Life Span and Disability XXV, 2 (2022), 273-293

Group intensive cognitive activation in patients with Major or mild Neurocognitive Disorder: Comparison between two subsequent cycles of treatment

Simonetta Panerai[1], *Domenica Tasca*[1], *Sabrina Musso*[1], *Donatella Gelardi*[1], *Giuseppina Prestianni*[1], *Stefano Muratore*[1], *Valentina Catania*[1] *& Raffaele Ferri*[1]

Abstract

The options for treating Major and mild Neuro Cognitive Disorders (M-NCD and m-NCD, respectively) include both pharmacological and non-pharmacological interventions. At present, no drugs appear to be decisive, which has grown the interest towards non-pharmacological interventions. Three main cognition-based approaches have been described in the scientific literature: cognitive stimulation, cognitive training, and cognitive rehabilitation. The studies on the effects of the cognitive interventions have shown controversial results. In our Institute the group-Intensive Cognitive Activation (g-ICA) was arranged whose effectiveness was demonstrated in a previous study.

The aim of the present study was to further investigate whether the g-ICA approach was effective in improving the cognitive skills in patients with M-NCD and m-NCD, by comparing two subsequent g-ICA treatments, one year apart; these included pre- and post-treatment assessments, by using a comprehensive neuropsychological battery. Twenty-nine participants with M- or m-NCD were recruited. Results showed

Received: October 1, 2022; *Revised:* November 3, 2022; *Accepted:* December 19, 2022

[1] Oasi Research Institute – IRCCS, Troina, 94018, Italy.

Corresponding author: Simonetta Panerai, Unit of Psychology, Oasi Research Institute – IRCCS, Troina, 94018, Italy. Phone: +39 0935 936374; E-mail: spanerai@oasi.en.it.

Conflict of Interest: The author reports no conflicts of interest.

Funding: This study was funded by the Italian Ministry of Health – "Ricerca Corrente 2022-2024".

Acknowledgements: We acknowledge the valuable contribution of all participants to the study, and their families. We are grateful to Eleonora Di Fatta for her contribution to the final version of this paper.

statistically significant differences between the pre- and post-treatment phases for each measure both at the first and at the second administration of treatment; a worsening in cognitive skills during the pause between the first and second treatment was recorded, while a recovery of cognitive functions was seen following the second treatment. g-ICA has proved to counteract the progressive cognitive impairment of NCDs.

Keywords: Dementia; M-NCD; m-NCD; Non-pharmacological treatment; Cognitive stimulation.

1. Introduction

In the Statistical Manual of Mental Disorders – fifth edition (DSM-5) (American Psychiatric Association, 2013) the Major Neuro Cognitive Disorder (M-NCD) is largely synonymous with dementia, characterized by the evidence of significantly acquired deficits in one or more cognitive domains, that interfere with independent daily functioning. Mild Neuro Cognitive Disorder (m-NCD) is synonym of Mild Cognitive Impairment (MCI), a clinical picture of great interest as it might represent (although not always) a precursor of dementia and might orient the intervention to prevent or postpone its onset (Langa & Levine, 2014). m-NCD is characterized by a mild-acquired cognitive decline, not interfering with independence in daily activities, even though greater effort or compensatory strategies may be required. M- and m-NCD may be caused by many different neurological or medical conditions. Two broad etiological categories have been conceptualized, such as a degenerative (e.g., due to Alzheimer's or fronto-temporal degeneration) and a non-degenerative condition (e.g., vascular disease, or traumatic brain injury related disorder). The management of NCDs requires a multidisciplinary synergy to preserve the cognitive and daily functioning abilities, as well as the quality of life of the patient and his/her family.

The options for treating M- and m-NCD include both pharmacological and non-pharmacological interventions (NPIs). Currently, no drugs appear to be decisive (Hildreth & Church, 2015); therefore, a growing interest has been shown in non-pharmacological interventions and in the combined use of both pharmacological and NPIs. NPIs do not present adverse effects and are often administered by involving patients, caregivers and/or other family members (Vandepitte, Van Den Noortgate, Putman, Verhaeghe, Faes, & Annemans, 2016).

Neuronal plasticity and cognitive reserve are behind the implementation of NPIs, especially the cognitive-based interventions. Furthermore, the lack of cognitive activity hastens cognitive decline, both in normal ageing individuals and in those with NCDs.

Three main cognition-based approaches have been described in the scientific literature: cognitive stimulation, aiming at enhancing general cognition and social functioning (Clare & Woods, 2004; Buschert, Bokde, & Hampel, 2010); cognitive training, including computer-based or paper-and-pencil exercises targeting specific cognitive functions (Cipriani, Bianchetti, & Trabucchi, 2006; Raggi, Iannaccone, Marcone, Ginex, Ortelli, Nonis *et*

al., 2007; Talassi, Guerreschi, Feriani, Fedi, Bianchetti, & Trabucchi, 2007; Alves, Magalhães, Machado, Gonçalves, Sampaio, & Petrosyan, 2013), and cognitive rehabilitation, targeting on individual relevant difficulties and including learning compensatory methods through repeated practices (Loewenstein, Acevedo, Czaja, & Duara, 2004; Choi & Twamley, 2013).

