Article

Autobiographical Cerebral Network Activation in Older Adults Before and After Reminiscence Therapy: A Preliminary Report

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Abstract

Introduction: Reminiscence therapy (RT), which engages individuals to evoke positive memories, has been shown to be effective in improving psychological well-being in older adults suffering from PTSD, depression, and anxiety. However, its impact on brain function has yet to be determined. This paper presents functional magnetic resonance imaging (fMRI) data to describe changes in autobiographical memory networks (AMN) in community-dwelling older adults. **Methods:** This pilot study used a within-subject design to measure changes in AMN activation in 11 older adults who underwent 6 weeks of RT. In the scanner, participants retrieved autobiographical memories which were either recent or remote, rehearsed or unrehearsed. Participants also underwent a clinical interview to assess changes in memory, quality of life, mental health, and affect. **Findings:** Compared to pretreatment, anxiety decreased ($z = -2.014$, $p = .040$) and activated significant areas within the AMN, including bilateral medial prefrontal cortex, left precuneus, right occipital cortex, and left anterior hippocampus. **Conclusion:** Although RT had subtle effects on psychological function in this sample with no evidence of impairments, including depression at baseline, the fMRI data support current thinking of the effect RT has on the AMN. Increased activation of right posterior hippocampus following RT is compatible with the Multiple Trace Theory Theory (Nadel & Moscovitch, 1997).

Keywords

autobiographical memory, functional MRI, older adults, reminiscence therapy

Introduction

Autobiographical memory (AM) refers to information and personally-relevant events acquired in a specific spatio-temporal context which have been accumulated from childhood, enabling us to construct a sense of identity and continuity (Conway & Pleydell-Pearce, 2000). It is formed of different types of representations, from general knowledge about oneself (semantic component) to very specific personal events (episodic component; Tulving et al., 1988; Conway, 2001). AMs are complex and draw on multiple brain regions involved in processing emotion (amygdala, insula), language (lateral temporal and inferior frontal gyri, angular and supramarginal gyri), different sensory modalities (medial parietal and occipital cortices) and more (Rubin, 2005). This network of brain areas is referred to as the AM network, which includes the medial prefrontal cortex, hippocampus, lateral temporal, medial parietal, and occipital cortices.

By evoking the AM network, Reminiscence Therapy (RT) may have many benefits for community dwelling older adults by having persons engage in recalling and discussing past experiences and memories, which in turn, may minimize cognitive decline, evoking memory of social engagement and encouraging social interactions. Well-being may also improve

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by lifting one's mood, minimizing anxiety and reducing stress (for reviews, see Allen et al., 2018, Syed Elias et al., 2015; Song et al., 2014). A number of studies of persons residing in nursing homes report that RT can evoke significant improvements in mood, self-esteem (Chao et al., 2006; Song et al., 2014), social interactions (Chao et al., 2006; Chiang et al., 2010), feelings of accomplishment, well-being (Chiang et al., 2010; Henkel et al., 2017), life satisfaction (Song et al., 2014), quality of life (Wu et al., 2018), positive effects on physical health (Henkel et al., 2017), as well as alleviating depression (Lopes et al., 2016; Song et al., 2014; Wang, 2005; Wu et al., 2018) or anxiety symptoms (Lopes et al., 2016), reducing loneliness (Ren et al., 2021) and psychological distress (King et al., 2019). The aim of this paper is to assess the benefits of RT on psychological functioning in community dwelling older adults and, using functional magnetic resonance imaging (fMRI), its effects on brain activation in key regions of the AM network.

The mechanism by which RT influences mood in healthy adults remains unclear. It is thought that RT impacts mood through plasticity-driven changes to AM traces due to regular, repeated activations, mediated by executive function and subjective factors including mood and stress/anxiety (see Allen et al., 2018 for a review and putative model). In particular, the "mental time travel" or *autonoesis* (see Irish et al., 2008; Tulving, 2005) associated with reminiscence may represent an important factor in these effects. The ability to mentally re-experience an event from a first-person perspective, thereby activating the respective sensory areas associated with the sights, sounds, smells, tastes, and other sensory modalities engaged at the time of the memory's formation, may enhance the sense of "presence" during retrieval, in turn heightening the emotional connection to the event (see Sant'Anna et al., 2020; D'Argembeau & Van der Linden, 2006).

Different methods have been used to probe AM during fMRI scanning. Addis et al. (2003) had a pre-scan interview in which participants produced specific (episodic) and general (semantic) AMs that were later presented to them in the MRI scanner. Other research has examined brain activity in response to cues presented in the scanner without pre-scanning rehearsal, either by using artefacts (family photographs) selected by people known to the participants (Gilboa et al., 2004) or interviewing the spouse (Viard et al., 2007) to prevent recent reactivation (and preserve remote memory traces). However, there has been a lack of research examining the effect of repetition on AM recall and underlying brain activity. Recalling different AMs through repeated sessions of remembering is possible with RT, in addition to uplifting mood, increasing social interactions and well-being. At the brain level, we would expect that the repeated sessions of AM remembering would increase activation within the AM network after RT.

