

The effect of creative expression program in neurocognitive networks performance measured by task and resting-state functional MRI

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ABSTRACT

Background: The current study examined the effects of a 16-week creative expression program on brain activity during a story creating task and resting-state functional network connectivity in mild cognitive impairment (MCI) adults.

Method: Thirty-six MCI adults were allocated to either the creative expression program (CrExp, n = 18) or control group (CG, n = 18). Before and after intervention, all participants were scanned with functional magnetic resonance imaging (fMRI) during story creating task performance and a resting state. The two-group comparison was calculated between the blood oxygenation level-dependent (BOLD) signal changes for each cluster to investigate the differences in fMRI activation and functional connectivity (FC) between two groups.

Results: Task activation analyses showed an increase in the right anterior cingulate gyrus (ACG), right medial frontal gyrus (MFG), right lentiform nucleus (LN), left hippocampus (HIP), left middle occipital gyrus (MOG), and left cerebellum posterior lobe (CPL) ($p < 0.05$). Story creating performance improvements were associated with greater activation in the left HIP region. Resting-state functional connectivity (FC) between left HIP and certain other brain areas shown a significant interaction of creative expression group versus control group. Moreover, connectivity between the right angular gyrus (ANG), right inferior temporal gyrus (ITG), right superior occipital gyrus (SOG), left ANG, and left MFG were related to improved cognitive performance ($p < 0.05$).

Conclusion: These data extend current knowledge by indicating that the creative expression program can improve cognitive activation in MCI, and these enhancements may be related to the neurocognitive network plasticity changes induced by creative expression training.

Key words: mild cognitive impairment, magnetic resonance imaging, functional network connectivity, brain activity, aged care

Introduction

Mild cognitive impairment (MCI), the most common early dementia clinical manifestation, is characterized by significant complaining of memory, language, executive functioning, attention, and visual-spatial abilities. Currently, there is little

effective recognition and treatments in patients at high risk of dementia, and some potential preventive medications currently being tested had certain side effects. Although disease progress slowly, patients may suffer a long unstable cognitive state, but the specific pathological changes appeared during this period may be a prediction marker of developing dementia (Shim *et al.*, 2017). In the early stage of cognitive impairment, the benefits of cognitive intervention in improving cognitive function in old adults with MCI or dementia have been widely reported (Chan *et al.*, 2017; Marlats *et al.*, 2019; Savulich

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et al., 2017; Steinbeisser *et al.*, 2020). Novel cognitive intervention therapy such as TimeSlips showed positive effects in target population (Kim *et al.*, 2020; Lin *et al.*, 2020). The creative expression program (CrExp), which is based on the concepts of art therapy, showed that when the patients were immersing in a group-centered activity, it may specifically benefit one's emotional expression and communication skills in older adults with AD or dementia (Shimada *et al.*, 2017; Vigliotti *et al.*, 2019). The program primarily consists of five steps of executive tasks related to picture presentation, including topic naming, scenery description, story pitch, character features, and the tale ending. All the elements like lines, numbers, symbols, graphs, and colors can be used for drawing the feelings or emotions in order to storytelling vividly during the group activities.

The brain regions supporting cognitive intervention show great correlation with the target functional regions affected in the early process of creative cognitive express processing. In the early stage of AD, exercise training may preserve neuronal plasticity and increase brain activity in enhanced neurocognitive function in older adults (Haeger *et al.*, 2020). Several neuroimaging studies have confirmed that the aerobic exercise has neuroprotective effects and associated with neuronal reserve (Chen *et al.*, 2020; Hsu *et al.*, 2018). Regions of the right frontal, parietal, and temporal are robustly activated when executing control training. Activity in this region is augmented for selective attention relative to predict behavioral outcome (Jor'dan *et al.*, 2017). Free recall performance also activates temporal pole and nucleus accumbens region, with some unique memory-specific connections (Coynel *et al.*, 2017). Moreover, the frontoparietal cortex and visual regions activities are greatest when changing task sets (Lamichhane *et al.*, 2020). Non-pharmaceutical intervention as a complementary therapeutic method for treating cognitive decline in pre-dementia may improve the brain neurocognitive function network of the target population.

