Original Article

Effects of creative expression program on the event-related potential and task reaction time of elderly with mild cognitive impairment

Junyu Zhao [a], Hong Li [b, *], Rong Lin [a], Minzhi Xie [c], Yinzhou Wang [c], Huiying Chen [d]

[a] School of Nursing, Fujian Medical University, Fuzhou, China
[b] Department of Nursing, Fujian Provincial Hospital, Fuzhou, China
[c] Department of Neurology, Fujian Provincial Hospital, Fuzhou, China
[d] Center of Patients Admission and Discharge Service, Fujian Provincial Hospital, Fuzhou, China

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ABSTRACT

Objectives: This study aimed to evaluate the effects of a 16-week creative expression intervention program (CrExp) on the event-related potential (ERP) and task reaction time in older individuals with mild cognitive impairment (MCI).
Methods: This study is a randomized controlled clinical trial conducted in the Memory Center of Fujian Provincial hospital. Thirty-six MCI patients were randomly distributed into two groups. One group underwent a 16-week creative expression program (CrExp, $n = 18$) and the other performed as a control group (CG, $n = 18$) by general social activities. The amplitude and latency of ERP-P300 from the central (Cz), parietal (Pz), frontal (Fz) cortices and task reaction time (RT) were assessed at baseline, post-interventi on, and 24-week follow-up.
Results: The CrExp group showed greater differences than CG of P300 latency in Cz ($F = 4.37$, $P = 0.015$), Pz ($F = 2.78$, $P = 0.009$), Fz ($F = 6.45$, $P = 0.031$) brain area after 16 weeks of intervention and in Fz ($F = 3.23$, $P = 0.028$), Cz ($F = 3.79$, $P = 0.024$), and Pz ($F = 5.60$, $P = 0.036$) at 24 weeks follow-up. Also, we analyzed the task reaction time between two groups and found that a shorten reaction time at post-intervention ($F = 4.47$, $P = 0.011$) and 24 weeks follow-up ($F = 3.12$, $P = 0.007$) in the CrExp group. However, there was no difference in P300 amplitude in either brain area between the two groups.
Conclusion: The electrophysiological results of the creative expression cognitive therapy group were more obvious than those of the general cognitive therapy group, and the latency and task reaction time may be considered as supported parameters in diagnosing the effects during non-drug therapy intervention in clinical practice.

What is known?

- Cognitive intervention is the most common and effective non-pharmaceutical therapy in patients with mild cognitive impairment.
- The event-related potential (ERP) P300 has been used in detecting the changeable of neuro-electrophysiology during cognitive processing.

What is new?

- The task reaction time is shortened following the period of the creative expression program.
- The P300 latency has been proved as supported parameters during the specific cognitive therapy program.

1. Introduction

Mild cognitive impairment (MCI) is known as a transitional phase or stage between normal aging and dementia. It is considered to be a series of the cognitive problem caused by early progressive degeneration or deterioration of brain function [1,2]. As MCI is without symptoms at an early stage of the disease, and, there

has been no efficient drug up to date, numbers of people suffer from undiagnosed MCI were delaying effective preventive treatment. The non-pharmaceutical therapies have proven effective in improving cognitive, independent functioning, and psychological health outcomes [3,4]. Nevertheless, only a few MCI patients who develop Alzheimer's disease (AD) receive timely administration of cognitive therapy or intervention.

The benefits of non-pharmaceutical cognitive intervention in improving cognitive function in old adults with MCI or dementia have been wildly reported [5–7]. Novel cognitive intervention programs such as timeslips build upon humanities and art therapy illustrated the positive effects in the target population [8,9]. The creative expression therapy (CrExp), which is based on the concepts of the timeslips program, suggested that the engaging nature of this group-centered activity may specifically benefit patients emotionally and improve communication skills and memory in older adults with AD or dementia [10,11]. It mainly involves five steps of functional tasks related to the presentation of a picture, including the topic of the picture, the background scenery, the development of a story, the actions of the leading character, and the ending of the story. The details of this CrExp program have been reported in our previous publications [12].