To date, most studies of RT in older adults have not been conducted in healthy older adults, but rather focused on those with anxiety disorders, obsessive-compulsive disorder (Ma et al., 2021; Schiepek et al., 2013), post-traumatic stress disorder (Beauregard, 2014; Karlsson, 2011), or major depression (Won Jeon & Kim, 2015; Wu et al., 2020; Dichter et al., 2010). From this prior work, we would hypothesize that RT will be associated with improved well-being, as well as decreased depression and anxiety scores. At the brain level, we would predict heightened activation in regions of the AM network during the AM task (i.e., medial prefrontal cortex, hippocampus, lateral temporal, medial parietal and occipital cortices; see reviews, Cabeza & St Jacques, 2007; Svoboda et al., 2006).

Methods and Participants

Participants

Eleven right-handed older adults aged 63–83 years old (mean age +/− s.d., 74.27 +/− 5.14 years old, 7 women, 4 men) with no history of psychiatric, neurological disorder,or history of traumatic brain injury were recruited from Dublin and surrounding areas via flyers or newspaper advertisements and community groups (e.g., aging or retirement group associations). Hand preference was measured using the Edinburg Handedness Scale. The study was approved by Maynooth University's Biomedical Sciences Ethics Sub-Committee (BSRESC) and the Trinity College Dublin School of Medicine Ethics Committee (Application Number: 20171002). Written informed consent was obtained from all participants prior to participation in the study. Participants had no abnormality on their T_1-weighted high-resolution magnetic resonance imaging (MRI). The inclusion of participants was also based on the absence of signs of depression (BDI or Beck Depression Inventory; Beck et al., 1988; cutoff is 0-9 for normal range) or of memory complaints (MFS or Memory Functioning Scale; Clare et al., 2002). No medication known to impair memory was allowed. Participants had on average 15.5 years of education (+/− 3.9 years) and were all living in their own homes. All participants were current non-smokers.

Reminiscence Therapy

The reminiscence therapy (RT) was delivered in small groups of 3-7 participants at a number of different venues. The RT comprised 6 weekly sessions, with each session lasting approximately one hour. A simple reminiscence approach, based on the 6-week program "Remembering Yesterday, Caring Today" program (Schweitzer & Bruce, 2008), was used in which participants were encouraged to share their past memories. In addition to past autobiographical memories, participants were prompted and encouraged to share memories of historical events in the public sphere (e.g., Pope John Paul II's visit to Ireland in the 1970s). The topics for each session were as follows: Session 1: Introduction, childhood and family life; Session 2:

Schooldays; Session 3: Historical session A; Session 4: Homes, gardens and animals, going out and having fun; Session 5: Historical session B; Session 6: Weddings, babies, children, rounding up. A facilitator (APA) would suggest a few themes, if conversation stopped, or reorient the conversation, if, for example, it became more focused on current affairs. He would ensure equal time for all participants to share memories during the group RT sessions. The form of reminiscence therapy employed here, Simple RT (Bhar, 2015; Lopes et al., 2016), encourages participants to focus on positive memories, thereby minimizing the risk of negative emotional experiences. With participants' permission, sessions were recorded, and audio recordings of highlights were added to an online digital archive. Between sessions, participants were encouraged to listen to memories provided by other people, to facilitate further retrieval (these are available at the following link: https://repository.dri.ie/catalog/wp98p078n).

Task and fMRI Experimental Design

The fMRI experiment was divided into 2 visits and, on each visit, participants underwent a battery of psychological tests (detailed below, with APA) and an MRI session with anatomical and functional scans (with APA).

Psychological Tests

All participants received a clinical interview with an experimenter. *Autobiographical memory* was assessed with the Episodic Autobiographical Memory Interview (EAMI; Irish et al., 2008), an autobiographical memory test distinguishing covering the whole lifespan (0-15, 15-30, 31–45 years of age, 46 years of age-last 5 years, last 5 years), hence distinguishing recent from remote memories. Memories elicited by participants during the EAMI for the remote (15–30 years old) and recent (past 5 years) life time periods were used as cues for the fMRI scanning session. Participants were asked to think about different memories at visits 1 and 2.

The following *self-report measures* of memory, subjective quality of life and satisfaction with life, mental health and affect were used. The *Memory Functioning Scale* (MFS, part of the Memory Awareness Rating Scale or MARS; Clare et al., 2002) to assess one's memory functioning. The Positive and Negative Affect Schedule (PANAS; Watson et al., 1998) was used to quantify affect. The *Control, Autonomy, Self-Realisation and Pleasure* (CASP-19; Netuveli et al., 2006) was used to evaluate quality of life. The *Satisfaction With Life Scale* (SWLS; Diener et al., 1985) was used to evaluate one's satisfaction with life. The *Beck Depression Inventory* (BDI; Beck et al., 1988) was used to measure depression and the trait items from the *State-trait Anxiety Inventory* (STAI; Spielberger et al., 1983) was used to measure anxiety (see Supplementary Figure 1).