The studies on the effects of the cognitive interventions have shown controversial results (Gates & Sachdev, 2014; Giovagnoli, Manfredi, Parente, Schifano, Oliveri, & Avanzini, 2017; Na, Yang, Yeom, Kim, Byun, Kim *et al.*, 2019; Yorozuya, Kubo, Tomiyama, Yamane, & Hanaoka, 2019), therefore additional evidence is needed on their efficacy.

In our Institute the group-Intensive Cognitive Activation (g-ICA; Panerai, Tasca, Musso, Catania, Ruggeri, Raggi *et al.*, 2016) was arranged to enrich the traditional rehabilitation provided in hospitals, generally based on physical and speech therapy. g-ICA is a combined treatment, based on the patient's central role and the mediation of pedagogy principles, and is delivered in an inpatient hospital setting to individuals with M- and m-NCD. Results of the aforementioned study showed improvements after treatment on general cognitive functioning, executive functions, attention, praxis, and visual memory (Panerai *et al.*, 2016).

2. Aims and hypothesis

The aim of the present study was to verify whether the g-ICA approach was effective in improving the cognitive skills in patients with M-NCD and m-NCD. For this scope, we compared two subsequent g-ICA treatment cycles, carried out approximately 12 months apart.

Based on our previous results, we hypothesized a significant improvement of the patients' cognitive performances both in the first and in the second administration of treatment.

Since our sample included patients with M- and m-NCD, we expected a progressive decline over time; therefore, we hypothesized that the cognitive performances reached at the end of the first treatment cycle wouldn't have been maintained in the absence of treatment and that the second pre-treatment assessment would have been worse than the final assessment of the first cycle.

3. Methods

3.1. Study design

A repeated AB study design was used, which included four phases: namely A1 (first pre-treatment assessment), B1(first g-ICA treatment implementation and post-treatment assessment), A2 (second pre-treatment assessment after about one year from the first), and B2 (second g-ICA treatment and post-treatment assessment). Several cognitive measures were administered during the assessments. In this study design each participant functioned as a control for him/herself.

3.2. Participants

Twenty-nine participants were recruited, 13 males and 16 females, 11 with mild (N = 8) to moderate (N = 3) M-NCD and 18 with m-NCD. The diagnoses were made based on the DSM-5 criteria by a multidisciplinary team (including a geriatrician, a neurologist, a physiatrist, and a neuropsychologist) prior to their admission at the Rehabilitation Unit of our Institute. The neuro-degenerative and nondegenerative etiologies were diagnosed in 12 and 17 participants, respectively. Patients with M-NCD due to AD were treated with cholinesterase inhibitors soon after the completion of the diagnostic process. Mean chronological age was 58 years (±11.5 *SD*).

M-NCD inclusion criteria were: (a) DSM-5 diagnostic criteria for M-NCD; (b) score between 10 and 23 at the Mini Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975); (c) score between 40 and 85 (mild or moderate cognitive decline) at the Milan Overall Dementia Assessment (MODA; Brazzelli, Capitani, Della Sala, Spinnler, & Zuffi, 1994); (d) score between 1 and 2 at the Clinical Dementia Rating (CDR; Hughes, Berg, Danziger, Coben, & Martin, 1982); (e) loss of almost one ADL (Katz, Downs, Cash, & Grotz, 1970) and Instrumental Activities of Daily Living (IADL; Lawton & Brody, 1969); (f) some communication abilities, no major sensorial (sight and hearing) or physical illnesses and no behavioral problems impairing the participation to group activities. Inclusion criteria to be met for m-NCD were: (a) DSM-5 diagnostic criteria for m-NCD; (b) score between 24 and 26 at the MMSE; (c) score between 85.5 and 89 (borderline cognitive level) at the MODA; (d) score .5 at the CDR; (e) ADL and IADL globally maintained; (f) no major sensorial (sight and hearing) or physical illnesses impairing the participation to group activities.

3.3. Procedures

g-ICA is an intensive combined cognitive treatment carried out for six weeks, preceded and followed by a comprehensive neuropsychological assessment. It integrates cognitive stimulation and cognitive training. It was delivered in an inpatient hospital setting by a trained clinical neuropsychologist, supported by a practicing psychologist, and included daily morning sessions (from Monday to Friday).

More details are provided in paragraph 3.5 and in our previous article (Panerai *et al.*, 2016).

3.4. Neuropsychological measures

A comprehensive neuropsychological battery was used, as suggested by Bianchi and Dai Prà (2008), to overcome the weakness resulting from the administration of only one or two measures, as well as to obtain a wide-spectrum neuropsychological profile and demonstrate the specific effects of the intervention (Lissek & Suchan, 2021).

The MMSE (Folstein *et al*., 1975), the MODA (Brazzelli *et al*., 1994) and the Montreal Cognitive Assessment (MoCA; Nasreddine, Phillips, Bédirian, Charbonneau, Whitehead, Collin *et al.*, 2005) were used to check the global cognitive functioning; the Coloured Progressives Matrices (CPM; Basso, Capitani, & Laiacona, 1987) for reasoning ability; for the frontal functions the Frontal Assessment Battery (FAB; Dubois, Slachevsky, Litvan, & Pillon, 2000) was used; short-term memory was assessed by means of the Digit Span (Orsini, Grossi, Capitani, Laiacona, Papagno, & Vallar, 1987), the Two-syllabic word span (Spinnler &Tognoni, 1987), and the visuo-spatial span (Corsi's test; Orsini *et al*., 1987); Rey's 15 words (Carlesimo, Caltagirone, & Gainotti, 1996) and Rey's Complex Figure-memory reproduction (Carlesimo, Buccione, Fadda, Graceffa, Mauri, Lorusso Bevilacqua *et al.*, 2002) were used to assess verbal episodic memory (immediate and delayed recall) and delayed visuo-spatial memory, respectively; for the constructional apraxia the copy of Rey's Complex Figure (Caffarra, Vezzadini, Dieci, Zonato, & Venneri, 2002) was used; selective attention was evaluated using the Digit Cancellation test (Spinnler & Tognoni, 1987); finally, the language abilities were investigated by means of the Aachener Aphasia Test (Italian version) (Luzzatti, Willmes, & De Blaser, 1996).

