The role of limbic structures in financial abilities of mild cognitive impairment patients

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ABSTRACT

Mild Cognitive Impairment (MCI) patients experience problems in financial abilities that affect everyday functioning. To date, the neural correlates of decline in this domain are unclear. This study aims at examining the correlation between the pattern of brain atrophy of MCI patients and performance on financial abilities. Forty-four MCI patients and thirty-seven healthy controls underwent structural magnetic resonance imaging, and assessment of financial abilitiesby means of the Numerical Activities of Daily Living Financial battery (NADL-F). As compared to healthy controls, MCI patients showed impaired performance in three out of the seven domains assessed by NADL-F: Item purchase, percentage, and financial concepts. The patients' performance in the NADL-F correlated with memory, language, visuo-spatial, and abstract reasoning composite scores. The analysis also revealed that volumetric differences in the limbic structures significantly correlated with financial abilities in MCI. Specifically, the patients' performance in the NADL-F was correlated with atrophy in the left medial and lateral amygdala and the right anterior thalamic radiation. These findings suggest that completing daily financial tasks involves sub-cortical regions in MCI and presumably also the motivational and emotional processes associated to them. Involvement of altered limbic structures in MCI patients suggests that impairment in financial abilities may be related to emotional and reflexive processing deficits.

1. Introduction

Older adults hold a comparatively high share of wealth of a nation. Age-related impairment in financial capacity (Widera et al., 2011) and decision-making is, therefore, not only a serious risk to individuals but also to society (Marson, 2013). Patients with Mild Cognitive Impairment (MCI) (Griffith et al., 2003, 2010; Okonkwo et al., 2006; Sherod et al., 2009) and mild Alzheimer's Disease (AD) (Martin et al., 2019; Triebel et al., 2009) experience significant impairments in financial conceptual knowledge, bank statement management, and the ability of paying bills. Previous studies exploring the neural correlates of decline in financial capacity (Griffith et al., 2010; Han et al., 2014, 2016; Marson, 2016; Stoeckel et al., 2013) indicated that areas traditionally associated with executive functions, i.e. the angular gyrus (Griffith et al., 2010; Stoeckel et al., 2013), precuneus (Stoeckel et al., 2013), medial and dorsolateral frontal cortex (Stoeckel et al., 2013), can predict financial capacity scores in MCI Critically, these studies analyzed only a few brain regions, which may be restrictive considering the multidimensional nature of financial abilities that presumably draw upon numerous brain networks, cortical hubs, and associated cognitive and emotional processes (Knight and Marson, 2012; Sherod et al., 2009). Moreover, previous approaches focused on the neuroanatomical correlates of the performance in a specific task, not on how the MCI brain-induced alterations may affect daily living financial abilities.

Recently, we developed the Numerical Activities of Daily Living-Financial (NADL-F battery, which is a series of tests capable of capturing impairments in financial abilities (Arcara et al., 2019), specifically related to counting currencies, reading abilities, item purchase, percentages, financial concepts bill payment and financial judgments. The test takes into account the crucial domains of the financial competence previously highlighted in the literature and it also adapts to properly assess participants within the Italian socio-cultural context. The NADL-F battery was tested both in healthy participants and patients with neurological disorders such as MCI and Alzheimer's disease (Arcara et al., 2019).

This study aims to examine the correlation between cortical and sub-cortical brain volume alterations and reduced performance in the NADL-F battery in MCI patients. It was anticipated that finance management and economical decisions could also rely on emotional aspects (Spinella et al., 2009) that have being associated with various structures of the limbic system in cognitively healthy individuals (Bermejo et al., 2011; Samanez Larkin et al., 2007) and that have not been previously investigated in relation to the financial capacities in MCI.

2. Methods

2.1. Participants

Eighty-one older adults were included in this study, of which 44 patients had MCI and 37 were healthy controls. Patients with MCI were older adults who presented for clinical evaluation to the IRCCS San Camillo Hospital (Venice, Italy). They were subsequently recruited to undertake a comprehensive clinical and neuropsychological examination. The diagnosis of MCI was made according to the Petersen et al. (2001) criteria. Following cognitive assessment (see Section 2.2.1), MCI patients were categorized as single domain amnestic ($N = 11$), multiple-domain amnestic ($N = 24$), and non-amnestic ($N = 9$). Control participants were 37 older adult volunteers recruited from the community and among family members. These participants underwent neurological evaluation and neuropsychological testing to ensure the absence of medical and psychiatric conditions that could compromise cognition. Other sources of cognitive impairment such as focal lesions were ruled out by visual inspection of MRI scans, carried out by an experienced neuro-radiologist unaware of the aims of this study. Participants were excluded if the MRI scans evidenced significant vascular pathology or micro bleeds, or head motion artefacts that affect T1w3d quality and segmentation. One MCI patient was excluded for these reasons. All but three participants were right-handed and none of them had a history of psychiatric disorders or drug or alcohol abuse.

The data analyzed in the current study were collected in accordance with the Helsinki Declaration. Written informed consent was obtained from all participants after the nature of the study was fully explained. The study was approved by the Ethics Committee for ULSS 12 and IRCCS San Camillo Hospital Foundation, (Venice, Italy), reference number 2016.07.

2.2. Measures

2.2.1. Cognitive assessment

MCI patients underwent a neuropsychological assessment as part of their clinical evaluation and the same battery of tests was also administrated to the healthy control group. The assessment evaluated global cognitive function as measured by MMSE and specific cognitive domains frequently affected by dementia, including measures of attention, executive functions, reasoning, language, memory, visuospatial abilities and basic arithmetic (see Table 1 for the full neuropsychological assessment). All participants were tested individually by trained neuropsychologists. The aim was to obtain cognitive profiles that could be clinically informative and sensitive to the impact of early stage neurodegeneration.