Procedure

Participants completed the psychological measures in a small testing room one at a time. This testing session lasted approximately one hour. Participants completed the questionnaires at their own pace (i.e., with no time limit) prior to the first group session. After completing the 6 RT sessions, participants completed the same measures again (visit 2). Parallel versions of tests were used wherever available for the post-intervention study visit, to minimize learning or other carryover effects.

Scanning Sessions

The scanning session consisted of 2 functional runs, each corresponding to one time period (recent or remote). Each functional run was composed of 20 experimental and 20 control trials. During the experimental trials, participants were instructed to read a cue presented visually on a screen in the scanner (duration of each stimulus was jittered between 8-12 sec) and mentally retrieve the corresponding past memory, with as much phenomenological detail as possible (e.g., emotions, mental visual images), without moving their head. Each visual cue prompted a specific memory which had been collected prior for each participant with the EAMI. Memories were either *recent* (past 5 years) or *remote* (when participants were 15 to 30 years old. This approximately corresponds to the *reminiscence bump*, a life epoch associated with the formation of personal memories that are likely to be retrieved at a relatively high rate later in life (Jansari & Parkin, 1996; Rubin et al., 1986). Additionally, half of the memories consisted of *rehearsed* memories and the other half of *unrehearsed* memories. *Rehearsed* memories were collected during the initial interview prior to the fMRI scanning session, where participants informed the researcher of the memories and then, with guidance from the researcher, developed brief cues that would later be used during the scanning session to prompt the participant to think of that particular memory. The *unrehearsed* memories were prompted by novel prompts/cues that participants had not seen before, and participants were instructed to retrieve an autobiographical memory that had not been discussed previously during their participation. There were 10 cues for each condition (i.e., 10 remote rehearsed, 10 remote unrehearsed, 10 recent rehearsed, 10 recent unrehearsed memories). Different memories were collected at visit 1 (before the 6 sessions of RT) and at visit 2 (after the 6 sessions). After cue presentation, participants had to rate the level of detail, between 1 and 5, by pressing on the corresponding button on the response pad. Recent versus remote memory retrieval, and rehearsed versus unrehearsed retrieval, were carried out in counterbalanced order.

Two control tasks were interleaved between the experimental trials in a randomized order; this order differed between visit 1 and 2 and recent versus remote memory, although the order of control and experimental stimuli for visit 1 and 2 and recent versus remote memory were kept the same for each participant

(see Figure 1 and Table 1). These control tasks consisted of sentence completion (to control for information retrieval; control task 1) or size comparison (to control for visuospatial processing; control task 2) tasks, based on previous literature (Addis et al., 2003). For the sentence completion task, participants had to complete phrases with one appropriate word (semantic information retrieval), without speaking aloud (e.g., the bird ate a …). In the size comparison task, participants had to decide which was the larger from 2 objects presented on the screen (visuospatial processing; e.g., which is the larger between a flower or a tree), without speaking aloud. These tasks were chosen to control for retrieval of semantic information (for the sentence completion task) and visuospatial processing (for the size discrimination task). There were 10 cues for each control condition for each functional run (i.e., 10 sentence completion, 10 size discrimination). Control task durations were jittered between 8-12 seconds. After cue presentation, participants had to rate the level of difficulty, between 1 and 5, by pressing on the response pad. The interstimulus interval (ISI) was jittered between 3-8 seconds.

Cues for the experimental and control tasks were presented visually using Presentation v.16.1 (Neurobehavioral Systems, Albany, CA) and response durations (detail for AM task, difficulty for control tasks) were jittered between 3-8 sec. Before the fMRI scan, participants were familiarized with the tasks in a training phase which lasted approximately 30 minutes, outside of the scanner.

MRI Acquisition

A Philips Intera Achieva 3.0 T MR system (Best, The Netherlands) was used to acquire the MRI data. A T1-weighted sequence was used to collect a high-resolution, 3-dimensional anatomical image (isotropic voxel at 0.9 mm) for structural localization and visualization. Structural scans lasted 11 minutes and 9 seconds. Functional images were acquired with echo planar imaging blood oxygen level-dependent (BOLD) sequences (repetition time = 2000 msec, echo time = 25 msec, flip angle = 90°, slice thickness = 3 mm). Functional scans lasted 5 minutes and 46 seconds. Each volume of data covered the entire brain with 40 slices, voxel dimensions of 3 × 3 × 3 mm, and a total of 330 volumes were acquired. The total duration of an MRI session was 22 minutes and 41 seconds.