3.5. The g-ICA protocol

The g-ICA is an intensive group treatment based on the patient-centered principle and the mediation pedagogy. The first considers the patients' needs and expectations, therefore g-ICA includes activities tapping on a wide spectrum of cognitive abilities, which appeal to the cognitive strength of patients. The mediation pedagogy comes from the Structural Cognitive Modifiability theory (Feuerstein, 1999) and is focused on interpersonal relationships (positive feedbacks between patients and mediator, empathy, sense of humor, and making the cognitive activities as pleasant as possible). The physical setting consists of a comfortable room, adequately equipped; the session organization includes errorless learning, variation of activities and materials, variation of task difficulties, use of social positive reinforcements, and a 20-min break with a snack. The session contents was organized on a weekly basis to stimulate a wide range of cognitive functions; the level of difficulties was adapted to the cognitive features of the group. The group was made of four/five participants.

3.6. Statistical analysis

Asymmetry and kurtosis calculations failed to show a normal distribution for most of the variables analyzed in this study, which led to resorting to nonparametric statistics.

The results obtained from all the measures at A1, B1, A2, and B2 were compared by means of the Friedman Anova and Kendall Coefficient of concordance, both for all the neuropsychological measures at the same time, and for each measure taken separately. The Wilcoxon matched pairs test was used for comparisons in pairs only if the p value was statistically significant (significance level was set as $p < .05$). More in detail, we compared: A1 vs B1 and A2 vs B2 to evaluate the benefits of the g-ICA treatment; B1 vs B2 for any differences in improvements obtained after the two cycles of treatment; B1 vs A2 to assess any maintenance of the improvements obtained during the first cycle of treatment; A1 vs A2 to get any quantitative information on the patients' progressive impairment over the year; A1 vs B2 in order to verify any differences between the final cognitive performances shown by patients and those shown during the first assessment. The r effect sizes $(r = z/\sqrt{N})$ were calculated for each difference that was statistically significant; effect sizes of .1 were considered small, .3 medium, and .5 large (Field, 2005).

3.7. Ethics approval

This study was approved by the Local Ethics Committee. Written informed consent was obtained by all volunteering subjects, in accordance with the Declaration of Helsinki, since our participants, although vulnerable, were able to personally give their consent. Furthermore, in the cases of dementia, caregivers were also informed about the study.

4. Results

Table 1 shows the median scores and interquartile ranges obtained at the neuropsychological battery at A1-B1-A2-B2. The scores at both B1 and B2 were higher than those in the respective pre-treatment phases (A1 and A2). At A2 the median scores were generally lower than those obtained at B2.

Table 1 – *Median scores and interquartile ranges at the neuropsychological battery at A1-B1-A2-B2*

A1	B1	A2	B2
GLOBAL COGNITIVE FUNCTIONS			
Milan Overall Dementia Assessment			
78.3 (70.85 - 84.7)	85.15 (81.2 - 90.15)	72.7 (58.1 - 81.4)	83.6 (72.4 - 88.3)
Mini Mental State Examination			
23.07 (19.27 - 25.49)	24.2 (20.27 - 27.97)	21.24 (14.15 - 25)	23.42 (18.56 - 27.15)
Montreal Cognitive Assessment			
16.9 (12.7 - 21.75)	21.62 (16.11 - 26.56)	16.05 (12.7 - 19)	21.87 (17.2 - 25)
REASONING AND COGNITIVE LEVEL			
Color Progressive Matrices			
23.75 (17.95 - 27.65)	25.9 (18.7 - 31.2)	25.65 (18.45 - 29.75)	29.25 (24 - 33.7)
FRONTAL FUNCTIONS			
Frontal Assessment Battery			
11.75 (9.00 - 13.3)	14.5 (12.3 - 15.7)	9.9 (7.3 - 12.7)	12.9 (10 - 15.5)