Functional magnetic resonance imaging (fMRI) combined with the targeted cognitive tasks brings a directly powerful technique to detect neurological potential deterioration related to cognitive dysfunction. In previous studies, the fMRI was used for tracing the internal strategic memory across the brain region and the functional brain activity during dynamic adaptive coding tasks or cognitive behavioral therapy processing in patients with impaired performance (McKenzie *et al.*, 2020; Qiao *et al.*, 2017). Another study has found that the hippocampus (HIP) plays an indispensable role in episodic memory in AD patients, by playing a critical role in successful memory retrieval and memory

consolidation process (Liechti *et al.*, 2019). However, few fMRI studies have focused on the activity and connections of creative expression on different brain regions in MCI patients. Hence, exploring the brain activity regions and connection status mainly affected in MCI patients may prove the mechanisms of how the creative expression achieves its therapeutic effects. In addition, the activation degree and connectivity strength of the target brain region should also be considered in order to properly study the actual effect of creative expression. In the current study, task-fMRI and resting-state fMRI were both used to investigate whether the creative expression program improved neurocognitive network functional plasticity in MCI adults. We compared the effects of 16-week (25 sessions) creative expression program on cognitive rehabilitation in MCI adults with the effects of a control condition with general social activities. In addition to completing an image task that measured functional network activation. We hypothesized that (a) MCI adults in the creative expression program group will exhibit more significant improvement in brain functional network connectivity than MCI adults in the control group; and (b) MCI adults in the creative expression program group will exhibit greater changes in the neurocognitive network (intrinsic brain activity and connectivity) than MCI adults in the control group.

Materials and methods

Participants

Neuropsychological screening and detailed medical records for eligibility were obtained in the Department of Geriatrics and Neurology service from September 2018 to May 2019. Forty-one participants met MCI inclusion criteria: (1) clinical records of probable MCI, as defined by the DSM-V (Luck *et al.*, 2017); (2) at least one domain cognitive impairment; and (3) no obvious impairment of daily living ability was reported. Exclusion criteria including: (1) cognitive dysfunction caused by depression or anxiety; (2) any cognitive declines related histories, like brain lesion, psychoactive substance abuse, or medical records; (3) taken medications that may affect cognitive function; and (4) contraindications to MRI, such as previous implantation with a metal device (e.g. pacemaker, arterial stent, aneurysm clamp, and dental implant).

All subjects underwent extensive neuropsychological assessment by a professional cognitive assessor at baseline. The assessment scales including Montreal Cognitive Assessment (MoCA) (Nasreddine *et al.*, 2005), the Digital Span Test (DST) (Gignac and Weiss, 2015), Activities of Daily Living

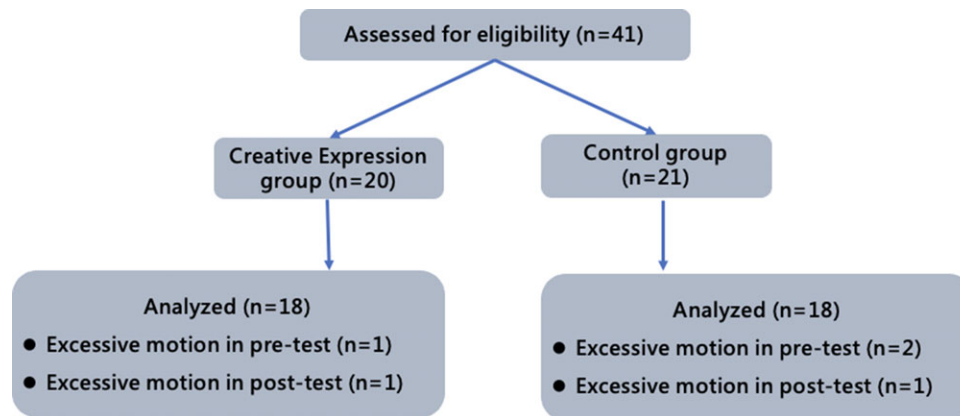


Figure 1. Flow diagram for participant enrollment.

scale (ADL) (Graf, 2008), Trail-Making Tests A and B (TMT-A, TMT-B) (Llinàs-Reglà *et al.*, 2017), Auditory Verbal Learning Test (AVLT) (Zhao *et al.*, 2012), and Category Verbal Fluency Test (Mok *et al.*, 2004) (CVFT). We used the STATA 12.0 (StataCorp, College Station, TX) for data analysis and compared the demographics at baseline by appropriate commands (Fisher's exact test, Chi-square test, or independent samples t-test). The level of statistical significance was set at $p < 0.05$ (two-tailed).

