
Received 8 March 2010
Received in revised form 26 August 2010
Accepted 30 August 2010
Available online 22 September 2010

Keywords:
Aging
Dementia
Decisions
Neuropsychology
Framing

ABSTRACT

Background: It is not known whether and in which way patients with mild cognitive impairment (MCI) and patients with mild Alzheimer's disease (AD) are affected by the information frame when judging the outcome of a medication. This study aimed to compare framing effects between healthy older adults, MCI patients, and mild AD patients.

Methods: Participants performed a framing task where they had to judge the outcome of unknown medications on a 7-point scale. Medications were described either by using positive terms (positive frame) or by using negative terms (negative frame).

Results: All three groups showed framing effects and judged more favourably the positively-framed medications than the negatively-framed medications. However, framing effects were more pronounced in MCI patients and mild AD patients than in healthy older adults.

Conclusions: This study suggests that the way information is conveyed is critical and that health-related decisions of patients with slight cognitive impairment may be relevantly biased by positive and negative formulations. The development of standardised, easily understandable means of patient information is recommended.

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1. Introduction

Understanding risk information is essential to participate actively in medical care and to make informed decisions. The way information is presented strongly influences human attitudes and choices, which is known as *framing effect* [1]. For example, although logically equivalent, a 50% chance of survival (positive frame) impacts differently on human decisions than a 50% chance of mortality (negative frame). In medical care, people typically show a more favourable attitude towards positively-framed treatments than towards negatively-framed treatments [2]. Recent studies have suggested that framing effects are the product of heuristic/holistic information processing [3] and that older adults are affected by framing effects because they tend to rely more on holistic information processing than on analytic information processing to conserve cognitive resources for other tasks [4,5].

To the best of our knowledge, there has been no study assessing framing effects in older adults with mild cognitive impairment (MCI) and in older adults with Alzheimer's disease (AD). Recent investigations have found that MCI patients and mild AD patients perform more poorly than healthy aging peers on standards of medical decision-making capacity measuring treatment appreciation (appreciating the consequences of a treatment choice), treatment reasoning (providing reasons for a treatment choice), and treatment under-

standing (understanding the treatment situation, treatment choices, and related risks and benefits) [6]. Mild AD patients also make less advantageous decisions than healthy controls in laboratory tasks that require advantageous decision making under ambiguity and under risk [7,8]. Thus far, however, it is unknown whether and in which way MCI patients and mild AD patients are affected by the information frame when judging the outcome of a medication. Understanding framing effects is crucial to develop adequate means of patient information and to assist patients with slight cognitive impairment in making informed decisions.

This study compared framing effects between healthy older adults, MCI patients, and mild AD patients. We hypothesised that all three groups show framing effects and judge more favourably the positivelyframed medications (e.g., effective in 71% of cases) than the negativelyframed medications (e.g., not effective in 29% of cases). As cognitive resources are reduced in MCI patients and mild AD patients as compared to healthy aging peers, we expected the patient groups to show stronger framing effects than the healthy control group. This study also examined the correlation of framing effects with neuropsychological test performance. Following recent investigations [9-11], we hypothesised that pronounced framing effects in the patient groups are associated with deterioration in specific neuropsychological domains. Specifically, we expected the participants with lower numerical skills or with poorer executive functions to be more influenced by the information frame than the participants with better cognitive functions. Reading abilities and sentence comprehension should also have an impact on healthrelated judgements of verbally presented information.

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Finally, this study assessed the percentage of MCI patients and the percentage of AD patients who show extreme framing effects in comparison to the healthy control group. Extreme framing effects can be taken as evidence of strongly context-driven judgements, which may lead to disadvantageous health-related decisions with serious negative consequences.