MEMORY			
Digit span			
4.25 (3.5 - 4.75)	4 (3.5 - 4.5)	3.75 (3 - 4.25)	4 (3.75 - 4.5)
Two-syllabic word span			
2.75 (2.38 - 3.25)	3.13 (2.75 - 363)	3 (2.5 - 3.25)	3.25 (2.75 - 3.75)
Visuo-spatial span (Corsi's test)			
3.75 (3.25 - 4.25)	4 (3.25 - 4.25)	3.75 (2.5 - 4.25)	4.25 (3.5 - 4.75)
Rey's 15 words-Immediate Recall			
28 (19 - 33.3)	28.05 (23.15 - 40.35)	27.1 (19.7 - 32.8)	32 (21 - 44.3)
Rey's 15 words-Delayed Recall			
4.7 (2.4 - 6.3)	4.8 (3.25 - 9.95)	4.5 (3.3 - 6.2)	5.4 (3.4 - 8.2)
Rey's Complex Figure-memory reproduction			
10.63 (4.25 - 16.6)	12.88 (7.8 - 22.44)	16.5 (2.25- 22.1)	22.25 (4.25 - 25.25)
PRAXIS			
Rey's Complex Figure-copy			
20.5 (15 - 30)	29 (22.6 - 33)	26.6 (14.4 - 30.6)	31.5 (18.25 - 33)
SELECTIVE ATTENTION			
Digit cancellation test			
33.38 (22.88 - 40.88)	41.5 (32.25 - 47.38)	33.25 (25.5 - 43)	41.88 (31.25 - 50.25)
LANGUAGE			
AAT- Token test			
59 (54 - 65)	63 (58 - 74)	59 (54 - 63)	62 (56 - 66)
AAT - Repetition			
58 (56 - 64)	62.5 (59 - 67)	58 (56 - 64)	61 (57 - 66.5)
AAT - Written Language			
67 (56 - 69)	66 (58 - 78)	65 (54.7 - 68)	67 (59 - 74)
AAT - Naming			
67 (59 - 74)	71 (63 - 80)	66 (53 - 80)	67 (60.5 - 80)
AAT - Comprehension			
56 (55 - 62)	59 (54 - 68)	57 (47 - 65.5)	57 (53 - 67)

Table 2 shows the results of the statistical analysis. Since the comparisons between all the measures turned out to be statistically

significant (Friedman Anova and Kendall Coefficient of concordance), comparisons were made between A1-B1-A2-B2 of each measure. Statistically significant differences were found in about all the measures, therefore we proceeded with the comparisons in pairs (Wilcoxon matched pairs test), except for the verbal and visuo-spatial span (Two-syllabic and Corsi's test), the copy of Rey's Complex Figure, and Naming and Written language, in which no statistical significance was found.

In the comparisons between both A1 vs B1 and A2 vs B2, to evaluate the effectiveness of the g-ICA treatment, findings showed statistically significant differences between the pre- and post-treatment phases for each measure, with large effect sizes (medium effect sizes were found only in the CPM and in the delayed recall of Rey's 15 words).

The comparisons between B1 (first post-treatment) vs A2 (second pre-treatment), aimed at assessing any loss of improvements reached at the end of the first cycle of treatment, showed statistically significant differences with large effect sizes (medium effect size was found only in the delayed recall of Rey's 15 words), except for verbal comprehension.

The comparisons between B1 and B2 (the two post-treatment phases), for the evaluation of any differences in improvements obtained after the two cycles of treatment, showed no statistically significant differences, except for the MODA, the Token test (with large effect size), and the MMSE (with medium effect size).

The comparisons between A1 vs A2 (the two pre-treatment phases), to obtain any information on the patients' progressive impairment over the year, showed statistically significant differences only in the MODA, MMSE, the memory reproduction of Rey's Complex Figure (with large effect size), and in the Digit span (with medium effect size).

Finally, the comparisons between A1 (first pre-treatment phase) vs B2 (second post-treatment phase), to check any differences between patients' final cognitive performances and those shown during the first assessment, showed statistically significant differences in the MoCA, FAB, memory reproduction of Rey's Complex Figure and the Digit cancellation test (with large effect size), as well as in the CPM and delayed recall of Rey's 15 words (with medium effect size).

Table 2 – *Statistically significant differences in the comparison of the scores obtained at A1-B1-A2-B2*

		A1 vs B1**			A1 vs A2**			A1 vs B2**			B1 vs A2**			B1 vs B2**			A2 vs B2**		
	p = *	*z*	*p* =	*r*	*z*	*p* =	*r*	*z*	*p* =	*r*	*z*	*p* =	*r*	*z*	*p* =	*r*	*z*	*p* =	*r*
All the measures	.00001																		
Milan Overall Dementia Assessment	.00001	4.08	.00005	.77	3.48	.0005	.67	1.19	ns		4.43	.000009	.87	3.26	.001	.64	4.07	.00005	.78
Mini Mental State Examination	.00001	3.43	.0006	.63	3.06	.003	.58	.83	ns		4.55	.000006	.78	2.54	.01	.48	3.81	.0001	.73
Montreal Cognitive Assessment	.00001	3.54	.0004	.69	1.47	ns		2.61	.009	.55	3.93	.00009	.84	.88	ns		4.14	.000034	.84
Color Progressive Matrices	.00008	2.48	.01	.47	1.32	ns		2.24	.025	.48	3.02	.0025	.64	.71	ns		3.62	.00029	.75
Frontal Assessment Battery	.00009	3.7	.0002	.74	1.12	ns		2.55	.012	.53	3.44	.0006	.73	.87	ns		3.88	.0001	.78
Digit Span	.044	.22	ns		2.38	.017	.44	.17	ns		2.25	.02	.42	.21	ns		3.01	.0027	.56
Two-syllabic word span	ns																		
Visuo-spatial span (Corsi's test)	ns																		
Rey's 15 words - Immediate Recall	.0005	2.45	.01	.46	1.93	ns		1.54	ns		3.17	.0015	.62	.07	ns		3.11	.019	.6
Rey's 15 words - Delayed Recall	.005	2.66	.008	.5	.06	ns		2.49	.012	.48	2.23	.025	.44	.83	ns		2.74	.006	.53
Rey's Complex Figure-memory reproduction	.02	2.62	.0003	.88	3.82	.00013	.88	3.62	.0003	.88	1.16	ns		.71	ns		2.75	.006	.65
Rey's Complex Figure-copy	ns																		
Digit cancellation test	.0003	3.53	.0004	.67	.88	ns		3.01	.0026	.6	2.73	.006	.56	.014	ns		2.61	.009	.52
AAT- Token test	.00001	3.74	.0002	.73	1.28	ns		1.55	ns		3.61	.0003	.83	3.35	.0008	.77	3.22	.001	.7
AAT - Repetition	.0003	3.35	.0008	.66	.41	ns		1.81	ns		3.18	.0015	.71	1.52	ns		3.13	.0018	.65
AAT - Written Language	ns																		
AAT - Naming	ns																		
AAT - Comprehension	.03	1.2	ns		1.2	ns		.37	ns		1.83	ns		.65	ns		2.72	.0065	.58