Behavioral Statistical Analysis

Non-parametric Wilcoxon Signed Ranks tests were conducted to compare the scores on the various psychological tests at visit 1 and visit 2.

fMRI Pre-Processing

Preprocessing was performed using FMRIPREP version 1.5.0 (Esteban et al., 2018, 2023), a Nipype (Gorgolewski et al., 2011, 2017) based tool. This is the standardized text

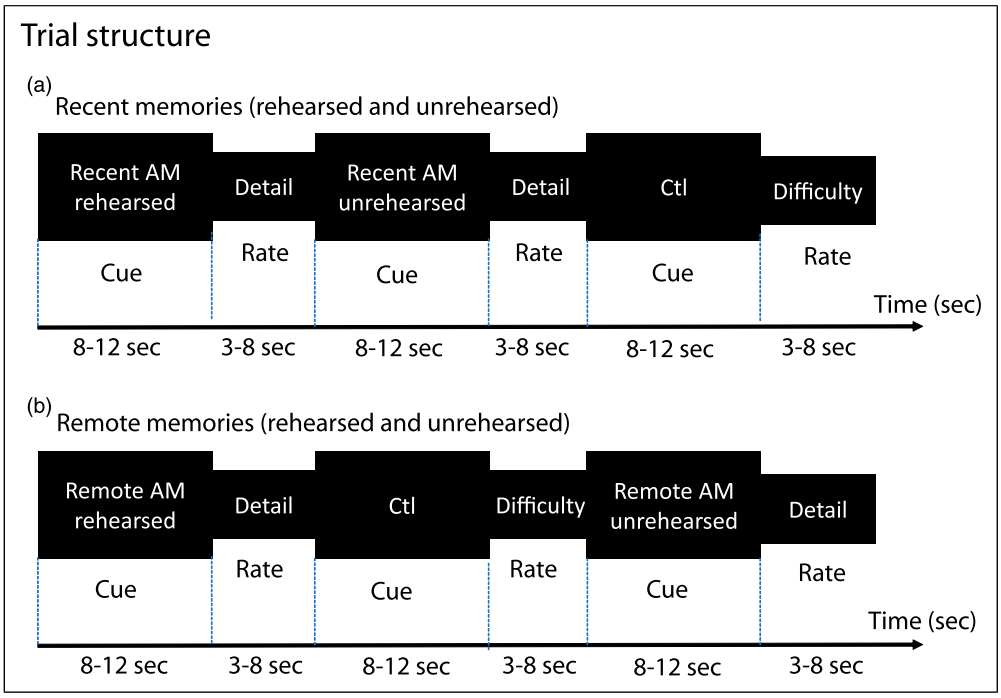

Figure 1. Trial structure showing the alternation between the experimental and control conditions. In the experimental condition, participants had to mentally recall (a) recent or (b) remote autobiographical memories, which were either rehearsed or unrehearsed from a visual cue presented on a screen in the scanner. In the control task, participants had to mentally complete a sentence with a missing word (sentence completion) or decide which of two words were biggest in size (size comparison). In-scanner ratings (between 1 and 5) were obtained for detail (memory task) or difficulty (control task).

Table 1. Example of Stimulus Presentation for the Run Visit 1 and Recent Memory.

Trial	Question	Trial	Question
1	Size	21	Complete
2	AM rehearsed	22	Complete
3	Size	23	AM unrehearsed
4	Size	24	AM unrehearsed
5	AM rehearsed	25	AM unrehearsed
6	AM rehearsed	26	Complete
7	AM rehearsed	27	Complete
8	Size	28	AM unrehearsed
9	AM rehearsed	29	Complete
10	Size	30	AM unrehearsed
11	AM rehearsed	31	AM unrehearsed
12	AM rehearsed	32	Complete
13	AM rehearsed	33	Complete
14	Size	34	Complete
15	Size	35	AM unrehearsed
16	Size	36	Complete
17	AM rehearsed	37	AM unrehearsed
18	AM rehearsed	38	Complete
19	Size	39	AM unrehearsed
20	Size	40	AM unrehearsed

Note. Abbreviations: AM rehearsed: recall of rehearsed autobiographical memory; AM unrehearsed: recall of unrehearsed autobiographical memory; Size: visuospatial processing/size comparison control; Complete: information retrieval/sentence completion control).

(boilerplate) provided by FMRIPREP with corresponding authorization (https://www.nipreps.org/intro/transparency/#citation-boilerplates). Each T1w (T1-weighted) volume was corrected for INU (intensity non-uniformity) using N4BiasFieldCorrection v2.1.0 (Tustison et al., 2010) and skull-stripped using antsBrainExtraction.sh v2.1.0 (using the OASIS template). Spatial normalization to the ICBM 152 Nonlinear Asymmetrical template version 2009c (Fonov et al., 2009) was performed through nonlinear registration with the antsRegistration tool of ANTs v2.1.0 (Avants et al., 2008), using brain-extracted versions of both T1w volume and template. Brain tissue segmentation of cerebrospinal fluid (CSF), white-matter (WM) and gray-matter (GM) was performed on the brain-extracted T1w using fast (Zhang et al., 2001) (FSL v5.0.9).