The project was registered in the Chinese Clinical Trials Registry and was approved by hospital ethics committee (No. K2018-003-01). Each participant has signed the informed consent before the research start.

Study design

Of the 41 patients met, some inclusion criteria and 5 patients were excluded due to the excessive motion. Each participant was scanned twice in the current study. MRI scanning in the creative expression program was performed as follows: task-processing scan during the intervention period (MRI 1) and a resting-state scan after completion of the 16-week creative expression program (MRI 2). The control group participants were scanned at the same time points. The flow diagram for participant enrollment is presented in Figure 1.

Intervention

This study utilized a 1:1 contemporaneous randomized, between-group design clinical trial. All the participants were randomized to either the group treated with creative expression program (CrExp) or the control group (CG). The study was conducted for a total of 25 sessions within 16 weeks. The CrExp program involved creative expression activities facilitated by a group of professional therapists. Each session lasted for 1 h and included a warm-up game (5–10 min), drawing (10 min), core storytelling

(30 min), discussion (5–10 min), and conclusion (5 min). The CG group performed standard social activities by social volunteers, nursing specialists, and physicians. Each session included 10 min of body-relaxing exercises, followed by 30 min of core cognitive strengthen items. More process information can be found in our previous publication (2021, Zhao *et al.*, 2018).

Story creating task

The story creating task requires storing information, gating information within one's mind, reorganized serial gist and details, and release associative thinking. The process is based on the storytelling group technique and also includes mind maps, the 5W1H dimensions (who, what, when, where, why, and how). Each story creating task included one image in random style (scenery, characters, animals, plants, etc.). The image consisted of a colorful image displayed at the center of a computer screen during the scanning processing. The first 30 s of the task were pre-scanning and adaptive, with the ready "story creating" as the stimulus displayed at the center of the screen, which prompted the participant to prepare to imagination. The task used an image displayed design (see Figure 2).

MRI data acquisition

Task-fMRI data acquisition

Participants underwent a scan to obtain high-resolution images of the whole brain (3T Siemens TIM Trio scanner) using the total imaging matrix. MRI scans were conducted at the Imaging Center for Affiliated Provincial Clinical Hospital of Fujian Medical University. Functional images were obtained using an echo-planar imaging (EPI) sequence with the following scan parameters: repetition time (TR), 2000 ms; echo time (TE),

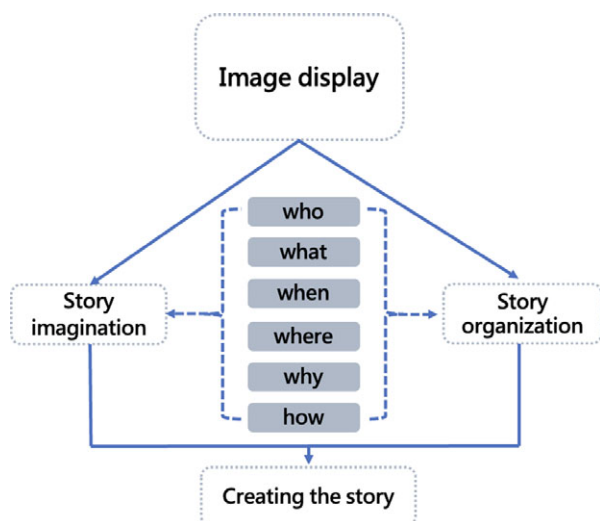


Figure 2. Design of the story creating task.

30 ms; gap, 1 mm; flip angle, 90 degrees; slice thickness, 3.0 mm; field of view, 200×200 mm; and inplane resolution, 64×64 . The data included 148 brain volumes with 31 axial slices. During the fMRI scans, all the participants were instructed to relax and remain as still as possible.

Resting-state fMRI image data acquisition

Participants were asked to close their eyes and avoid sleeping for the 9-min scan. A gradient-EPI sequence was acquired using the following fMRI parameters: TR/TE, 2000/3.30 ms; matrix size, 64×64 ; and slice thickness, 1.55 mm. The resting-state scan acquired 240 whole-head volumes over a total imaging time of 9 min.