*Friedman Anova and Kendall Coefficient of concordance
**Wilcoxon matched pairs test
ns = not significant

5. Discussion

The g-ICA is a short (six weeks) combined intensive intervention characterized by cognitive stimulation activities and cognitive tasks. Unlike other multi-component approaches (Avila, Bottino, Carvalho, Santos, Seral, & Miotto, 2004; Olazarán, Muñiz, Reisberg, Peña-Casanova, del Ser, Cruz-Jentoft *et al.*, 2004; Sitzer, Twamley, & Jeste, 2006; Raggi *et al.*, 2007; Olazarán, Reisberg, Clare, Cruz, Peña-Casanova, Del Ser *et al.*, 2010), our treatment was implemented both with M- and m-NCD, due to its flexibility and custom tasks. Combined interventions seem able to cope with the complexity of m-NCD, generally resulting in an improved status, both in cognitive terms (general and specific functions) and in terms of well-being (Lissek & Suchan, 2021). Our results show that the g-ICA turned out to be beneficial in both m- and M-NCD (Karssemeijer, Aaronson, Bossers, Smits, Olde Rikkert, & Kessels, 2017) although, to date, the possibility of preventing the onset of dementia in patients with m-NCD remains unclear (Hafdi, Hoevenaar-Blom, & Richard, 2021).

Our approach has already shown its effectiveness in improving general and specific cognitive skills (Panerai *et al.*, 2016). The aim of the current study was to confirm the effectiveness of g-ICA in subjects with M- and m-NCD by comparing the results obtained after two subsequent cycles of treatment, implemented at one year from each other. For this scope, four administrations of the neuropsychological battery were carried out, immediately before (A1 and A2) and after (B1 and B2) treatments. As hypothesized, the median scores obtained after the two cycles of treatment were higher than those in the respective pre-treatment phases, and at A2 the median scores were generally lower than those obtained at B1 (Table 1), thus leading to hypothesize a loss of previous improvements. However, statistically significant differences were not found in each neuropsychological measure (Table 2). The Friedman Anova test showed statistical significances between A1-B1-A2-B2 in all the measures, except for verbal and visuo-spatial span (Two-syllabic and Corsi's test), praxis (Rey's Complex Figure copy), naming and written language (AAT subtests), which have proven not to be amenable to increase.

In the comparisons between A1 vs B1 and A2 vs B2 (the two pre- and post-treatments), statistically significant improvements were found in: global cognitive functions (MODA, MMSE, MoCA); reasoning and cognitive level (CPM); frontal functions (FAB); verbal immediate and delayed recall (Rey's 15 words); non-verbal delayed recall (Rey's Complex

Figure-memory reproduction); selective attention (Digit cancellation); Token test and Repetition from AAT. The comparison between A2 vs B2 showed also significant differences in Digit Span and ecological verbal comprehension from AAT. Large effect sizes were found in all these comparisons, except for the CPM and for Rey's 15 words Delayed recall in A1 vs B1 (medium effect size). The findings on the general cognitive functions and language abilities, globally confirmed our previous results (Panerai *et al.,* 2016) and those reported in the scientific literature (Bahar-Fuchs, Martyr, Goh, Sabates, & Clare, 2019). However, not all language components improved after g-ICA treatment, but only repetition, and sentences and ecological comprehension. Given the relevant role of the verbal language in mediating interpersonal relationships, these results take on undoubted importance, probably because our approach included specific language tasks, as well as a continuous exposure to verbal language, which was the principal vehicle of communication between the patients as well as patients and mediator.

The effectiveness of the cognition-based interventions on delayed memory and executive functions is less evident in the scientific literature (Wang, Yu, Wang, Tan, Meng, & Tan, 2014); in our study both frontal functioning (FAB), and verbal and non-verbal delayed recall (Rey's 15 words and Rey's Complex figure, respectively) significantly improved. In contrast, the short-term memory (verbal, digit and visuo-spatial span) did not increase. This might be because the delayed memory tests were preceded by a learning phase (5 repetitions of the list of 15 words, and copy of the complex figure), instead in the span test an immediate repetition was required. This specific result leads to underline the crucial importance of learning materials to be recalled for patients with NCDs; on the other hand, the clear weakness of spontaneous memory, especially the recall of vocal stimuli, was also highlighted. Another result of our study was the increased performance of selective attention (Digit cancellation). This can be considered an important finding since attention, memory and executive functioning are the cognitive functions that first deteriorate in dementia (Traykov, Rigaud, Cesaro, & Boller, 2007).