Functional data was slice time was corrected using 3dTshift from AFNI v16.2.07 (Cox, 1996) and motion was corrected using mcflirt (FSL v5.0.9, Jenkinson et al., 2002). This was followed by co-registration to the corresponding T1w using boundary-based registration (Greve & Fischl, 2009) with 9 degrees of freedom, using flirt (FSL). Motion correcting transformations, BOLD-to-T1w transformation and T1w-to-template (MNI) warp were concatenated and applied in a single step using antsApplyTransforms (ANTs v2.1.0) using Lanczos interpolation.

Physiological noise regressors were extracted applying CompCor (Behzadi et al., 2007). Principal components were estimated for the 2 CompCor variants: temporal (tCompCor) and anatomical (aCompCor). A mask to exclude signal with cortical origin was obtained by eroding the brain mask, ensuring it only contained subcortical structures. Six tCompCor components were then calculated including only the top 5% variable voxels within that subcortical mask. For aCompCor, 6 components were calculated within the intersection of the subcortical mask and the union of CSF and WM masks calculated in T1w space, after their projection to the native space of each functional run. Frame-wise displacement (Power et al., 2013) was calculated for each functional run using the implementation of Nipype.

fMRI Statistical Analysis

fMRI statistical analyses were performed with SPM12 (Statistical Parametric Mapping; Wellcome Trust Centre for Neuroimaging, London, UK). fMRI time series were modeled by a general linear model including separate regressors for each of the experimental (visit1/visit2, recent/remote, rehearsed/unrehearsed) and control conditions. All regressors were convolved with the canonical hemodynamic response function. Data were high-pass filtered (cutoff period, 128 s). At the first level, contrasts were calculated for each regressor of interest, by subtracting the control conditions, and were then brought to the second level analysis. A 3-way flexible factorial design (ANOVA) was used at the second level with the following factors: visits (1 vs. 2), remoteness (remote vs. recent) and rehearsal (rehearsed vs. unrehearsed). Based on our a priori hypotheses, resulting statistical maps were thresholded at an uncorrected voxel-level p-value of .001 and an extent threshold of 10 voxels. This threshold has been used previously in fMRI studies of AM retrieval (Daselaar et al., 2008; Donix et al., 2010; Hur et al., 2021; Steinvorth et al., 2006; Viard et al., 2007).

Results

Psychological Results

Comparison of psychological scores revealed no statistical difference between visits 1 and 2 for the various tests used (see Table 2), except for the STAI: participants reported significantly less anxiety at visit 2 compared to visit 1 ($z = -2.014$, $p = .040$). Concerning in-scanner ratings scales, there were no significant differences on ratings of detail between visits 1 and 2.

fMRI Results

fMRI results revealed differences between conditions and interactions, as described below.

Visit Versus Control Condition

At visit 1, results showed activation in regions of the AM network, including the precuneus, medial, middle and superior

frontal gyri, medial (hippocampus, parahippocampal gyrus) and lateral (middle and superior) temporal gyri, fusiform and angular gyri and cerebellum. At visit 2, similar activations within the same areas of the AM network were observed (precuneus, frontal gyri, medial and lateral temporal gyri, angular gyrus, cerebellum) suggesting a sustained level of activation within regions supporting AM. All results are reported in Table 3.

Visit 1 versus Visit 2

Hyperactivations were detected for visit 2 compared to visit 1 in the following regions, all of which are part of the autobiographical memory (AM) network: bilateral superior medial frontal cortex, right middle and left inferior frontal gyri, left precuneus, left insula, right middle occipital gyrus and left anterior hippocampus. Table 4 shows the x, y, z coordinates which are specific voxels within the specified brain area. In the reverse comparison, visit 1 showed no differential activation compared to visit 2 (see Table 4 and Figure 2(a)).

Recent versus Remote Memories

Hyperactivations were detected for remote compared to recent memories in the following regions, also parts of the AM network, including the left precuneus and right-lateralized areas: posterior hippocampus, middle temporal and fusiform gyri, middle and inferior frontal gyri, supramarginal gyrus, calcarine sulcus, basal ganglia (putamen, globus pallidus) and cerebellum. In the reverse comparison, no differential activation was detected for recent compared to remote memories. A significant interaction was detected between the factors *remoteness and rehearsal*, whereby the rehearsal effect was greatest for remote compared to recent memories in the right fusiform gyrus, inferior temporal gyrus and insula (see Table 4 and Figure 2(b)).

Rehearsed versus Unrehearsed Memories

Hyperactivation of the right posterior hippocampus was detected for rehearsed compared to unrehearsed memories. For the opposite comparison, no activations were detected for unrehearsed compared to rehearsed memories (see Table 4 and Figure 2(c)).