The event-related potentials (ERPs) are one of the most useful tools in detecting the neuroelectrophysiological changes in the brain during cognitive processing [13,14]. Due to objectivity and noninvasiveness, it is often used in spectating cerebral electrophysiological changes involved in specific cognitive functions of brain areas. The P300 is the most noteworthy cerebral wave reflected in the process from receiving stimulus to primary cognitive information processing. Some studies have found any significant differences in cognitive performance during a sustained task between MCI patients and controls [15–17]. Given the positive effects of non-drug cognitive interventions, it is necessary to explore the P300 of creative expression cognitive therapies or general cognitive activities.

This study aimed to characterize the differences in P300 after conducting the CrExp or general cognitive intervention in MCI patients. We hypothesized that CrExp participants have prolonged P300 latency and/or a reduced amplitude, and shorten reaction time were as expected outcomes after 16 weeks and at 24-week follow-up.

2. Materials and methods

2.1. Study design

This study is a simple-randomized clinical trial which is conducted in the Memory Center of Fujian Provincial Hospital, China. The patients were allocated to either the Creative expression program (CrExp) or the control group (CG). The study was conducted a total of 25 sessions over 16 weeks.

2.2. Participants and sample size

36 older adults who met the following inclusion criteria for MCI were included in the study [18]: 1) memory/cognitive issue reported by the individual themselves or their caregivers within the past year; 2) clinical reports indicating suspected cognitive deterioration by Diagnostic and Statistical Manual of Mental Disorders (DSM-IV, 4th Edition); 3) objective cognitive weakening in a single or higher number of domains as shown by neuropsychological evaluations (MoCA) [19]; 4) ability to take care of oneself or perform activities of daily living normally. The exclusion criteria included: 1) cognitive dysfunction caused by a known factor; 2) clinical depression or anxiety; 3) medical history of brain lesions,

psychotropic substance/drug abuse, medical reports indicating comorbidities linked with deterioration in cognitive function; 4) administered medications that may affect cognitive function.

2.3. Instruments

The NDI-092 evoked potentiometer was used to record and analyze various indicators of brainstem auditory ERP-P300 of the subjects. Each participant was seated in a comfortable chair and was performed in a sound-attenuated room with a warm light. According to the 10/20 international system, the electrode was continuously recorded at the central (Cz), parietal (Pz), frontal (Fz) cortices sites. The auditory oddball paradigm consisted of a series of standard tones (500 Hz) and deviant tones (2,000 Hz) binaurally through a headset. The sound level for each tone was 85 dB, with a duration of 100 ms and inter-stimulus-interval (ISI) of on average 1,600 ms. The deviant tones made up 20% of the presentations and the test lasted approximately 10 min. All the participants were instructed to press the button as accurately and quickly as possible when they heard the deviant sounds. The participants performed the pre-test first to make sure they have understood the task. The P300 latency (μV) and amplitude (ms) are significant factors used for analyzing ERP results. Also, the reaction time (ms) was defined as the length between hearing the deviant tone and pressing the button accurately.

2.4. Procedure of data collection

Data were collected over 24 weeks. After admission to the memory center, all participants have signed informed consent and ensured his eligibility for the entire study. The demographic data and MoCA score were collected as part of the baseline information for 30 min personally interviewed before the intervention section in the consulting room. The research was approved by the ethical committee of the hospital and was registered in the Chinese Clinical Trials Registry (Trial registration number: ChiCTR-ONN-16007776).

The CrExp program involved creative storytelling activities facilitated by a group of professional therapists. Each session lasted for 1 h and included: a warm-up interaction game (5–10 min), drawing period (10 min), core storytelling activity (30 min), discussion (5–10 min), conclusion (5 min).

The CG performed standard social activities facilitated by a group of social workers, nursing specialists, and physicians. Each session included 10 min of body-relaxing exercises, followed by 30 min of core cognitive strategy items (including an activity, a game, or a course), which required that certain tasks be completed. More process information can be found in our previous publication [12].