In contrast to what has been reported in the literature (Bahar-Fuchs *et al*., 2019), in our study the improvements obtained at the end of the first g-ICA treatment were not maintained in the medium-term (from 3 to 12 months), except for the ecological comprehension. Therefore, a worsening of cognitive performance was clear in the absence of treatment.

In summary, an initial improvement in cognitive performance after the first g-ICA treatment was seen, followed by a cognitive loss in the absence of treatment, and a recovery during the second administration of g-ICA intervention. However, the condition of the patients in A2 was like that shown in A1, even if the scores obtained in some tests (MMSE, MODA, Memory reproduction of Rey's Complex Figure, and Digit Span) were lower than those obtained in A1. In our study the MODA and the MMSE, as measures of global cognitive functions, appeared to be more efficient than MoCA or CPM to detect cognitive deterioration over time. The cognitive status of the patients in B2 was like that in B1; in addition, it appeared better (MoCA, CPM, FAB, Delayed Recall of the 15 Rey's words, Memory reproduction of Rey's Complex Figure, and Digit Cancellation) or similar (all the other measures) than the one shown in A1. Therefore, after a year, following a second g-ICA treatment, an improvement in some cognitive abilities and the maintenance of others were clear. Consequently, we might state that g-ICA is able to counteract the natural tendency to loss of cognitive skills, typical of NCD patients.

Our study presents, however, some strengths and some limitations. Among the strengths we can include the use of a large neuropsychological battery, to demonstrate the specific effects of the intervention, and the sustainability of our approach. According to some authors, the multi-component interventions are very time-consuming and cost intensive (Lissek & Suchan, 2021). In our case, g-ICA was intensive, but short-lived (six weeks plus two weeks for the pre-and post-treatment assessments). It was implemented in an inpatient hospital setting funded by the Regional Health System. It represented an enrichment of the routine rehabilitation programs, as defined by the local regulations (Italian Government Essential Assistance Levels).

Another strength was the use of the mediation pedagogy and the errorless learning, and the group format, because they facilitated enhancement of motivation and removal of personal psychological barriers for engaging in treatment.

One of the main limitations was the small sample size of our group. The recruitment of a greater number of participants might allow to analyze the results obtained not only by the whole group, but also by m- and M-NCD separately. Thus, we might add information on possible differences in efficacy in the two clinical groups. Since g-ICA is a combined cognitive intervention, it is impossible to determine the relation between the strategies used and their specific effects.

A critical question related to the meaning of cognitive improvements (measured through neuropsychological tests) in daily life remains to be explored; some other measures on functional living skills and quality of life should be added in future research.

References

Alves, J., Magalhães, R., Machado, A., Gonçalves, O. F., Sampaio, A., & Petrosyan, A. (2013). Non-pharmacological cognitive intervention for aging and dementia: Current perspectives. *World Journal of Clinical Cases*, *1* (8), 233-241. https://doi.org/10.12998/wjcc.v1.i8.233.

American Psychiatric Association (2013). *Diagnostic and statistical manual of mental disorders* (*5th ed.*). Arlington, VA: American Psychiatric Publishing.

Avila, R., Bottino, C. M., Carvalho, I. A., Santos, C. B., Seral, C., & Miotto, E. C. (2004). Neuropsychological rehabilitation of memory deficits and activities of daily living in patients with Alzheimer's disease: a pilot study. *Brazilian Journal of Medical and Biological Research*, *37* (11), 1721-1729. https://doi.org/10.1590/s0100-879x2004001100018.

Bahar-Fuchs, A., Martyr, A., Goh, A. M., Sabates, J., & Clare, L. (2019). Cognitive training for people with mild to moderate dementia. *The Cochrane Database of Systematic Reviews*, *3* (3): CD013069. https://doi.org/10.1002/14651858.CD013069.pub2.

Basso, A., Capitani, E., & Laiacona, M. (1987). Raven's coloured progressive matrices: normative values on 305 adult normal controls. *Functional Neurology*, *2* (2), 189-194.

Bianchi, A., & Dai Prà, M. (2008). Twenty years after Spinnler and Tognoni: new instruments in the Italian neuropsychologist's toolbox. *Neurological Sciences: Official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology*, *29* (4), 209-217. https://doi.org/10.1007/s10072-008-0970-x.

Brazzelli, M., Capitani, E., Della Sala, S., Spinnler, H., & Zuffi, M. (1994). A neuropsychological instrument adding to the description of patients with suspected cortical dementia: the Milan overall dementia assessment. *Journal of Neurology, Neurosurgery, and Psychiatry, 57* (12), 1510-1517. doi: 10.1136/jnnp.57.12.1510.

Buschert, V., Bokde, A. L., & Hampel, H. (2010). Cognitive intervention in Alzheimer disease. *Nature Review Neurology, 6* (9), 508-517. https://doi.org/10.1038/nrneurol.2010.113.

Caffarra, P., Vezzadini, G., Dieci, F., Zonato, F., & Venneri, A. (2002). Rey-Osterrieth complex figure: normative values in an Italian population sample. *Neurological Sciences: Official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology, 22* (6), 443-447. https://doi.org/10.1007/s100720200003.