2.2.2. Financial abilities assessment: the NADL-F test battery

The Numerical Activities of Daily Living – Financial (NADL-F battery was administered to all participants. The battery includes the following tests: Counting Currencies (NADL-F A), Reading Numbers Abilities in ecological contexts (NADL-F B), Item Purchase (NADL-F C), Percentages in real life concrete situations (NADL-F D), Financial Concepts particularly relevant to the Italian cultural context (NADL-F E), Bill Payments (NADL- F), Financial Judgments in fraudulent and other common scenarios (NADL-F G) (Arcara et al., 2019).

2.3. MRI acquisition

MRI resonance images were acquired using a 1.5 T Philips Achieva MR scanner with an 8-channel head coil. MRI study protocol included a high resolution 3D T1-weighted anatomical acquisition (repetition time/echo time: 7.6 ms/ 3.58 ms; FOV 250 × 250 × 168; acquisition voxel dimensions 1.1 × 1.1 × 1.2 mm); a T2-weighted axial scan and a coronal fluid attenuated inversion recovery (FLAIR) scan to detect the presence of significant vascular pathology or micro bleeds, which might be not compatible with the diagnosis of MCI prodromal to AD and induce a suboptimal segmentation of the T1-weighted images.

2.3.1. Cortical and subcortical voxel based morphometry

Structural data were analyzed with CAT12 pipeline in SPM12 (http://dbm.neuro.uni-jena.de/cat/). Gray matter (GM) and white matter (WM) were segmented and then processed separately. For processing- and analysis-steps, preset parameters in accordance with a standard protocol (http://www.neuro.uni-jena.de/cat12/CAT12-Manual.pdf) were used, applying default settings unless indicated otherwise. To identify potential outliers and segmentation failure sample homogeneity implemented in CAT12 SPM toolbox was checked using covariance matrix. Spatial normalization and segmentation into three voxel classes (gray matter (GM), white matter (WM) and cerebrospinal fluid [CSF]) was adopted by using an adaptive maximum posterior segmentation and partial volume segmentation. Estimated total intracranial volume (eTIV) for all scans was calculated as the sum of GM, WM and CSF volumes as provided by CAT12 toolbox. Modulated normalized GM and WM maps were then smoothed using a 6 mm FWHM kernel to reduce the impact of gyri variability across participants in statistical analyses.

In order to avoid tissue mis-assignment, the gray matter VBM mean template was binarized using 0.2 fractional intensity value as threshold for gray-matter inclusion, and then used as mask for statistical GLM estimation. White-matter VBM mask was obtained based on fractional anisotropy (FA) FSL (FMRIB's Software Library, Oxford University) mean template, binarized using 0.3 fractional intensity value as threshold. Smoothed-modulated-normalized-masked GM and WM maps were then included in statistical analyses.

2.4. Statistical analyses

Differences between MCI patients and healthy controls on demographical and clinical features were assessed by means of the Mann Whitney test. For discrete variables a Pearson chi squared Test was adopted. The financial capacities of the two groups were also compared using the Mann Whitney test. Bonferroni corrected threshold of $p < 0.007$ (0.05/7 NADL-F sub-tests) was considered.

Additionally we investigated the relationship between the NADL-F and various neurocognitive and socio-demographic aspects including the Cognitive Reserve index (CRIq, Nucci et al., 2011), the number of years of formal education (i.e., Education), and composite scores in neuropsychological tests representing each cognitive domain (see Table 1). The participants' raw scores on the neuropsychological tests were converted into z scores and averaged to form the composite measures. The use of composite values reduced the redundancy of task scores tapping the same cognitive domain. The following

Table 1
Composite measures of the neuropsychological tests for MCI patients.

Cognitive domains	Functions/tests
MMSE	General cognitive status (Folstein et al., 1975)
Executive functions and attention	Phonemic verbal fluency (Novelli et al., 1986a)
	Stroop task - Interference inhibition (sec) (Caffarra et al., 2002a)
	Attentive matrices (Spinnler and Tognoni, 1987)
	Digit span backward (Orsini et al., 1987)
Language	Semantic verbal fluency (Novelli et al., 1986a)
	Token test (Spinnler and Tognoni, 1987)
Short-term memory	Digit span forward (Orsini et al., 1987)
	Immediate story recall (Spinnler and Tognoni, 1987)
	Spatial span (Orsini et al., 1987)
Long-term memory	Delayed recall Rey-Osterrieth complex figure (Caffarra et al., 2002b)
	Delayed story recall (Spinnler and Tognoni, 1987)
	Spatial supraspan (Orsini et al., 1987)
	Paired associate word learning (Novelli et al., 1986b)
Visuo-spatial abilities	Rey-Osterrieth complex figure immediate copy (Caffarra et al., 2002b)
Abstract reasoning	Raven Progressive Matrices (Carlesimo et al., 1996)
	Similarities (from WAIS-R; Orsini and Laiacona, 1997)
Instrumental Activities of Daily Living	IADL (Lawton and Brody, 1969)
Basic Arithmetic	Mental calculation, Rules and Principles, Written operations from NADL (Semenza et al., 2014)

neurocognitive domains were included in this analysis: Executive functions and Attention, Language, Short-Term Memory, Long-Term Memory, Visuo-spatial abilities and Abstract Reasoning. A sub-sample ($N = 15$ MCI; $N = 5$ controls) also completed a Basic Arithmetic assessment which was also included (for the MCI group) in the correlation analyses. We calculated the Pearson's correlation between the neuro-cognitive and socio-demographic variables and the NADL-F subtests and total score. The correlations were calculated separately for MCI patients and healthy controls. All p-values in these analyses were corrected with Bonferroni correction (separately for MCI patients, and healthy controls), to compensate for multiple comparisons inflation of Type 1 error.

In order to define the subcortical and cortical volumetric differences related to the presence of MCI, GM and WM GLM group comparison between healthy controls and MCI patients was performed using SPM12 (Welcome Trust Centre for Neuroimaging, UCL, London, UK) including age, gender, and eTIV as nuisance variables. In order to reduce false positives (Spisák et al., 2018), a bayesian *Probabilistic Threshold-free Cluster Enhancement (TFCE) method* was used to define GM e WM patterns in MCI, with significance threshold set to $p < 0.05$.