MRI data preprocessing and analysis

Task-fMRI preprocessing and analysis

Functional image preprocessing and statistical analyses were conducted using Statistical Parametric Mapping (SPM12) (<https://www.fil.ion.ucl.ac.uk/spm/software>) and Resting-State fMRI Data Analysis Toolkit (REST) V1.8 (<http://www.restfmri.net/forum/REST>). The first five volumes were discarded to eliminate the nonequilibrium effects of magnetization and allow the participants to adapt to the EPI scanning environment. Subsequent functional images underwent the following preprocessing steps: slice-timing correction, realignment, co-registration, and New Segment + Diffeomorphic Anatomical Registration Through Exponentiated Lie algebra (DARTEL) with high-resolution structural scans. The DARTEL tool was used to compute transformations from an individual's native space to

Montreal Neurological Institute (MNI) coordinate space. The segmented blood oxygenation level-dependent (BOLD) volumes were normalized to standardized MNI space using the DARTEL template and resampled to 3-mm isotropic voxels. Finally, the normalized images were smoothed to a $9 \times 9 \times 9$ mm full-width at half-maximum (FWHM) using a Gaussian kernel.

Functional changes were analyzed using SPM12 concerning individuals and groups. Individual analysis: statistical parametric maps were computed for individual participants using the general linear model with separate hemodynamic basis response function modeling of MR signal responses for each participant. Statistical analyses were performed on a voxel wise basis across the whole brain, and the threshold was set at $p < 0.05$, combined with an individual voxel threshold of $p < 0.01$ and a cluster size > 200 voxels.

Resting-state fMRI preprocessing and analysis

We utilized DPARSFA advance edition (DPARSFA 5.2, <http://rfmri.org/DPARSFA>), which was based on SPM12 (<https://www.fil.ion.ucl.ac.uk/spm/software>) for the resting-state fMRI data analysis. Preprocessing comprised the following steps: 1) removal of the first eight functional volumes; 2) slice-timing correction; 3) three-dimensional motion correction; and 4) co-registration of individual's structural images to the functional images using a linear transformation, which were segmented into white matter, gray matter, and cerebrospinal fluid using a new segment algorithm in REST; 5) spatial normalization using the MNI template and resampling to $3 \times 3 \times 3$ -mm voxels; 6) linear detrending and nuisance signal removal (white matter, cerebrospinal fluid, global signal, 6-head motion parameters, 6-head motion parameters at one time point earlier, and the 12 corresponding squared items (Friston 24-parameter model) as covariates via multiple regressions; 7) spatial smoothing with a 4-mm FWHM Gaussian kernel; and 8) bandpass filtering (ranging from 0.01 to 0.01 Hz) to reduce the effects of low-frequency drift and high-frequency noise. In this study, we excluded four subjects according to the head motion criteria of a maximum spin (x, y, z) of $< 2.0^\circ$ and a maximum cardinal direction displacement (x, y, z) of < 2.0 mm. Seed-based, voxel-wise, whole-brain connectivity analysis was performed to the resting-state fMRI image data. Functional connectivity (FC) analyses between the seed point and all voxels of the whole-brain statistical parametric Z-maps for individual participants were computed by DPARSFA.