2. Methods

2.1. Participants

Healthy older adults, MCI patients, and AD patients participated in the study (each group $n\!=\!18$). Groups were comparable in age and education (Table 1). There were no significant differences between healthy controls and MCI patients as well as between healthy controls and AD patients in the gender distribution (Table 1). Healthy volunteers were recruited among relatives and friends of clinical staff, who never participated before in framing studies. AD patients and MCI patients were recruited consecutively from the outpatient memory clinic of the Department of Neurology. They were evaluated prospectively using standard neurological and neuropsychological test procedures. Additional investigations included an informal family interview, brain CT and/or MRI, routine blood tests, and, when necessary, PET, EEG, and other diagnostic procedures. Diagnosis of probable AD was based on the

criteria proposed by Dubois et al. [12] (gradual and progressive change in memory function as reported by patients or informants over more than 6 months; objective evidence of episodic memory impairment on testing, in isolation or in association with other cognitive deficits; presence of medial temporal lobe atrophy; exclusion of other medical disorders). As the cognitive deficits were not pronounced, AD patients were classified as mild AD. Diagnosis of MCI was based on the criteria proposed by Petersen et al. [13] (memory complaint; no functional impairment; slight objective cognitive deficits on formal neuropsychological testing, with scores within 1.5-2 SD from the average range of standardised norms). Overall, exclusion criteria were history of stroke, head trauma, substance abuse, and major metabolic, psychiatric, or neurological disorders (other than AD or MCI) that may compromise cognition. This study complies with the ethical rules stated in the Declaration of Helsinki and was approved by the local ethics committee. Informed consent was obtained from participants or caregivers.

2.2. Neuropsychological background tests

All participants performed the CERAD battery (Consortium-to-Establish-a-Registry-of-Alzheimer's-Disease) [14], which contains tests of global cognitive status (Mini Mental State Examination, MMSE), verbal memory, figural memory, naming to confrontation, visuo-construction, and verbal fluency. All participants also performed a test of planning and

 Table 1

 Demographic information, scores in neuropsychological tests, group comparisons and results of the correlation analysis (significant p-values are in bold).