Carlesimo, G. A., Buccione, I., Fadda, L., Graceffa, A., Mauri, M., Lorusso Bevilacqua, G., & Caltagirone, C. (2002). Standardizzazione di due test di memoria per uso clinico: Breve Racconto e Figura di Rey. *Nuova Rivista di Neurologia, 12*, 1-13.

Carlesimo, G. A., Caltagirone, C., & Gainotti, G. (1996). The Mental Deterioration Battery: normative data, diagnostic reliability and qualitative analyses of cognitive impairment. The Group for the Standardization of the Mental Deterioration Battery. *European Neurology, 36* (6), 378-384. https://doi.org/10.1159/000117297.

Choi, J., & Twamley, E. W. (2013). Cognitive rehabilitation therapies for Alzheimer's disease: a review of methods to improve treatment engagement and self-efficacy. *Neuropsychology Review, 23* (1), 48-62. https://doi.org/10.1007/s11065-013-9227-4.

Cipriani, G., Bianchetti, A., & Trabucchi, M. (2006). Outcomes of a computer-based cognitive rehabilitation program on Alzheimer's disease patients compared with those on patients affected by mild cognitive impairment. *Archives of Gerontology and Geriatrics, 43* (3), 327-335. https://doi.org/10.1016/j.archger.2005.12.003.

Clare, L., & Woods, R. T. (2004). Cognitive training and cognitive rehabilitation for people with early-stage Alzheimer's disease: a review. *Neuropsychological Rehabilitation, 14* (4), 385-401. doi:10.1080/09602010443000074.

Dubois, B., Slachevsky, A., Litvan, I., & Pillon, B. (2000). The FAB: a Frontal Assessment Battery at bedside. *Neurology, 55* (11), 1621-1626. https://doi.org/10.1212/wnl.55.11.1621.

Feuerstein, R. (1999). *Mediated learning experience (MLE): theoretical, psychosocial and learning implications.* Tel Aviv: Freund Publishing House.

Field, A. (2005). *Discovering statistics using SPSS* (2nd ed.). London: Sage Publication, Inc.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research, 12* (3), 189-198. https://doi.org/10.1016/0022-3956(75)90026-6.

Gates, N. J., & Sachdev, P. (2014). Is cognitive training an effective treatment for preclinical and early Alzheimer's disease? *Journal of Alzheimer's Disease, 42* (Suppl. 4), S551-S559. https://doi.org/10.3233/JAD-141302.

Giovagnoli, A., Manfredi, V., Parente, A., Schifano, L., Oliveri, S., & Avanzini, G. (2017). Cognitive training in Alzheimer's disease: a controlled randomized study. *Neurological Sciences: Official Journal of the Italian Neurological Society and the Italian Society of Clinical Neurophysiology, 38,* 1485-1493. doi: 10.1007/s10072-017-3003-9.

Hafdi, M., Hoevenaar-Blom, M. P., & Richard, E. (2021). Multi-domain interventions for the prevention of dementia and cognitive decline. *The Cochrane database of Systematic Reviews, 11* (11): CD013572. https://doi.org/10.1002/14651858.CD013572.pub2.

Hildreth, K. L., & Church, S. (2015). Evaluation and Management of the Elderly Patient Presenting with Cognitive Complaints. *Medical Clinics of North America*, *99* (2), 311-335. https://doi.org/10.1016/j.mcna.2014.11.006.

Hughes, C. P., Berg, L., Danziger, W. L., Coben, L. A., & Martin, R. L. (1982). A new clinical scale for the staging of dementia. *The British Journal of Psychiatry: the Journal of Mental Science*, *140*, 566-572. https://doi.org/10.1192/bjp.140.6.566.

Karssemeijer, E., Aaronson, J. A., Bossers, W. J., Smits, T., Olde Rikkert, M., & Kessels, R. (2017). Positive effects of combined cognitive and physical exercise training on cognitive function in older adults with mild cognitive impairment or dementia: A meta-analysis. *Ageing Research Reviews*, *40*, 75-83. https://doi.org/10.1016/j.arr.2017.09.003.

Katz, S., Downs, T. D., Cash, H. R., & Grotz, R. C. (1970). Progress in development of the index of ADL. *The Gerontologist*, *10* (1), 20-30. https://doi.org/10.1093/geront/10.1_part_1.20.

Langa, K. M., & Levine, D. A. (2014). The diagnosis and management of mild cognitive impairment: a clinical review. *JAMA*, *312* (23), 2551-2561. https://doi.org/10.1001/jama.2014.13806.

Lawton, M. P., & Brody, E. (1969). Assessment of older people: Self-monitoring and instrumental activities of daily living. *Gerontologist*, *9* (3), 179-186. doi: 10.1111/j.1532-5415.1983.tb03391.x.

Lissek, V., & Suchan, B. (2021). Preventing dementia? Interventional approaches in mild cognitive impairment. *Neuroscience and Biobehavioral Reviews*, *122*, 143-164. https://doi.org/10.1016/j.neubiorev.2020.12.022.

Loewenstein, D. A., Acevedo, A., Czaja, S. J., & Duara, R. (2004). Cognitive rehabilitation of mildly impaired Alzheimer disease patients on cholinesterase inhibitors. *The American Journal of Geriatric Psychiatry: Official Journal of the American Association for Geriatric Psychiatry*, *12* (4), 395-402. https://doi.org/10.1176/appi.ajgp.12.4.395.