Table 1. Baseline demographics and neuropsychological findings

CHARACTERISTICS	CREXP GROUP (N = 18)	CG GROUP (N = 18)	P-VALUE
Age, years, [range/mean (SD)]	64–83/71.61 (5.38)	63–84/71.61 (5.86)	0.584 ^a
Gender, n (%), (female/male)	10 (55.6)/8 (44.4)	8 (44.4)/10 (55.6)	0.290 ^b
Education level, n (%), (illiterate/primary/secondary/tertiary)	0 (0)/1 (5.6)/13 (72.2)/4 (22.2)	0 (0)/2 (11.1)/12 (66.7)/4 (22.2)	0.473 ^b
Social status, n (%), (living with family/alone)	15 (83.3)/3 (16.7)	14 (77.8)/4 (22.2)	0.834 ^b
Exercise per day, n (%), (<30min/30 ~ 60min/> 60 min)	6 (33.3)/10 (55.6)/2 (11.1)	5 (27.7)/12 (66.7)/1 (5.6)	0.972 ^b
Ambulatory level, n (%), (unaided/with stick)	17 (94.4)/1 (5.6)	18 (100)/0 (0)	0.986 ^b
Medical history, n (%), (Hypertension/Diabetes/Dyslipidemia)	8 (44.4)/12 (66.7)/4 (22.2)	7 (38.9)/13 (72.2)/3 (16.7)	0.637 ^b
MoCA, score [mean (SD)]	21.93 (2.12)	21.67 (2.36)	0.193 ^a
NCSE, composite score [mean (SD)]	22.17 (1.84)	21.96 (1.88)	0.317 ^a
NCSE, normal domain [mean (SD)]	51.36 (11.91)	50.58 (12.13)	0.794 ^a
CVAULT totally recall, score [mean (SD)]	13.32 (1.87)	13.19 (1.93)	0.188 ^a
CVAULT delay recall, score [mean (SD)]	4.92 (1.35)	5.04 (1.03)	0.185 ^a
CVCVFT, score [mean (SD)]	9.67 (1.23)	9.45 (1.43)	0.227 ^a
DST, score [mean (SD)]	7.16 (1.33)	7.18 (1.35)	0.243 ^a
TMT-A, score [mean (SD)]	135.47 (33.60)	134.14 (32.67)	0.211 ^a
TMT-B, score [mean (SD)]	240.56 (12.11)	238.77 (13.92)	0.175 ^a

MoCA, Montreal Cognitive Assessment; NCSE, Neurobehavioral Cognitive Status Examination; CVAULT, Chinese Version Auditory Verbal Learning Test; CVCVFT, Chinese Version Category Verbal Fluency Test; DST, Digital Span Test; TMT-A, Trail Making Test-Part A; TMT-B, Trail Making Test-Part B; CrExp, intervention group; CG, control group.

^aIndependent-sample t-test.

^bFisher's exact test.

Statistical analysis

To investigate the differences between CrExp and CG changes in fMRI activation and FC, the BOLD signal changes in each reported fMRI cluster for the individual and the change scores were calculated for cognitive activation performance. Then, the two-group t-test was used to compare the differences of the between-group scores in task activation and resting connectivity.

Results

Participant characteristics

Participant demographic details are presented in Table 1. Two sample t-test revealed no significant statistical differences between the control and creative expression intervention groups in characteristics (range $p = 0.290$ – 0.986) or neuropsychological assessment results (range $p = 0.175$ – 0.794) at baseline, suggesting that the two groups have similar demographic backgrounds.

Results of task-fMRI

Whole-brain activation results from the group (creative expression intervention and control) by time (pretest and posttest) t-test revealed that the following regions showed a significant difference:

the right anterior cingulate gyrus (ACG) ($t = 4.77$, $p < 0.0001$), right middle frontal gyrus (MFG) ($t = 3.50$, $p = 0.0013$), right lentiform nucleus (LN) ($t = -4.59$, $p < 0.0001$), left hippocampus (HIP) ($t = 3.56$, $p = 0.0011$), left middle occipital gyrus (MOG) ($t = -5.27$, $p < 0.0001$), and left cerebellum posterior lobe (CPL) ($t = -4.36$, $p < 0.0001$). In all these regions, the creative expression program group showed a pattern of increasing activation after intervention, while the control group showed a stable pattern over time. For further details, see Table 2 and Supplement Figure 1. Besides, the left HIP showed a significant correlation between increased mean BOLD signal and improved behavioral performance in the task-fMRI.