The correlation between each MCI's cortical and subcortical volumetric differences and financial autonomic functionalities was calculated using a VOI (volumes of interest) approach after atlas based parcellation of cluster areas included in the thresholded GM and WM maps. For this purpose Brainnetome atlas areas (http://atlas.brainnetome.org/download.html) and ICBM-DTI-81 atlas tract (https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/Atlases), normalized in MNI-space, resampled in 1.5 mm isotopical voxel dimension, and thresholded at 30%, were applied as masks for GM and WM maps, respectively. VOI areas that survived the masking process were added to a regression model including participants' NADL-F total score. This pathology-centered approach allows to investigate the role of specific alterations due to MCI pathology and its associations with the patients' performance in NADL-F. After exploring how MCI might correlate with financial functionalities as a whole, the same VOI approach was applied to single NADL-F sub-tests that resulted significantly impaired in MCI participants (as compared to healthy controls). eTIV, age and gender were again included as covariates. Whole-brain voxel-based multiple regression analyses were also carried out to investigate linear correlations between GM and WM volumes and MCI scores on the NADL-F battery (See Supplementary Material, Table S1 and S2, and Figure S1). The same analysis was not carried out among healthy participants that showed highly preserved financial abilities and consequently lack of variability in the NADL-F scores, which reduces the meaning of the

regression analyses.

MRIcron (https://www.nitrc.org/projects/mricron) and SPM12 slice overlay tools were used to visualize the significant clusters maps overlaid onto a brain template in MNI space.

3. Results

There were no significant differences in terms of years of education and gender between MCI patients and the control group ($p = 0.248$ and $p = 0.888$, respectively). Significant differences between the two groups were found for age ($p < 0.003$) (see Table 2), and it was thus included as covariate in the voxel-based regression models. Although gender distribution did not differ between groups, it was also included as a covariate as it can actively contribute at the variability pattern in

Table 2
Demographical and clinical characteristics.

	MCI (N = 43)		HC (N = 37)		Mann–Whitney
	Mean	SD	Mean	SD	P value
Education	11.00	21.67	12.35	19.57	0.248
Age	75.44	47.44	68.89	113.99	0.003
Sex (% Male)	58%		54%		0.888*
NADLF TOT	43.81	63.11	52.46	11.20	<0.001
ADL	6	0	6	0	–
IADL	13.81	0.5	13.33	1.13	0.042
MMSE (raw)	26.39	2.84	28.73	1.17	0.001
Executive Functions[++]	−0.15	.62	.26	.34	0.013
Language[++]	−0.31	.77	.55	.51	<0.001
Short-term memory[++]	−0.35	.57	.60	.14	<0.001
Long-term memory[++]	−0.45	.66	.79	.53	<0.001
Visuo-Spatial abilities[++]	−0.26	1.05	.64	.08	<0.001
Abstract reasoning[++]	−0.16	.92	.50	.65	<0.001
Basic arithmetic[++°]	−0.27	0.85	–	–	–
CRI	104.68	19.25	115.18	18.09	.092

Note. Comparison between MCI's and healthy participants' demographical characteristics.

* For discrete variables a Pearson chi squared Test was adopted. NADLF TOT = NADL-F total score. ADL = Activities of Daily Living. IADL = Instrumental Activities of Daily Living. MMSE = Mini Mental State Examination; MCI = patients with MCI; HC = healthy controls; in Bold: Variables that significant differed between groups. CRI = Cognitive Reserve Index.

[++] Composite Z-scores are reported. °No values are reported for Basic arithmetic abilities given the small number of available observations in the control group ($N = 5$).

Table 3
Financial abilities in MCI and control groups.

	MCI (N = 43)				HC (N = 37)				Mann–Whitney
	Mean (SD)	Min	Max	N below cut-off	Mean (SD)	Min	Max	N below cut-off	P value
NADLF-A Counting Currencies	4.21 (1.22)	1	5	4	4.68 (0.34)	3	5	0	0.045
NADLF-B Reading abilities	5.79 (1.41)	3	7	7	6.46 (0.42)	5	7	0	0.010
NADLF-C Item Purchase	11.49 (5.21)	2	14	3	13.08 (1.52)	10	14	0	**< 0.001****
NADLF-D Percentages	5.35 (4.95)	1	9	7	7.24 (1.91)	3	9	1	**< 0.001****
NADLF-E Financial Concepts	6.86 (5.60)	2	12	7	9.65 (3.18)	6	13	0	**< 0.001****
NADLF-F Bill Payments	4.95 (1.28)	2	6	3	5.65 (0.40)	4	6	0	**0.001****
NADLF-G Financial Judgments	5.16 (1.66)	1	6	5	5.70 (0.27)	4	6	0	0.074
NADLF-Total (Performing below cut-off in at least one domain)	44.07 (8.03)	26	58	18	52.46 (3.35)	44	59	1	**< 0.001****

Note: Performance on financial abilities was compared between MCI and healthy participants. A Bonferroni corrected threshold of $p < 0.007$ was considered.
  ** In bold: tasks in which there were significant differences between groups.

VBM (see Voevodskaya et al., 2014).

Global cognitive performance, as assessed with the MMSE scale, was significantly impaired in MCI patients compared to controls ($p < 0.001$). Moreover, various specific cognitive capacities were significantly reduced in the MCI group compared to controls (see Table 2). IADL, although in the normal range in both groups, was significantly reduced in MCI patients ($p < 0.042$).

3.1. NADL-F battery performance in MCI and healthy controls

Financial abilities as measured by the total NADL-F score, were significantly impaired in MCI patients ($p < 0.001$). In particular, item purchase ($p < 0.001$), percentage ($p < 0.001$), and financial concepts ($p < 0.001$), were found to be significantly impaired also after Bonferroni correction. Moreover, 18 out of 43 MCI patients scored below cut-off in at least one domain of the NADL-F battery while only 1 out of 37 healthy participants showed an impairment in one NADL-F domain (see Table 3 for details).