Discussion

This preliminary study on the effects of RT in older adults revealed several significant effects. Psychological measures before and after RT revealed that participants reported less anxiety at visit 2 compared to visit 1. Functional MRI data highlighted 3 main results. First, recalling autobiographical memories at visit 2 hyperactivated a network of brain regions typically activated during AM recollection (i.e., bilateral medial PFC, left precuneus, right middle occipital cortex, left anterior hippocampus) compared to memories from visit 1. Second, remote memories hyperactivated brain regions in the AM network (i.e., left precuneus, right posterior hippocampus, right middle temporal gyrus, right fusiform gyrus, right middle and inferior frontal gyri, parieto-occipital areas and cerebellum) compared to recent memories. Third, rehearsed memories hyperactivated the right posterior hippocampus compared to unrehearsed memories.

Table 2. Psychological Measures, Depicting Means and Standard Deviations (S.D.) for Participants (N = 11, 7 Women, 4 Men) at a Significant Threshold of $p < .05$.

Psychological tests	Visit 1		Visit 2		Z value	
	Mean	S.D.	Mean	S.D.	z value	*p*
MFS	38.45	3.8	39	6.4	−.268	.789
PANAS						
Positive	34.54	6.3	35.27	4.8	−.415	.678
Negative	13.81	3.0	15.27	5.7	−.359	.719
CASP-19	46.18	6.3	46.63	3.8	−.141	.888
SWLS	27.72	6.7	30.0	2.9	−1.541	.123
BDI	4.50	4.1	3.1	3.4	−1.364	.172
STAI	32.63	9.5	29.63	7.3	−2.014	**.04***

Note. Abbreviations:. BDI: Beck Depression Inventory; CASP-19: Control, Autonomy, Self-Realisation and Pleasure; MFS: Memory Functioning Scale; PANAS: Positive and Negative Affect Schedule; STAI: State-trait Anxiety; SWLS: Satisfaction With Life Scale. Bold font: significant results.

Psychological Results

Six sessions of RT had no significant effects on the different psychological measures, except on reported anxiety (as assessed with the STAI), suggesting little psychological effect of such therapy (Allen et al., 2020; Woods et al., 2016; see review, Woods et al., 2018). However, we did find lower anxiety ratings after therapy (visit 2) compared to before (visit 1) suggesting an effect of RT on anxiety (Lopes et al., 2016; see review, Allen et al., 2018), supporting studies showing a positive effect of psychological therapy, notably in patients suffering from anxiety disorders (Ribeiro Porto et al., 2009; Hur et al., 2021; Ma et al., 2021; Schiepek et al., 2013; book chapter, Beauregard, 2014). Here, we replicate these findings in healthy older adults. Lower anxiety scores at visit 2 compared to visit 1 may also have arisen because participants had already partaken in both psychological and scanning phases at visit 1 (6 weeks prior) and were thus more familiar with the (potentially stressful) context of experimentation, hence possibly lowering their anxiety. It is also possible that behavioral improvements in other psychological domains may surface later, e.g., after more sessions of RT.

fMRI Results

Visit 1 and Visit 2. Concerning neuroimaging findings, results showed activation in regions of the AM network at visit 1 and

Table 3. Results of the 3-Way ANOVA Depicting Differences in MRI Activations Between Each Visit and the Control Condition at p_{unc} < .001 Uncorrected, k > 10 Voxels. L: left; R: Right.

		MNI coordinates			
Region	Laterality	x	y	z	z score
Visit 1 > control					
Precuneus	L	−3	−57	31	5,54
	R	9	−51	18	4,99
Superior frontal gyrus	L	−18	27	57	4,09
	R	21	30	54	3,63
Medial frontal gyrus	R	3	57	−12	3,85
Superior medial frontal gyrus	R	3	63	31	3,83
Posterior hippocampus	R	33	−24	−12	3,78
Parahippocampal gyrus	L	−24	−24	−22	3,82
	R	24	−18	−19	3,51
Middle temporal gyrus	L	−60	−3	−15	4,00
Superior temporal gyrus	R	63	−3	−12	3,76
Fusiform gyrus	L	−21	−36	−15	3,48
Angular gyrus	R	39	−63	41	3,45
Cerebellum	L	−6	−54	−45	3,83
Visit 2 > control					
Middle temporal gyrus	L	−63	0	−19	5,25
Parahippocampal gyrus	L	−18	−15	−25	5,14
	R	21	−12	−29	3,62
Anterior hippocampus	L	−27	−21	−15	3,92
Caudate	R	6	0	14	5,09
Precuneus	L	−6	−60	34	5,01
Medial frontal gyrus	L	−3	45	−12	4,16
	R	6	57	−5	4,06
Superior frontal gyrus	L	−21	39	47	3,98
Angular gyrus	L	−42	−72	37	3,80
Cerebellum Crus 1	R	27	−75	−29	3,78
Cerebellum Crus 2	R	15	−87	−38	3,57
Cerebellum	R	9	−54	−42	3,69
	L	−6	−54	−42	3,51