2.5. Data analysis

The STATA 12.0 (StataCorp, College Station, TX) software was used for statistical calculations. Fisher's exact test, an independent sample t-test, or a Chi-square test were appropriately used to compare group demographic differences as well as all quantitative data metrics. Repeated measures of ANOVA were used to evaluate the intervention effects over time from baseline to 16 weeks, and from baseline to 24 weeks follow-up. The between-group differences at post-intervention and 24 weeks follow-up, were performed by ANCOVA with baseline age, education, and MoCA score as covariates. Bonferroni analyses were evaluated when significant between-group differences were revealed. Missing data were replaced for an average value from the individual's available data (from baseline session to follow-up session). All the results were considered to be significant at $P < 0.05$.

2.6. Ethical consideration

All of the participants continued with their routine medical care or out-patient follow-up. The study protocol was conducted according to the Helsinki Declaration and was approved by the ethics committee of Fujian Provincial Hospital (No. K2016-003-01).

3. Results

3.1. Demographic and neuropsychological assessment

Table 1 showed that there were not significant statistical differences in demographics (ranging from $P = 0.290$ to $P = 0.986$) or neuropsychological test outcome (MoCA score, $P = 0.193$) between the CrExp (21.93 ± 2.12) and CG group (21.67 ± 2.36) before the study initiated. A total of 36 participants (18 MCI patients were examined in each group) comprised the sample. Within 16 weeks, 25 sessions were carried out at the same time for both groups.

3.2. The event-related potential outcome

Table 2 shows the results of P300 latency and amplitude between the CG and CrExp. After 16 weeks of intervention, the CrExp group showed greater differences than CG in latency on Cz ($F = 4.37$, $P = 0.015$), and Pz ($F = 2.78$, $P = 0.009$). When education and MoCA scores were entered as covariates, there was also a significant difference between groups in latency on Fz ($F = 6.45$, $P = 0.031$). Moreover, at 24 weeks follow-up, significant group differences remained in latency Fz ($F = 3.23$, $P = 0.028$), Cz ($F = 3.79$, $P = 0.024$), and Pz ($F = 5.60$, $P = 0.036$). There were no obvious differences in amplitude at post-intervention and at 24 weeks follow-up. Meanwhile, the results of repeated measures ANOVA showed significant differences in the CrExp group in latency Fz ($F = 3.13$, $P = 0.039$), Cz ($F = 5.11$, $P < 0.01$) and Pz ($F = 6.78$, $P < 0.001$) at post-intervention and in latency Fz ($F = 2.33$,

$P = 0.041$), Cz ($F = 2.41$, $P = 0.047$), Pz ($F = 2.19$, $P = 0.049$) at 24 weeks follow-up. Contrarily, there were no significant differences in all indexes in CG.

3.3. Task reaction time outcome

There was no significant group difference in the baseline reaction time between CG (601.42 ± 33.23) and CrExp (589.17 ± 38.16, $P = 0.372$). During the creative expression program, repeated measures analysis (interaction effect group x time) revealed a significant decrease at post-intervention ($F = 4.47$, $P = 0.011$) and 24 weeks follow-up ($F = 3.12$, $P = 0.007$) compared to the CG. After the intervention, the average reaction time of the CG group was 594.51 ± 33.90 ms, whereas that of the CrExp group was found to be 454.67 ± 33.88 ms, and the intragroup analysis showed that the CrExp group decreased reaction time ($F = 16.36$, $P = 0.001$). Similarly, at 24 weeks follow-up, the mean reaction time of the CG group was 597.45 ± 39.06 ms, whereas the CrExp group was found to be 465.67 ± 37.89 ms, and the intragroup analysis showed that the CrExp group decreased reaction time ($F = 5.23$, $P = 0.029$). (Fig. 1).

4. Discussion

The present study revealed that creative expression participants had significantly decrease latency and higher reaction time than controls on the ERP test. The poorer P300 performance exhibited by the control group may be associated with cognitive intervention.

Our findings showed that the difference in latency between CrExp and CG at post-intervention. This supports the view of non-pharmaceutical therapy in MCI as a consequence of the cognitive improvement, or an influencing factor. There are two principal electrophysiological markers of P300: latency and amplitude, which have been considered as objective parameters of cognitive processing [20]. Using the P300 may detect the response of specific cognitive activities in several areas involving the temporal, frontal, parietal lobes, and hippocampus of brain areas. These areas are related to the encoding and processing of memory, as well as even the language and executive of expressive activities reprocessing. Furthermore, the difference in latency result between the two groups remained even after the 24 weeks follow-up period. This may indicate that, within a given time frame, creative expression cognitive activity has a sustained effect on the effects of brain cognitive remodeling, helping to monitor the treatment progression and development of patients with MCI.