3.2. Neurocognitive correlates of financial abilities

There was no significant correlation between Neuropsychological tests and NADL-F scores in the Control group (See Table 4b). In the patient group, instead, several significant correlations were found, in particular for Percentages and NADL-F Total score. The Percentages subtest showed significant and high correlation with Education, Language, Short-Term Memory, Long-term Memory, Visuo-spatial abilities, and Abstract Reasoning composite scores. The NADL-F total score showed significant correlations with Language, Short-Term Memory,

Long-Term Memory, Visuo-spatial abilities, and Abstract Reasoning composite scores (see Table 4a). No significant correlations were found with CRIq, and Basic Arithmetic abilities. Detailed results on correlations can be found in the Supplementary material: Table S3 and Table S4.

3.3. Brain volume differences in MCI patients and its correlation with the NADL-F battery test total score

In order to explore how brain volume differences in MCI influence financial abilities, participants' performance on the NADL-F battery was correlated with GM and WM density in each cluster associated with MCI regressing out eTIV, age and gender. gray and white matter anatomical differences in MCI patients are shown in Fig. 1. Volumetric differences were found in the hippocampi, basal ganglia, insula, corpus callosum and anterior thalamic radiation, among other areas. A complete list of the areas and the corresponding MNI coordinates is presented in the Supplementary material (Table S5 and Table S6).

Correlations between NADL-F scores and volumetric differences in GM and WM were generally found to be positive. That is: the better the performance in the test, the greater the volume, and the lower the performance in the test, the greater the atrophy (or the smaller the volume). A significant positive correlation between brain volume differences in MCI patients and the NADL-F battery test total score was found with GM in medial ($p < 0.034$), lateral parts of amygdala ($p < 0.030$) and inferior temporal gyrus ($p < 0.051$) in the left hemisphere. A negative correlation between NADL-F and volumetric differences in WM at the anterior thalamic radiation in the right hemisphere ($p < 0.022$) was also found (see Fig. 2).

Table 4a
Correlations between neurocognitive and socio-demographic variables and NADL-F scores in MCI patients. Asterisks indicate significant correlations after Bonferroni correction for multiple comparisons.

	TOT_A	TOT_B	TOT_C	TOT_D	TOT_E	TOT_F	TOT_G	NADL-F_TOTAL
Executive function	0.24	0.31	0.54*	0.41	0.25	0.38	− 0.11	0.45
Language	0.29	0.54*	0.57*	0.61*	0.47	0.56*	0.22	0.7*
Memory-short	0.48	0.55*	0.47	0.63*	0.64*	0.37	0.13	0.72*
Memory-long	0.42	0.4	0.43	0.53*	0.5	0.31	0.04	0.62*
Visuo-spatial	0.42	0.47	0.44	0.58*	0.5*	0.39	0.22	0.65*
Abstract reasoning	0.42	0.54*	0.55*	0.72*	0.5*	0.51*	0.16	0.74*
Education	0.18	0.44	0.09	0.49	0.42	0.19	0.21	0.43
CRIq	0.11	0.36	0.13	0.38	0.24	0.16	− 0.29	0.27
Basic Arithmetic	0.58	0.56	0.35	0.63	0.57	0.43	0.26	0.68

Table 4b

Correlations between neurocognitive and socio-demographic variables and NADL-F scores in healthy participants. Asterisks indicate significant correlations after Bonferroni correction for multiple comparisons. No significant correlations were found, after Bonferroni correction for multiple comparisons.

	TOT_A	TOT_B	TOT_C	TOT_D	TOT_E	TOT_F	TOT_G	NADL-F_TOTAL
Executive function	0.26	0.28	0.15	0.11	−0.14	−0.02	−0.16	0.1
Language	0.25	0.2	0.02	0.26	0.06	0.18	−0.3	0.21
Memory-Short	0.14	0	0.12	0.4	0.34	0.01	−0.28	0.37
Memory-Long	0.29	0.42	0.08	0.42	0.18	0.04	−0.17	0.4
Visuo-spatial	0.33	0.03	−0.26	−0.05	0.06	0.28	−0.18	0
Abstract reasoning	0.36	0.39	−0.04	0.26	0.2	0.21	−0.25	0.33
Education	0.31	0.35	−0.08	0.24	0.14	0.19	−0.34	0.25
CRIq	0.22	0.1	−0.08	0.2	0.25	0.26	0.02	0.25