2 separately, suggesting a sustained level of activation of the nodes within the network supporting AM. There were hyperactivations of the AM network for memories recalled at visit 2, compared to visit 1, including the medial and lateral PFC, precuneus, occipital cortex and left anterior hippocampus. Medial PFC regions are typically associated with self-referential processing (see reviews, Cabeza & St Jacques, 2007; Svoboda et al., 2006), while lateral PFC are more frequently associated with memory search and strategic retrieval processes (Cabeza & St Jacques, 2007). Precuneus and occipital areas presumably reflect processes of mental visual imagery and visuospatial processes (Svoboda et al., 2006), operating and facilitating AM retrieval. Left hippocampal activation has a well-known role in episodic contextual retrieval (Burgess et al., 2001; for review, Svoboda et al., 2006) through its role in binding details in memory (Eichenbaum, 2017; Moscovitch et al., 2005). It has also been shown to reflect richness of re-experiencing (Gilboa et al., 2004) and retrieval of particularly detailed and personally-significant AMs (Addis et al., 2003). Its anterior part may serve to extract the general context of a specific memory (Audrain & McAndrews, 2022). Overall, hyperactivation of the AM network after 6 sessions indicates that RT stimulates the neural circuits of AM, supporting studies suggesting a biological effect of RT (book chapters, Karlsson, 2011; Won Jeon & Kim, 2015).

Recent versus Remote Memories. Remote memories hyperactivated regions of the AM network (i.e., lateral PFC and temporal areas, medial and lateral parietal cortices, occipital areas and right posterior hippocampus) compared to recent memories. Remote memories being encoded many decades ago have presumably undergone greater repetition processes over time, compared to recent memories that have been encoded only recently. The Multiple Trace Theory (MTT, Nadel & Moscovitch, 1997) posits that each time an event is

Table 4. Results of the 3-Way ANOVA Depicting Differences in MRI Activations Between the Factors (Visit 1 vs. Visit 2), Remoteness (recent vs. remote) and Rehearsal (Rehearsed vs. Unrehearsed memories) at $p_{unc} < .001$ Uncorrected, k > 10 Voxels. L: left; R: Right.

		MNI coordinates			
Region	Laterality	x	y	z	Z score
Visit 1 > Visit 2	-	-	-	-	-
Visit 2 > Visit 1					
Medial superior frontal gyrus	L	−9	57	8	4.17
	L	0	57	1	4.04
	R	12	66	−5	3.60
Insula	L	−27	18	−9	3.98
Inferior frontal gyrus	L	−48	42	−12	3.72
Middle occipital gyrus	R	51	−75	28	3.67
Precuneus	L	−6	−63	61	3.62
Middle frontal gyrus	R	42	48	28	3.59
Precentral gyrus	R	57	6	44	3.52
		60	12	34	3.22
Anterior hippocampus	L	−15	−6	−15	3.48
Recent > Remote	-	-	-	-	-
Remote > Recent					
Fusiform gyrus	R	42	−48	−15	4.77
	R	39	−42	−22	4.63
Middle temporal gyrus	R	54	−54	21	4.14
Postcentral gyus	L	−66	−9	21	4.42
	L	−54	−9	21	4.16
	R	63	−3	34	4.35
Rolandic area	L	−63	0	11	4.12
Precentral gyrus	R	66	3	21	4.17
Rolandic area	R	66	−6	8	3.65
Paracentral lobule	R	0	−27	61	4.24
	R	3	−36	64	3.86
Precuneus	L	−12	−42	61	3.66
Putamen	R	27	9	−5	4.01
	R	33	−15	4	3.44
Posterior hippocampus	R	33	−27	−5	4.00
Pallidum	R	30	−12	−5	3.40
Supramarginal gyrus	R	63	−30	44	3.97
Inferior frontal gyrus	R	48	36	1	3.70
Calcarine sulcus	R	27	−66	11	3.50
Middle frontal gyrus	R	39	21	41	3.38
Cerebellum 8	R	18	−63	−42	3.33
Rehearsed > Unrehearsed					
Posterior hippocampus	R	21	−24	−12	3.42
Unrehearsed > Rehearsed	-	-	-	-	-
Rehearsal x Remoteness interaction					
Fusiform gyrus	R	39	−42	−22	3.76
Inferior temporal gyrus	R	54	−51	−12	3.59
Insula	R	30	15	18	3.41

retrieved (i.e., re-activated), a new hippocampal trace is created, with its accompanying sparse and distributed connections, thus strengthening that memory. Hence, remote memories are represented by a greater number of traces than recent memories, and the hippocampus and neocortical areas continuously interact over time. Here, compared to recent memories, remote memories hyperactivated a set of brain regions belonging to the AM network, in particular, the right (posterior) hippocampus, concordant with MTT and previous neuroimaging studies (Bonnici et al., 2012; Gilboa et al., 2004; Maguire, 2001; Oddo et al., 2010; Piolino et al., 2004; Rekkas et al., 2005; Ryan et al., 2001; Santangelo