In our study, the ERP reaction time was found to be shortened in the CrExp group after post-intervention. This support is consistent with our expectations. In terms of the reaction time of P300, task-familiar participants processed all stimuli faster than task-unfamiliar participants [21]. The reaction time of behavioral is key information for concealing the probe stimuli [22] when the cortical activity is required and its reaction time is largely determined by the amount and strength of intervention [23]. For the electrophysiology profile, the symptom of cognitive deficiency becomes more and more obvious with the increase of reaction time. According to the result mentioned facts, it could be suggested that CrExp have a shorten P300 reaction time, which represents a reduced cognitive processing period. Some studies have shown that RT-related activity reflects task-specific processes that are periodically-engaged, particularly during less demanding tasks [24,25]. Furthermore, the effect was still found to exist in reaction time at the 24-week follow-up. This further indicates that the CrExp program might trigger the persistent effects of an individual's endogenous cognitive neurobiological response and promotes the self-compensation of cognitive damage.

Table 1
Baseline demographic and neuropsychological evaluation of participants.

Characteristics	CrExp (n = 18)		CG (n = 18)		χ^2	P
	n	%	n	%		
Age (years)						
60–70	8	44.5	7	38.9	2.13	0.584
71–80	8	44.5	9	50		
>80	2	11.1	2	11.1		
Gender						
Male	8	44.5	10	55.6	2.57	0.290
Female	10	55.5	8	44.4		
Education level						
Primary	1	5.5	2	11.1	–	0.473*
Secondary	13	72.3	12	66.7		
Tertiary	4	22.2	4	22.2		
Social status						
Living with family	15	83.3	14	77.8	−0.12	0.834
Alone	3	16.7	4	22.2		
Exercise per day (min)						
<30	6	33.3	5	27.8	–	0.972*
30–60	10	55.6	12	66.7		
>60	2	11.2	1	5.5		
Ambulatory level						
Unaided	17	94.5	18	100	–	0.986*
With stick	1	5.5	0	0		
Medical History						
Hypertension	8	44.5	7	38.9	−0.43	0.637
Diabetes	12	66.7	13	72.3		
Dyslipidemia	4	22.2	3	16.7		

Note: * Fisher exact test. CrExp = intervention group. CG = control group.

Table 2
Results of P300 latency and amplitude between control group and creative expression group (*Mean ± SD*).

ERP P300	Group	Baseline (Week 0)	Post-intervention (Week 16)	Follow-up (Week 24)	Postintervention (Week 16)				Follow-up (Week 24)			
	CG ($n = 18$)				Group$^\Delta$		Time$^\#$		Group$^\Delta$		Time$^\#$	
	CrExp ($n = 18$)				F	P	F	P	F	P	F	P
Latency (ms)												
Fz	CrExp	398.87 ± 26.05	368.57 ± 21.25	363.71 ± 23.04	6.45	0.031*	3.13	0.039*	3.23	0.028*	2.23	0.041*
	CG	394.41 ± 17.55	386.48 ± 23.87	388.57 ± 24.53			2.29	0.057			0.67	0.350
Cz	CrExp	408.80 ± 37.97	367.57 ± 34.18	380.90 ± 26.58	4.37	0.015**	5.11	<0.001**	3.79	0.024*	2.41	0.047*
	CG	407.11 ± 37.76	402.85 ± 34.01	414.15 ± 24.02			4.63	0.431			- 1.10	0.772
Pz	CrExp	386.17 ± 21.33	359.80 ± 25.79	360.93 ± 23.25	2.78	0.009*	6.78	<0.001**	5.60	0.036*	2.19	0.049*
	CG	387.06 ± 20.32	373.36 ± 24.40	376.45 ± 24.33			1.98	0.363			1.76	0.438
Amplitude (μV)												
Fz	CrExp	6.79 ± 1.25	7.05 (4.82,10.65) ^	7.10 (4.10,9.76) ^	0.51	0.087	−0.45	0.640	1.06	0.917	- 1.14	0.630
	CG	6.51 ± 1.28	6.97 ± 2.30	6.20 ± 2.52			−1.57	0.437			0.96	0.817
Cz	CrExp	5.41 ± 1.03	5.78 (3.19,8.62) ^	5.57 (2.76,9.13) ^	0.18	0.391	−1.22	0.571	0.05	0.520	- 0.68	0.528
	CG	5.70 ± 1.08	6.01 ± 2.38	5.98 ± 2.53			−1.24	0.508			- 1.06	0.677
Pz	CrExp	6.92 ± 1.14	7.18 (4.61,10.75) ^	7.13 (3.62,11.41) ^	0.57	0.104	−0.23	0.850	0.31	0.136	- 1.21	0.523
	CG	7.14 ± 1.77	6.96 ± 2.40	7.03 ± 3.17			0.77	0.913			- 0.15	0.906