A = Counting Currencies; B = Reading Numbers Abilities in ecological contexts, C = Item Purchase, D = Percentages in real life concrete situations, E = Financial Concepts particularly relevant to the Italian cultural context, F = Bill Payments, G = Financial Judgments in fraudulent and other common scenarios. CRIq = Cognitive Reserve Index questionnaire.
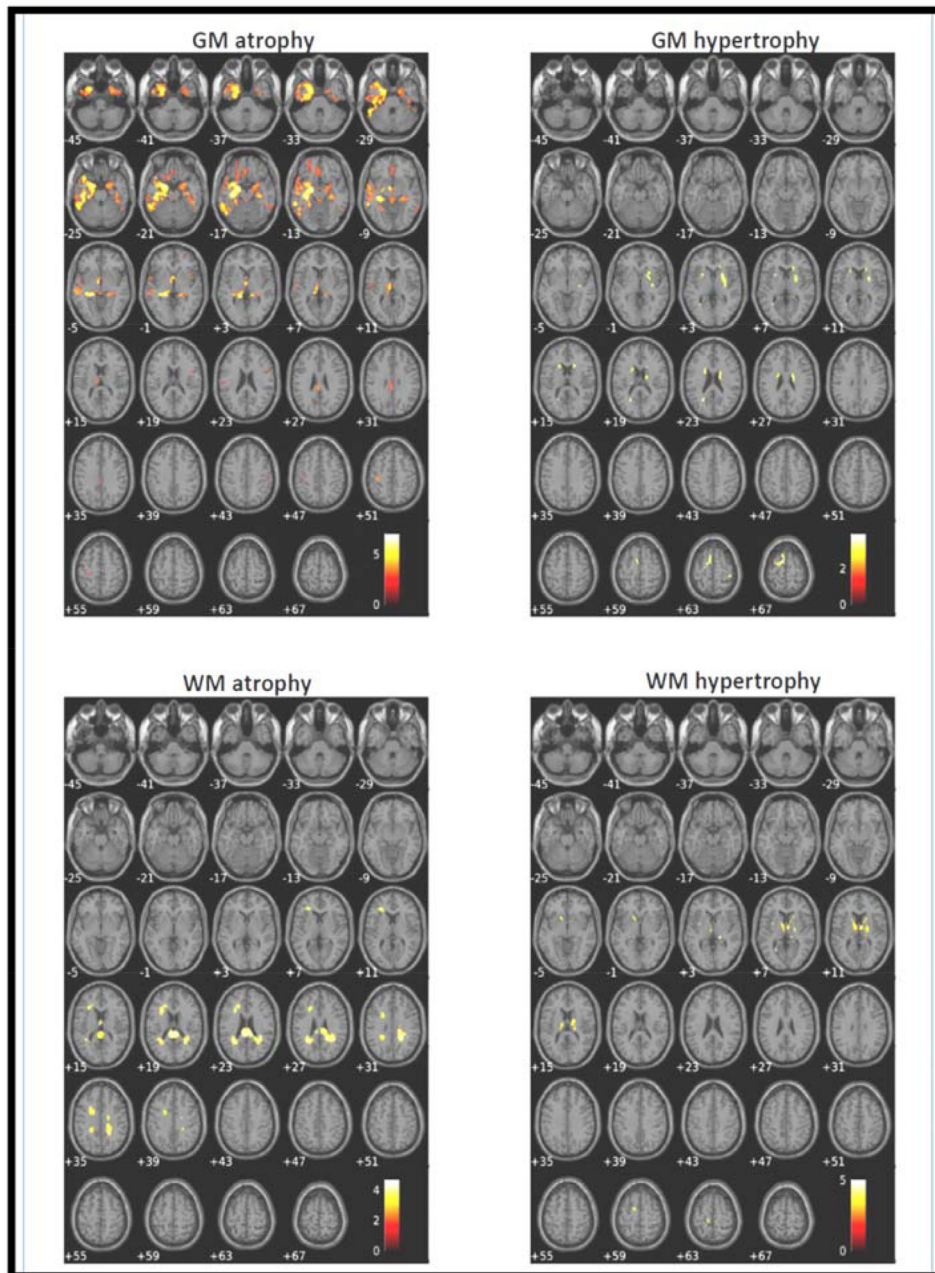
Fig. 1. WM and GM volumetric differences in MCI patients (MCI) versus healthy controls (HC). Significance was thresholded with a false discovery rate at $p < 0.05$ after bayesian TFCE correction enhancement.
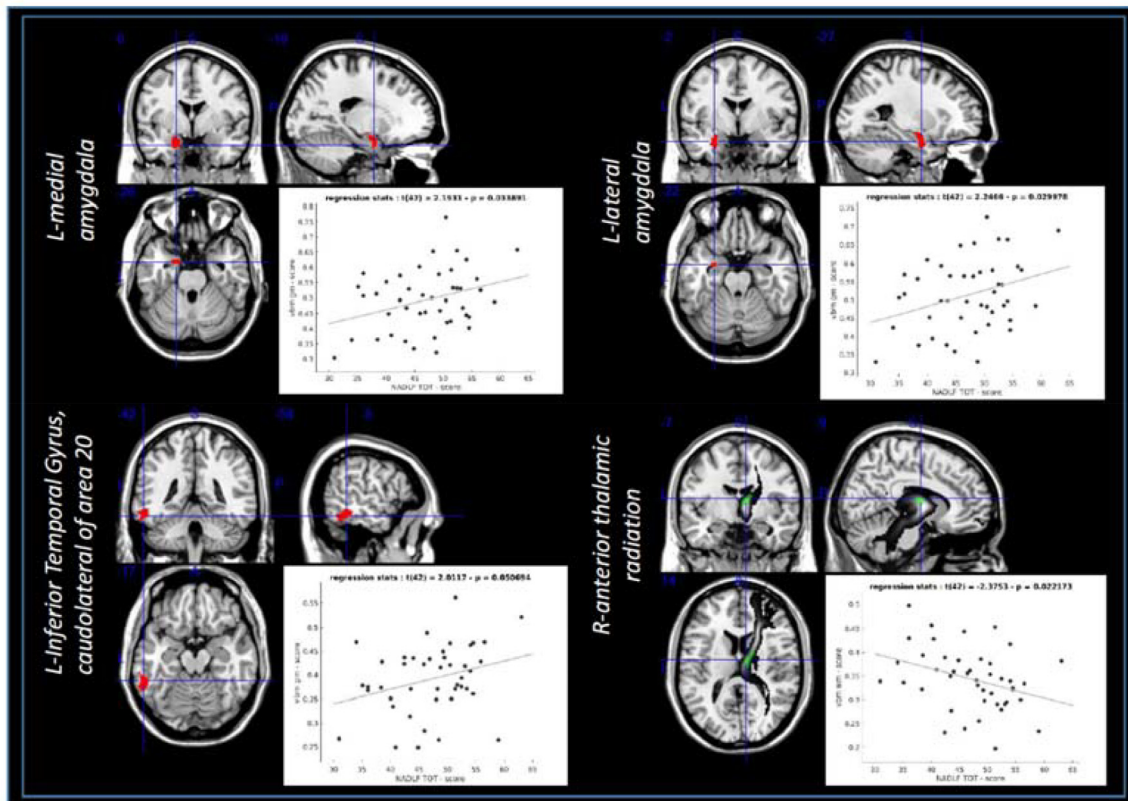
Fig. 2. Correlations between cortical and subcortical MCI-specific volumetric differences and NADL-F total score performance.