Results of resting-state fMRI

The results we obtained from the task-fMRI analysis suggested that the cognitive performance improvements were attributable to the higher activation in the left HIP. We then examined the HIP-based voxel-wise connectivity in the whole brain. The following regions showed a significant group difference: the right angular gyrus (ANG) ($t = 6.09$, $p < 0.0001$), the right inferior temporal gyrus (ITG) ($t = 4.77$, $p < 0.0001$), right superior occipital gyrus (SOG) ($t = 3.02$, $p = 0.0048$), the left ANG ($t = 4.12$, $p = 0.0002$), and left MFG

Table 2. Regional brain activation changes caused by the creative expression program

PRIMARY REGIONS	BROADMANN'S AREA	SIZE (VOXELS)	MAX T-STATISTIC	MNI COORDINATES		
				X	Y	Z
R_Lentiform nucleus	13	136	-4.59	30	-12	3
L_Hippocampus	27/29	105	3.56	-9	-45	9
R_Anterior cingulate gyrus	32	72	4.77	-6	42	18
L_Middle occipital gyrus	19	118	-5.27	-18	-93	24
L_Cerebellum posterior lobe	18	114	-4.36	11	-89	27
R_Medial frontal gyrus	20	76	3.50	-6	38	30

The statistical threshold was set at $p < 0.05$ using the AlphaSim correction for multiple comparisons with a threshold of $p < 0.01$ at the voxel level and a minimum cluster size of 115 voxels. All coordinates are reported in the MNI format.

Table 3. Functional connectivity changes based on the seed of the left hippocampus altered by creative expression program

PRIMARY REGIONS	BROADMANN'S AREA	SIZE (VOXELS)	MAX T-STATISTIC	MNI COORDINATES		
				X	Y	Z
R_Superior occipital gyrus	19	85	3.02	47	-77	0
R_Inferior temporal gyrus	37	40	4.77	45	-69	3
R_Angular gyrus	40	121	6.09	36	-69	6
L_Angular gyrus	39	131	4.12	-36	-63	9
L_Middle frontal gyrus	48	144	4.60	-27	-60	12

The statistical threshold was set at $p < 0.05$ using the AlphaSim correction for multiple comparisons with a threshold of $p < 0.01$ at the voxel level and a minimum cluster size of 115 voxels. All coordinates are reported in the MNI format.

($t = 4.60$, $p < 0.0001$) (see Table 3 and Supplement Figure 2).

Discussion

Brain activity changes in the network activation pattern

These results show that brain activities increased during the story creating task in specific brain regions are considered to be part of measured performance in neurocognitive network, including the right ACG, right MFG, right LN, left HIP, left SOG, and left CPL in the creative expression group. Specifically, the ACG and MFG have been implicated in imaging and expression indicator (Gu *et al.*, 2020; Brockett *et al.*, 2020; Roet *et al.*, 2019), and the HIP is likely to be essential for episode memory encoding (Zeidman and Maguire, 2016; Bartsch and Wulff, 2015). Within the LN, creative expression-related increases were seen in these regions, which are involved in planning and execution of internal representation, perform tasks (Dong *et al.*, 2020) and image stimuli response (Hwang *et al.*, 2017). Previous observations suggested that

the occipital lobe was also affected by visual imagery and may be necessary for specific aspect of cognitive efficiency, such as perception executive control and neurofeedback (De Marco *et al.*, 2017; Anderson *et al.*, 2019). A brain study in MCI participants demonstrated increased activation in the left CPL, which may be related to their higher connection on understanding and construction of the correct order (Van Overwalle *et al.*, 2020).

The present results are entirely consistent with our hypothesis that the creative expression intervention would significantly influence the activation pattern of neurocognitive-related brain regions in MCI older adults. These findings fit nicely into the literature that suggests specific brain activity pattern changes in MCI are heavily involved in period of creative expression program and cognitive function improvements. Besides, similar studies which were focused on the storytelling have indicated that improving the key components of the mentalizing network correlates with changes in specific brain activation patterns in undergraduate students and neurotypical adults (Yuan *et al.*, 2018; Alyahya *et al.*, 2020). The impaired function of HIP has been indicated as a valuable predictor of progression

from amnesic MCI to AD stage (Chen *et al.*, 2015). The cognitive flexibility underlying imagination is grounded in the complex interaction of HIP-included network and frontoparietal. Enhancement in FC between the HIP and frontoparietal cortex has been indicated to result in better imagination task performance. The trace transformation theory (TTT) initially proposed that neural and psychological transformations are linked and proceed in tandem (Sekeres *et al.*, 2018). It further illustrated that story creating intervention increased MCI adults' hippocampal activation, which was accompanied by improved episode memory function. In addition, Eleanor-Maguire *et al.* (2016) found that better perception and imagining fictitious were related to higher activation in the HIP, which suggests improved event details and specific information from episodic simulation in MCI adults (Thakral *et al.*, 2020). Thus, creative expression intervention could have beneficial effects on neurocognitive function in MCI adults by increasing brain activation patterns.