Luzzatti, C., Willmes, K., & De Blaser, R. (1996). *AAT – Aachener Aphasie Test. Italian Version.* Firenze: Giunti Organizzazioni Speciali.

Na, R., Yang, J. H., Yeom, Y., Kim, Y. J., Byun, S., Kim, K., & Kim, K. W. (2019). A Systematic Review and Meta-Analysis of Nonpharmacological Interventions for Moderate to Severe Dementia. *Psychiatry Investigation*, *16* (5), 325-335. https://doi.org/10.30773/pi.2019.02.11.2.

Nasreddine, Z. S., Phillips, N. A., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., Cummings, J. L., & Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *Journal of the American Geriatrics Society*, *53* (4), 695-699. https://doi.org/10.1111/j.1532-5415.2005.53221.x.

Olazarán, J., Muñiz, R., Reisberg, B., Peña-Casanova, J., del Ser, T., Cruz-Jentoft, A. J., Serrano, P., Navarro, E., García de la Rocha, M. L., Frank, A., Galiano, M., Fernández-Bullido, Y., Serra, J. A., González-Salvador, M. T., & Sevilla, C. (2004). Benefits of cognitive-motor intervention in MCI and mild to moderate Alzheimer disease. *Neurology*, *63* (12), 2348-2353. https://doi.org/10.1212/01.wnl.0000147478.03911.28.

Olazarán, J., Reisberg, B., Clare, L., Cruz, I., Peña-Casanova, J., Del Ser, T., Woods, B., Beck, C., Auer, S., Lai, C., Spector, A., Fazio, S., Bond, J., Kivipelto, M., Brodaty, H., Rojo, J. M., Collins, H., Teri, L., Mittelman, M., Orrell, M., Feldman, H. H., & Muñiz, R. (2010). Nonpharmacological therapies in Alzheimer's disease: a systematic review of efficacy. *Dementia and Geriatric Cognitive Disorders*, *30* (2), 161-178.

Orsini, A., Grossi, D., Capitani, E., Laiacona, M., Papagno, C., & Vallar, G. (1987). Verbal and spatial immediate memory span: normative data from 1355 adults and 1112 children. *Italian Journal of Neurological Sciences*, *8* (6), 539-548. https://doi.org/10.1007/BF02333660.

Panerai, S., Tasca, D., Musso, S., Catania, V., Ruggeri, F., Raggi, A., Muratore, S., Prestianni, G., Bonforte, C., & Ferri, R. (2016). Group Intensive Cognitive Activation in Patients with Major or Mild Neurocognitive Disorder. *Frontiers in Behavioral Neuroscience*, *10*: 34. https://doi.org/10.3389/fnbeh.2016.00034.

Raggi, A., Iannaccone, S., Marcone, A., Ginex, V., Ortelli, P., Nonis, A., Giusti, M. C., & Cappa, S. F. (2007). The effects of a comprehensive rehabilitation program of Alzheimer's Disease in a hospital setting. *Behavioural Neurology*, *18* (1), 1-6. https://doi.org/10.1155/2007/782959.

Sitzer, D. I., Twamley, E. W., & Jeste, D. V. (2006). Cognitive training in Alzheimer's disease: a meta-analysis of the literature. *Acta Psychiatrica Scandinavica*, *114* (2), 75-90. https://doi.org/10.1111/j.1600-0447.2006.00789.x.

Spinnler, H., & Tognoni, G. (1987). *Standardizzazione e taratura italiana di test neuropsicologici.* Milano: Masson Italia Periodici.

Talassi, E., Guerreschi, M., Feriani, M., Fedi, V., Bianchetti, A., & Trabucchi, M. (2007). Effectiveness of a cognitive rehabilitation program in mild dementia (MD) and mild cognitive impairment (MCI): a case control study. *Archives of Gerontology and Geriatrics*, *44* (Suppl. 1), 391-399. https://doi.org/10.1016/j.archger.2007.01.055.

Traykov, L., Rigaud, A. S., Cesaro, P., & Boller, F. (2007). Le déficit neuropsychologique dans la maladie d'Alzheimer débutante [Neuropsychological impairment in the early Alzheimer's disease]. *L'Encephale*, *33* (3 Pt 1), 310-316. https://doi.org/10.1016/s0013-7006(07)92044-8.

Vandepitte, S., Van Den Noortgate, N., Putman, K., Verhaeghe, S., Faes, K., & Annemans, L. (2016). Effectiveness of Supporting Informal Caregivers of People with Dementia: A Systematic Review of Randomized and Non-Randomized Controlled Trials. *Journal of Alzheimer's Disease: JAD*, *52* (3), 929-965. https://doi.org/10.3233/JAD-151011.

Wang, C., Yu, J. T., Wang, H. F., Tan, C. C., Meng, X. F., & Tan, L. (2014). Non-pharmacological interventions for patients with mild cognitive impairment: a meta-analysis of randomized controlled trials of cognition-based and exercise interventions. *Journal of Alzheimer's Disease: JAD, 42* (2), 663-678. https://doi.org/10.3233/JAD-140660.

Yorozuya, K., Kubo, Y., Tomiyama, N., Yamane, S., & Hanaoka, H. (2019). A Systematic Review of Multimodal Non-Pharmacological Interventions for Cognitive Function in Older People with Dementia in Nursing Homes. *Dementia and Geriatric Cognitive Disorders, 48*, 1-16. https://doi.org/10.1159/000503445.