3.4. Correlation between NADL-F battery single tests and MCI patients' brain volumetric differences

Among the NADL-F tests impaired in MCI patients [NADLF–C (Item purchase), NADL-D (percentages), NADLF-E (financial concepts, and NADLF-F (Bill payment)], only NADLF-D performance was significantly correlated with cortical and subcortical volumetric differences. In particular, a significant positive correlation was found with GM in middle temporal gyrus ($p < 0.027$) and inferior temporal gyrus ($p < 0.046$) in the left hemisphere and in inferior temporal gyrus ($p < 0.035$) in the right hemisphere. The same positive relationship was found with WM in the posterior part of the left anterior thalamic radiation (see Fig. 3). MCI Item purchase abilities were correlated with left medial and lateral amygdala as a trend ($p < 0.06$ and $p < 0.07$). Additionally, a negative correlation trend (WM alteration correlates with low performance) was found between financial concept and WM in anterior thalamic radiation ($p < 0.051$).

4. Discussion

The present study shows that financial deficits in MCI patients are predicted by sub-cortical structures alterations as the left medial and lateral amygdala and the anterior thalamic radiation. Atrophy in cortical areas as the inferior temporal and middle temporal gyrus, which are generally associated with reading (Turkeltaub et al., 2003) and visually encoding of complex stimuli like Arabic numbers (Shum et al., 2013), appear also related to financial abilities. Behaviorally, the patients' performance in the NADL-F correlated with short- and long-term memory, language, visuo-spatial and abstract reasoning composite scores.

The main novelty of our findings is the identification of the relation between financial deficits in MCI patients and the atrophy of limbic structures, in accordance with the white matter degradation that predicts declining financial skills and knowledge (Gerstenecker et al., 2017). These regions are typically active in the course of motivational and emotional processes, might play a fundamental role in strategic decisions (Damasio, 1994; Rosenbloom et al., 2012; Samanez-Larkin and Knutson, 2015) and particularly in stressful financial ones (Raggetti et al., 2017). The amygdala, for example, appears to play a key role in inhibiting actions with potentially deleterious economical outcomes (De Martino et al., 2010).

Other subcortical regions, including the anterior thalamic radiation, have been generally implicated in the reward circuitry responsible for the control of motivated behavior (Panksepp, 2004). We found that alterations to these subcortical regions appeared also correlated with financial abilities in MCI. The results suggest that, differently from other regions, the correlations between this WM sub-region and task performance was negative. However, caution in the interpretation of the direction of the latter correlation is warranted, as it might be influenced by the presence of WM hyperintensities (Karim et al., 2016) and might not be due to actual volume reductions associated with higher performance.

Previous studies exploring MRI volumetrics and financial tasks in MCI have not reported correlations with limbic structures (Griffith et al., 2010; Stoeckel et al., 2013). However, these studies might not be directly comparable with the current one due to various methodological differences, including the test used to assess financial abilities FCI in previous studies, and NADL-F in the present study), the varying sample sizes that impact on the statistical power (MCI $N = 38$ and $N = 16$ respectively in the two previous studies versus $N = 44$ in the current one), the algorithms implemented in previous versions of SPM used in these works that were not optimized for GM/WM assignment. Most crucially, previous studies have focused on specific regions of interest that excluded sub-cortical regions a priori, which, as we demonstrated here, are altered in the MCI patients and associated with the financial performance. Our study suggests, for the first time, that
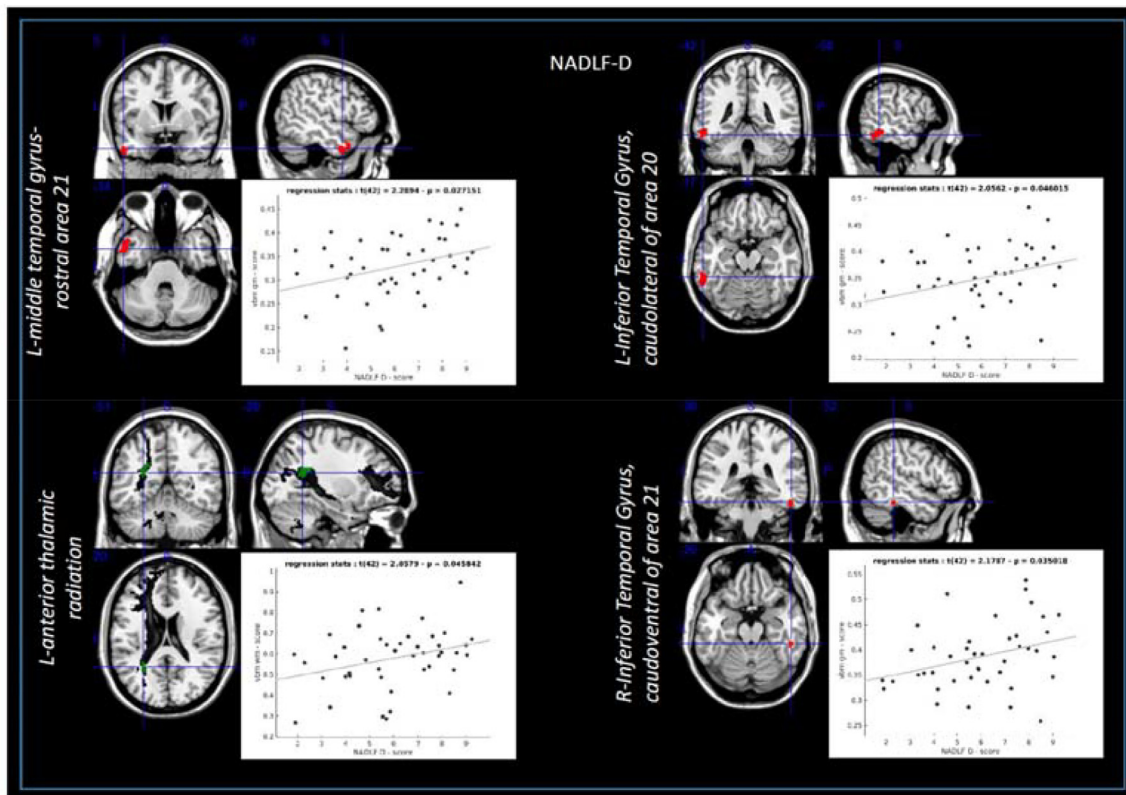
Fig. 3. Correlations between cortical and subcortical MCI-specific volumetric differences and NADL-F subtests score performance. Only NADLF-D performance was significantly associated with cortical and subcortical volumetric differences.