	Max. score	Healthy controls (1) $(n=18)$	MCI patients (2) $(n=18)$	AD patients (3) (<i>n</i> = 18)	All 3 groups	1 vs. 2	1 vs. 3	2 vs. 3	Framing-1 ^c	Framing-2 ^c
		Mean ± standard deviation [median]			p-value					
Age (years) Education (years) Gender (m:f) CERAD [14]		75.4 ± 6.4 [74.5] 9.3 ± 1.3 [9.0] 10:8	75.4 ± 4.9 [75.0] 8.7 ± 1.4 [8.5] 12:6	77.8 ± 4.8 [78.5] 8.9 ± 1.0 [9.0] 4:14	0.299 ^d 0.298 ^d 0.021 ^f	0.888 ^e 0.171 ^e 0.729 ^f	0.226 ^e 0.406 ^e 0.088 ^f	0.15 ^e 0.462 ^e 0.019 ^f		
MMSE Verbal memory, Learning (tot.) Free recall ^c	30 30 10	$28.1 \pm 1.0 [28.0]$ $20.2 \pm 2.4 [19.0]$ $6.7 \pm 1.7 [6.5]$	26.5 ± 2.0^{a} [26.5] 17.6 ± 4.4 [17.0] 4.9 ± 3.1 [4.5]	20.9 ± 3.2^{b} [22.0] 9.6 ± 3.9^{b} [10.5] 1.2 ± 1.6^{b} [0]	$\begin{array}{c} \textbf{0.000}^{\rm d} \\ \textbf{0.000}^{\rm d} \\ \textbf{0.000}^{\rm d} \end{array}$	0.008 ^e 0.014 ^e 0.051 ^e	0.000° 0.000° 0.000°	0.000° 0.000° 0.000°	0.000 ^g (r = -0.526)	0.001 ^g (r=-0.456)
Recognition (correct hits) Recognition (false positive) Figural memory, Free recall ^c	10 10 11	$9.7 \pm 0.7 [10.0]$ $1.3 \pm 3.2 [0]$ $9.2 \pm 2.5 [10.0]$	$8.7 \pm 1.6 [9.0]$ $1.2 \pm 2.7 [0]$ $5.7 \pm 2.2 [5.0]$	7.9 ± 1.6^{a} [8.0] 3.1 ± 3.9^{b} [1.0] 1.9 ± 2.4^{a} [1.0]	0.001 ^d 0.059 ^d 0.000 ^d	0.059 ^e 0.988 ^e 0.000 ^e	0.001 ^e 0.074 ^e 0.000 ^e	0.143 ^e 0.074 ^e 0.000 ^e	0.000^{g} ($r = -0.524$)	0.001^{g} $(r = -0.440)$
Verbal fluency (animals/min) ^c Visuo-construction	11	$20.7 \pm 3.3 [21.0]$ $10.6 \pm 0.6 [11.0]$	$15.9 \pm 4.7 [15.5]$ $10.5 \pm 0.8 [11.0]$		0.000 ^d	0.000 ^e 0.988 ^e	0.000 ^e	0.000 ^e	0.000^{g} $(r = -0.551)$	0.000^{g} $(r = -0.531)$
(copying geometrical shapes) Naming to confrontation (short version of the Boston naming test) ^c	15	13.9 ± 1.1 [14.0]	12.8 ± 2.0 [13.0]		0.026 ^d	0.047 ^e	0.014 ^e	0.501 ^e	0.024^{g} $(r = -0.308)$	0.012^{g} $(r = -0.340)$
Planning (CLOX1) [15] ^c	15	$12.9 \pm 1.8 \ [13.0]$	11.4 ± 1.5 [11.5]	$8.5 \pm 3.2^b \ [9.0]$	$0.000^{\rm d}$	0.003 ^e	0.000 ^e	0.002 ^e	0.000 ^g (<i>r</i> = -0.469)	0.000^{g} ($r = -0.548$)
Mental complex calculation [16] ^c	24	11.7 ± 5.0 [11.0]	8.9 ± 3.9 [9.0]	$5.0 \pm 4.3 [4.0]$	0.001 ^d	0.096	0.000 ^e	0.008 ^e	0.000^{g} $(r = -0.524)$	0.000^{g} $(r = -0.473)$
Simple arithmetic processing (NPC) [17] ^c	32	-	31.0 ± 1.2 [31.0]	$24.1 \pm 7.1^{a} [25.0]$	-	-	-	0.001 ^e	0.004^{g} $(r = -0.486)$	0.011^{g} $(r = -0.439)$
Verbal attention span (digit span forward, WMS-R) [19] ^c	14	-	5.9 ± 1.3 [6.0]	4.5 ± 1.3^{a} [4.0]		-	-	0.006 ^e	0.001^{g} $(r = -0.526)$	0.048^{g} $(r = -0.327)$
Verbal working memory (digit span backward, WMS-R) [19] ^c	14	-	4.4 ± 1.9 [5.0]	3.8 ± 1.3 [4.0]	_	-	-	0.196 ^e	0.100^{g} $(r = -0.275)$	0.219^{g} ($r = -0.207$)
Reading comprehension (AAT) [18] ^c	15	-	13.1 ± 1.7 [13.0]	12.9 ± 1.9 [13.0]	_	-	-	0.879 ^e	0.019^{g} $(r = -0.393)$	0.019^{g} $(r = -0.395)$
Anxiety (HADS-D) [20] Depression (HADS-D) [20]	21 21	- -	$5.8 \pm 4.2 [5.0]$ $4.7 \pm 3.4 [5.5]$	$4.6 \pm 2.7 [5.0]$ $4.6 \pm 3.1 [3.5]$	- -	 -	_	0.632 ^e 0.950 ^e		

 $MCI = mild\ cognitive\ impairment;\ AD = Alzheimer's\ disease;\ Framing-1 = positive\ frame-high\%\ minus\ negative\ frame-low\%;\ Framing-2 = positive\ frame-low\%\ minus\ negative\ frame-high\%).$

^a Group mean and median below 1.5 SD from the average range of standardised norms.

^b Group mean and median below 2 SD from the average range of standardised norms.

^c Variables entered in the Spearman-rank correlation analysis.

d Kruskall-Wallis test.

e Mann-Whitney test.

 $^{^{\}rm f}$ Chi-square test with Yates correction for 2×2 comparisons.

 $^{^{}m g}$ Spearman-rank correlation analysis for the groups pooled together (uncorrected p-values).

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