Note: ^ Median (P$_{25}$, P$_{75}$); $^\#$ANOVA; $^\Delta$ANCOVA; *P < 0.05; **P < 0.01. ERP = event-related potential. CrExp = intervention group. CG = control group.
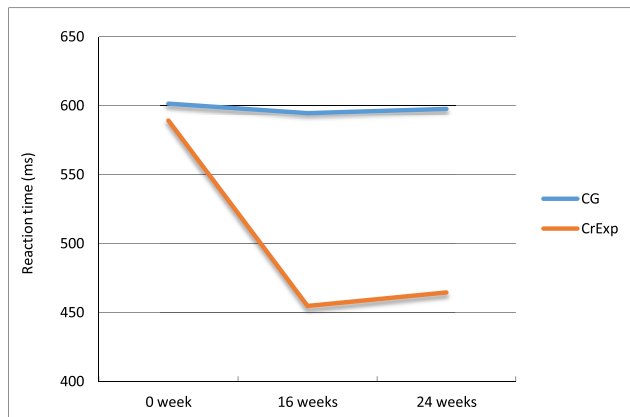

Fig. 1. Event-related potential P300 reaction time changes (interaction level group x time). Lines represent decreased reaction time at pre-intervention, post-intervention and 24 weeks follow-up for CG and CrExp group. CrExp= intervention group. CG=control group.

However, the present study revealed that CrExp had no significant differences amplitude than CG after intervention or follow-up. Meta-analysis has reported that the P300 amplitude of MCI patients was lower than that of the healthy CG and even lower for the AD population [26]. The divergence among our studies and others might be due to the selection of target populations, also maybe because both groups received different levels of cognitive intervention. Most of the studies were reported the amplitude comparison between MCI/AD and normal healthy [27], or young and elderly individuals [28]. Thus, we deem that the amplitude varieties in existing non-drug cognitive intervention may not correspond to a clinically relevant cognitive deterioration or improvement to some degree. This would be further explored in our future researches.

The benefits of implementing the CrExp program among MCI patients is demonstrated in this study, however, there exist various shortcomings. First, the small sample size of the MCI patients employed in this study, may attenuate the statistical analyses, predominantly affecting the nonsignificant findings. Also, participants of both experimental groups comprised mixed categories, including amnestic MCI patients and a smaller proportion of non-amnestic individuals. Future studies in this field should emphasize the certification of the effect of the CrExp program involving a larger homogenous sample size. Furthermore, recruitment of convenient samples was another shortcoming of this study. The MCI patients were employed from a geriatric hospital and thus were aware of their memory failure as compared to individuals who might not seek medical advice.

5. Conclusion

In summary, the study results have demonstrated that the CrExp program shows improvement in P300 latency and reaction time, which may be considered as a support parameter in the diagnosis of effects on non-drug therapy intervention in clinical practice.

CRediT authorship contribution statement

Junyu Zhao: Conceptualization, Writing - original draft, Methodology, Funding acquisition. **Hong Li:** Supervision, Project administration, Funding acquisition. **Rong Lin:** Investigation, Data curation. **Minzhi Xie:** Visualization, Investigation, Software. **Yinzhou Wang:** Resources, Validation. **Huiying Chen:** Resources, Validation.

Declaration of competing interest

No conflicts of interest are reported in this work.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.ijnss.2020.12.005.

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