the completion of some of the most common daily financial tasks entails the differential involvement of sub-cortical regions in MCI patients and conceivably also the motivational and emotional processes associated to them.

It is an open question whether a stronger association between financial abilities and areas linked to affective-based decisions progressively and independently occurs in pathological aging, or as a consequence of the fact that the cognitive processes become less effective (see Table 2). Indeed, limitations on executive resources and working memory are frequent in MCI (Saunders and Summers, 2011). Thus, it is conceivable that, when executive functions breakdown, the emotional processes normally related with decision making (Rosenbloom et al., 2012) prevail over the cognitive ones. Disinhibited impulsive behaviors as well as reduced capacities to, for example, carry out calculations and dealing with finances under pressuring conditions would be expected under such conditions. These behaviors were indeed verified in the present study (see Table 3). On the other hand, inadequate emotional processing, associated with reduced volumetric changes in limbic structures, might independently influence the individual's ability to correctly assess consequences of decisions (Bayard et al., 2014). This might negatively influence, for example, shopping decisions or the ability to trade-off due dates and available money when prioritizing bill payments. Decreasing emotional processes may further affect the person's ability to rate untrustworthy stimuli (Castle et al., 2012) to identify exploitive situations (Spreng et al., 2017), fake offers or difficult percentage-based discounts, and to avoid them (Glass et al., 2019). Most of these aspects, with the only exception of fraud detection, were indeed significantly impaired in MCI participants in the present study (see Table 3). It is thus conceivable that a combination of both processes (i.e., overreliance on emotional aspects as a consequence of executive deficits, and inadequate emotional processing due to atrophy of areas associated to them) predisposes to irrational financial decisions and increases the risk of financial exploitation. Measures on emotional

processing would be desirable in order to better understand the relationship between cognitive and emotional aspects, and financial abilities.In the absence of such measures, it seems reasonable to question a purely cognitive explanation of the financial deficits in MCI,as it would be at odds with the observed relationship between the performance in the financial task and the gray and white matter alterations in limbic structures.

Some brain areas might be particularly vulnerable to inter-subject volumetric variability and might thus spuriously and generally appear correlated with task performance above and beyond any specific alteration caused by pathological aging. We ruled out this possible interpretation of the present findings by exploring the whole brain variability map within the MCI sample (see Figure S1 in Supplementary Materials). Ninety-eight percent of the variance was explained by the first 9 independent components mapping across many cortical and subcortical regions. Moreover, we did not find increased variability as expressed by Coefficient of Variability (CV) in limbic areas (amygdala, middle and lateral parts) and in those that do not correlate with NADL-F scores (see Figure S2 in Supplementary Materials). This suggests that the link between financial deficits and limbic alterations is not merely due to greater volumetric variability of the latter compared to other brain areas.

This investigation was prompted by a previous study on the anatomical underpinning of basic daily life numerical abilities in the MCI. Benavides-Varela and colleagues (2015) found that numerical abilities in MCI patients were associated with regions, such as the frontal cortex, that are not typically involved in basic numerical skills, as the inferior parietal cortex is. In fact, the anatomical associations detected with VBM correlation models seem to reflect progressive reliance over more associative areas that would take over in supporting performance over time, to face the loss of computation power in math-specialized areas.

An analogous, albeit distinctive, pattern of evolution seems to characterize the more complex domain of financial capacity Our study

suggests that when cognitive decline takes over (see Table 2), limbic structures, which are also altered, are involved in financial tasks. Importantly, as demonstrated by Benavides-Varela et al. (2015), limbic structures are not crucial in MCI for basic math abilities. We may speculate that the involvement of brain structures dealing with emotional and motivational processing may emerge in tasks pertaining to domains such as the financial one in which this type of processing plays a major role or when risky conditions are perceived but not managed satisfactorily. Consequently, MCI patients are at risk of behaving less rationally when confronted with financial matters. This may result in non-mindful, unwise decisions and higher gullibility (Lichtenberg, 2016), ultimately leading to a disadvantageous course of action.

Finally, some comments on the neurocognitive correlates of financial capacities are warranted. Several correlations were found between neuropsychological tests and NADL-F scores for the MCI group only, in line with the data already reported for the standardization of NADL-F battery (Arcara et al., 2019). Specifically, the patients' performance in the NADL-F correlated with memory, language, visuospatial and abstract reasoning composite scores. Item purchase abilities also correlated with measures of executive functions and attention. The latter partially confirms previous literature indicating that attention (Okonkwo et al., 2006; Stoeckel et al., 2013) and executive functions significantly correlate with the MCI abilities to deal with numerical problems in ecologically valid settings (Zamarian et al., 2007a; 2007b; Pertl et al., 2017) and financial performance (Griffith et al., 2003; Okonkwo et al., 2006; but see also Sherod et al., 2009; Niccolai et al., 2017). There were no significant correlations with Basic Arithmetic and the NADL-F. However, given that the correlation values are remarkably high (see Table 4a), we suspect that the lack of statistical significance is related to the conservative approach used (Bonferroni correction) and, most importantly, the small degrees of freedom due to limited number of observations for which data on both NADL-F and NADL were available (see Table 2). We also noted that the cognitive reserve measure included in this study showed very low correlation with financial abilities. This weak relationship supports the idea that financial abilities similarly to numerical abilities (Arcara et al., 2017), are not strongly influenced by cognitive reserve, in particular less so than other variables such as years of formal education.