FC changes in the neurocognitive network

Voxel-wise resting connectivity analyses showed that the creative expression intervention caused connectivity increase in the left HIP-bilateral ANG, the left HIP-right ITG, and left HIP-bilateral SOG. Extensive research has been reported that the above regions are critical nodes of the neurocognitive network. Roni-Tibon *et al.* suggested that the ANG were involved in subjective mnemonic experience, which may play different roles during encoding and retrieval by different mnemonic task (Tibon *et al.*, 2019). The ITG presented an enhancement of stimulus selectivity when involving in visual shape categorization and passive viewing task (McKee *et al.*, 2014). Meta-analysis research concluded that the cognitive training programs have significantly increases in activation in altered clusters regions involving SOG, middle frontal gyrus, and posterior parietal cortex (Duda and Sweet, 2020). Similarly, task-related and resting-state FC studies have been found to be significantly changed after specific cognitive training in healthy, MCI, and AD older adults (Li *et al.*, 2015). Recently, new research characterized in particular altered FC between the HIP and frontal lobes, in which it is thought to be involved in higher cognitive domains and is a critical component of the working memory network (Velayudhan *et al.*, 2021). This finding is consistent of our previous hypothesis that the FC integrity between the HIP and other brain regions may have potential as an early diagnostic tool in identifying the effect of cognitive training when in large samples. The clinical utility of MRI scanning

has been broadly superior to the available international evidence in identifying positive outcomes or brain activation (Guinane and Ng, 2018; Tibon *et al.*, 2019).

Strengths and Limitations

A significant advantage of this study is the story creating design; to the best of our knowledge, this is the first study to combine the task-fMRI and resting-state fMRI data to perform this method and investigate the functional reorganization and neural pathways in neurocognitive network elicited by creative expression program in MCI older adults. By period of novel cognitive training with spontaneous brain-intensive response to this specific stimulus, the combination of both task-fMRI and resting-state fMRI enables a more accurate detection in exploring the effects of creative expression program on functional plasticity of target brain region. This study provided new insights into the non-pharmaceutical therapy methods via neurological effects of story creating training on working memory and brain plasticity.

Conclusion

The present study demonstrated that the story creating intervention improves the activation and connectivity of neurocognitive-related brain regions in MCI old adults and strengthens the neural network activation and neuron connectivity. These changes are related to neurocognitive performance improvements. Our findings are the first to suggest that story creating interventions improve the ability of cognitive impairment elders to allocate implicit and explicit memory by enhancing functional plasticity of neurocognitive network. Finally, these results highlight the involvement of story creating intervention in specific training in stimulating cognitive development in MCI older adults and imply the therapeutic potentials of adjuvant creative expression program in improving MCI with cognition dysfunction.

Conflict of interest

All authors of this article declare that we have no conflict of interest.

Description of authors' roles

JZ contributed to development of the CrExp or CG intervention and study design, wrote the first draft of

the manuscript, created tables and figures, and oversaw statistical analyses.

HL supervised all statistical analyses and overall statistical approach and contributed to manuscript writing.

RL contributed to development of the CrExp or CG intervention and study design.

JS contributed to development of the MRI scanning and study design, coordinated and oversaw data collection, and contributed to statistical analysis approach.

WC contributed to development of the MRI scanning and study design, coordinated and oversaw data collection, and contributed to statistical analysis approach.

MM supervised data collection and data entry, contributed to statistical analyses, and contributed to manuscript writing.

Impact statement

We certify that this work is novel clinical research. This research makes two major contributions to the literature. First, it demonstrates the feasibility and acceptability of an innovative cognitive intervention in older adults suffering from cognitive deficiency, using a randomized design and performing a creative expression program administered by trained research team. Second, it provides evidence that the activation and functional connectivity of the brain via story creating cognitive training could be detected by means of brain imaging diagnosis, and the MRI as a clinical sensitive tool in detecting or instructing specific intervention pattern.

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Supplementary material

To view supplementary material for this article, please visit <https://doi.org/10.1017/S104161022000382>

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