Figure 2. fMRI results depicting hyperactivations for (a) memories retrieved at visit 2 compared to visit 1, (b) memories of remote compared to recent periods, (c) memories that were rehearsed compared to unrehearsed ones, and corresponding color z scales.

et al., 2020; Sekeres et al., 2018; Söderlund et al., 2012; Steinvorth et al., 2006; Viard et al., 2007, 2010). Posterior hippocampal activation has already been detected for remote compared to recent AMs in younger (Bonnici et al., 2012) and older adults (Gilboa et al., 2004). For remote memories, Gilboa et al. (2004) showed that clusters of activations were detected all along the longitudinal axis of the hippocampus, whereas clusters were more anterior for recent memories, in line with predictions of the MTT (i.e., "repeated reinstatements of a memory lead(s) to the formation of new, distributed traces within the medial temporal lobe"). Here, additional confirmation was provided with the comparison of rehearsed versus unrehearsed memories, revealing right posterior hippocampus hyperactivation for rehearsed compared to unrehearsed memories, lending further support to MTT predictions. This result suggests a process of re-encoding in AM which, in turn, may contribute to better memory retention in healthy aging. At a methodological level, hippocampal hyperactivation for rehearsed compared to unrehearsed memories suggests that whether or not AMs are rehearsed shortly before retrieval in the scanner will impact upon the level of brain activation observed.

Hyperactivations were also detected in other regions of the AM network described previously (lateral PFC, precuneus, occipito-parietal areas) and in lateral temporal cortices which have a role in the retrieval of semantic AM information (Svoboda et al., 2006). The fusiform cortex has been linked to processing of object details (Donix et al., 2010). A significant interaction between remoteness and rehearsal confirmed that rehearsal (i.e., repetition) was greatest for remote compared to recent memories, in particular in the fusiform cortex, lateral temporal cortex and insula, which has a role in subjective experience of emotional AMs (Van Schie et al., 2019).

Limitations

This pilot study had a number of limitations. One notable caveat of this study is the small number of participants that took part, leading to low statistical power; future follow-up studies will aim for larger sample sizes and increased power. With this limitation in mind, our reported findings should be interpreted with caution. While retention was high overall, given the constraints of scanning both before and after therapy, we had 2 dropouts; while the reasons given were of a practical nature (holidays, time commitments), it is possible that lack of satisfaction with the intervention was also a factor. We intend to seek feedback regarding satisfaction with the intervention in future iterations of this study and have engaged significantly with Perspectives in Public and Patient Involvement (PPI) in our approach to our subsequent studies. Further, as

participants were healthy older adults, many of the assessed variables (such as depression) were close to floor/ceiling at baseline, and so it would be difficult to demonstrate a significant impact of 6 sessions of RT. In future studies of this nature, we will also seek to include measures of cognitive performance, including global cognition, attention, and memory. Finally, previous studies using 6-week programs have shown positive effects with samples of people living with dementia; to see comparable effects in healthy older adults living in the community, longer durations/greater intensity (i.e., more than one hour per week) may be required.

Conclusions

Reminiscence therapy applied to a group of healthy older adults was associated with a slight reduction in reported anxiety after 6 sessions (visit 2) compared to baseline (visit 1). Most interestingly, fMRI results indicated that the AM network was hyperactivated after therapy (visit 2) compared to before (visit 1), in regions subtending AM recall (medial PFC, hippocampus, visual imagery areas). Furthermore, recalling remote memories hyperactivated the AM network compared to recent memories, in particular the right posterior hippocampus, consistent with the MTT model (Nadel & Moscovitch, 1997), an area also hyperactivated when recalling rehearsed compared to unrehearsed memories. Altogether, these findings indicate a significant effect of RT in healthy older adults on the AM brain network, although effects at the psychological level were subtle. It is plausible that RT with an increased number of sessions (over several months) may have had more significant effects on psychological function, since effects were already observed at the brain level after only 6 sessions. Our study further validates the potential positive effects of RT in an older population and its potential interest in patients, in particular those with memory disorders.

Author Contributions

AV, APA, CMD, RAPR and SC contributed to the conception of the work. APA and CMD contributed to data acquisition. AV, MN and SC contributed to the data analysis. AV contributed to manuscript preparation. RAPR, SC, APA, SC, HP and FE contributed to revisions. AV contributed to figure preparation. All authors contributed to the article and approved the submitted version.

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Supplemental Material

Supplemental material for this article is available online.

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