The pattern of correlations may be compatible with the idea that difficulties in carrying out numerical ADL, and in particular financial ones, may be secondary to other cognitive difficulties in MCI (Griffith et al., 2003; Okonkwo et al., 2006; Stoeckel et al., 2013). However, given the correlational nature of the data, we can only speculate that these neurocognitive aspects are actually the bases of the financial deficit other potential explanations are plausible. For example, the observed correlation could indicate that a single common impairment is related to both the neurocognitive measures and the performance in the financial task Future clinical studies could address this potential explanation by intervening on specific aspects (e.g., a training focused on the memory impairment, emotion regulation techniques, etc.) and investigating if the intervention has some effects on financial abilities corroborating the idea that financial abilities impairment strongly stems from these abilities. In this complex scenario of results, a full picture of the relationship between neurocognitive measures, financial abilities and brain correlates would require further investigations (for example by means of mediation analysis, Vidoni et al., 2010). However, given that the knowledge of neurocognitive basis of financial abilities is still at the early stages, and the number of mediation models that can be defined is potentially very high, shading further light on this issue is outside the scopes of the present article. Future behavioral studies with larger samples can better investigate, for instance by structural equation modeling, potential complex structures of relationships between basic neurocognitive components, emotional, and financial abilities, and the results could serve as the basis for future VBM studies investigating the neural correlates. Lastly, the lack of

correlation among healthy controls is not surprising, as it probably derives from the reduced variability typically observed for healthy controls in neuropsychological tests.

4.1. Relevance and implications

Older persons' quality of life is associated with the ability to remain autonomous in daily activities. Financial abilities, in particular, are critical for job completion and other frequent roles in the society. When the ability to deal with money declines, the patient's family members might often increase their participation and supervision and look for potential ways to deal with this problem of significance in many life domains. The present study opens up new possibilities for programs aiming at potentiating financial abilities in MCI patients. Previous studies have successfully used brain stimulation techniques in combination with cognitive training programs to help MCI patients cope with other deficits (Birba et al., 2017; Das et al., 2019). Similarly, the cortical and subcortical brain structures altered in MCI patients and that we have found related to financial deficits might be employed as direct or, in case of subcortical structures, indirect targets (e.g., Abend et al., 2018) in specific programs using brain stimulation techniques (e.g. TMS/tDCS). The findings of the present work also suggest that when designing effective cognitive training programs, it might be informative to take into account the patients' personality traits (e.g. anxious traits, impulsiveness, etc.), which modulate the ability to deal with emotional decisions. Future work should shed more light in this sense.

Limitations of the current study should be acknowledged. Although we reported the various sub-types of MCI in our sample for descriptive purposes, we did not distinguish among different subtypes of MCI in the analyses because the sample sizes did not provide adequate statistical power within most sub-groups. Moreover, as the current work derives from a cross-sectional design, the ultimate clinical and neuropathological status of these participants is unknown. However, if we consider the annualized rate of conversion to AD from amnestic MCI (Belleville et al., 2017) along with the fact that the majority of the MCI patients were categorized as amnestic (Section 2.1), we might expect that a majority of the participants in this study will clinically manifest AD in the future. Replication of the findings within a larger sample and in longitudinal designs is needed to confirm the precision of these estimates and the confidence that these effect sizes generalize to the various MCI subtypes or even in early AD. Furthermore, financial skills might in principle correlate with different volumetric changes in MCI and in controls. One crucial aspect prevented a separate analysis of the groups: many control participants obtained the maximum scores in most tasks, and performed above cut-off in the entire battery reflecting a highly preserved financial abilities. In practical terms this translates in the lack of variability in the NADL-F scores among healthy controls, which would have limited the outcome of the VBM analysis. Our approach was thus straightforwardly focused on the pathology and on understanding how brain alterations in MCI may be related to the progressive impairment in the financial domain. Future studies should explore whether the same or additional structures influence financial abilities in healthy participants. Additionally, the voxel based WM alteration resulted from our T1w3D data does not allow to explore the nature of this deviation from the healthy population. Future studies, perhaps using a 3T scanner that benefit of recent advances in DTI (e.g., adopting Neurite Orientation Dispersion and Density Imaging – NODDI as in Wen et al., 2019) will consent to explore the relationship of specific intra-cellular and extracellular alterations related to MCI disease progression and the NADL-F performance. Finally, exploring the patients' awareness of these deficits and whether neuroimaging might help in defining patients at risk in their financial decision-making would also be desirable.

4.2. Conclusions

In conclusion, we present findings suggesting that cortical and subcortical brain volumes typical of the MCI pathology contribute to financial deficits in these patients. In particular, difficulties with financial matters showed a robust relationship with alterations in the limbic structures. These findings highlight the clinical significance of exploring how volumetric alterations and corresponding pathology may place MCI patients at risk in complex instrumental daily activities, such as financial ones and potentially suggest new remediation strategies to deal with risky financial behaviors.

CRediT authorship contribution statement

Silvia Benavides-Varela: Conceptualization, Methodology, Writing - review & editing. **Francesca Burgio:** Conceptualization, Methodology, Writing - review & editing, Funding acquisition. **Luca Weis:** Methodology, Formal analysis, Writing - review & editing. **Micaela Mitolo:** Data curation, Writing - original draft. **Katie Palmer:** Writing - original draft. **Roberta Toffano:** Investigation, Writing - original draft. **Giorgio Arcara:** Writing - original draft. **Antonino Vallesi:** Writing - review & editing. **Dante Mantini:** Writing - review & editing. **Francesca Meneghello:** Conceptualization, Writing - review & editing. **Carlo Semenza:** Conceptualization, Writing - review & editing, Supervision.

Declaration of Competing Interest

The authors declare no conflict of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.nicl.2020.102222.

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