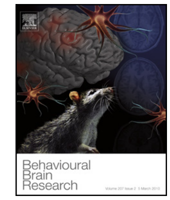
Behavioural Brain Research 293 (2015) 125–133

Contents lists available at ScienceDirect

Behavioural Brain Research

journal homepage: www.elsevier.com/locate/bbr



Research report

Better together: Left and right hemisphere engagement to reduce age-related memory loss

Michela Brambilla, Rosa Manenti, Clarissa Ferrari, Maria Cotelli*

Neuropsychology Unit, IRCCS Centro San Giovanni di Dio Fatebenefratelli, Brescia, Italy

HIGHLIGHTS

- Youngs and high-performing elders exhibited similar performances on memory task.
- Youngs and high-performing elders showed a symmetrical hemisphere recruitment.
- Low-performing elders showed asymmetrical engagement of the hemispheres (left > right).
- The maintenance of hemispheric symmetry had a direct positive correlation with memory.
- These findings drew attention to brain maintenance hypothesis.

ARTICLE INFO

Article history:
Received 15 April 2015
Received in revised form 10 July 2015
Accepted 11 July 2015
Available online 19 July 2015

Keywords:
Non invasive brain stimulation
tDCS
Aging
Cognition
Memory
Plasticity

ABSTRACT

Episodic memory is a cognitive function that appears more susceptible than others to the effects of aging. The main aim of this study is to investigate if the magnitude of functional hemispheric lateralization during episodic memory test was positively correlated with memory performance, proving the presence of a beneficial pattern of neural processing in high-performing older adults but not in low-performing participants.

We have applied anodal transcranial Direct Current Stimulation (tDCS) or sham stimulation over left and right hemisphere in a group of young subjects and in high-performing and low-performing older participants during an experimental verbal episodic memory task.

Remarkably, young individuals and high-performing older adults exhibited similar performances on episodic memory tasks and both groups showed symmetrical recruitment of left and right areas during memory retrieval. In contrast, low-performing older adults, who obtained lower scores on the memory tasks, demonstrated a greater engagement of the left hemisphere during verbal memory task. Furthermore, structural equation model was performed for analyzing the interrelations between the index of interhemispheric asymmetry and several neuropsychological domains. We found that the bilateral engagement of dorsolateral prefrontal cortex and parietal cortex regions had a direct correlation with memory and executive functions evaluated as latent constructs. These findings drew attention to brain maintenance hypothesis. The potential of neurostimulation in cognitive enhancement is particularly promising to prevent memory loss during aging.

1. Introduction

Episodic memory is a cognitive function that appears more susceptible than others to the effects of aging [1,2]. Age-related changes in episodic memory are critical for daily life functioning and their decline is accelerated in conditions like amnestic Mild Cognitive Impairment (aMCI) and Alzheimer's Disease (AD) [3,4]. Longitudinal population based studies have demonstrated that lower memory performances are reliable predictors of future cognitive decline [5].

Additionally, the results from previous studies demonstrated inter-individual differences in cognitive changes in older adults [6–10]. Progress regarding the study of physiological and pathological aging has provided strong evidence of neurochemical, structural and functional brain changes associated with age-related memory impairment [11–15].

Frontal cortex activation has been deeply investigated in older adults because higher prefrontal (PFC) activation is more prevalent in older adults than in younger adults during several cognitive

* Corresponding author at: IRCCS Centro San Giovanni di Dio, Fatebenefratelli, Via Pilastroni, 4 25125 Brescia, Italy.
E-mail address: mcotelli@fatebenefratelli.eu (M. Cotelli).

http://dx.doi.org/10.1016/j.bbr.2015.07.037
0166-4328/

tasks [16–20]. Neuroimaging studies have revealed an age-related reduction in occipito-temporal activity coupled with an increase in frontal activity, a pattern referred to as the posterior–anterior shift in aging [21]. However, recent works provide evidence in support of both age related reductions in efficiency and compensation in older adult participants, under the same cognitive task [22].

Moreover, PFC increased activity in elderly individuals has been repeatedly investigated in episodic memory tasks, highlighting that the functional asymmetry depicted for young individuals (left PFC specialized for encoding, right PFC crucial for retrieval [23,24]) is reduced in older individuals (hemispheric asymmetry reduction — HAROLD model suggests a reduction of this PFC asymmetry [25]). Different hypotheses have tried to explain the significance of these age-related changes that could represent a compensatory strategy to counteract age-related cognitive deficits [17,18,26,27] or a difficulty in recruiting specialized neural networks [28,29].

Another pattern of imaging findings described similar networks of brain regions recruited by younger and high-performing older adults [15,30–32] and leaded to discuss that the lack of functional changes could constitute a determinant of successful memory aging.

A procedure that can be used to investigate brain functional reorganization in physiological and pathological aging is transcranial Direct Current Stimulation (tDCS) [33]. TDCS is a neuromodulatory technique that utilizes the application of a very low direct current over the scalp facilitating or inhibiting spontaneous neuronal activity [34]. Moreover, this approach has the additional potential to serve as an effective cognitive enhancer to augment abilities in healthy populations as well as a therapeutic interventions to remediate deficits in individuals with neurological and psychiatric conditions [35,36].

Manenti et al. [37] applied tDCS over the dorsolateral prefrontal cortex (DLPFC) or over the parietal cortex (PARC) to facilitate verbal episodic memory in healthy older adults and in young participants. Overall, the results demonstrated that, in young and in older subjects, anodal tDCS applied during the retrieval phase facilitates verbal episodic memory. In particular, we found that tDCS applied over the left and right regions (DLPFC and PARC) induced better performance in young participants, whereas only tDCS applied over the left regions (DLPFC and PARC) increased retrieval efficacy in older subjects. However, it remains unclear whether this different hemispheric recruitment in young and in elderly individuals may be beneficial in order to maintain memory performance in older or instead if it may represent evidence of brain dysfunction [18,22,38]. To address this question we re-analyzed data acquired in a our previous study [37].

The purpose of this study is to investigate if the magnitude of functional hemispheric lateralisation (index of interhemispheric asymmetry: left–right tDCS effect) during episodic memory test is positively correlated with memory performance, proving the presence of a beneficial pattern of neural processing in high-performing older adults but not in low-performing participants. Based on previous imaging and brain stimulation studies [39,40], we predict that hemispherical symmetry during episodic memory would only be present in high-performing older adults.

Moreover, a structural equation model (SEM) was performed for analysing the interrelations between the index of interhemispheric asymmetry and different neuropsychological domains [41].

2. Materials and methods

2.1. Participants

Thirty-two healthy young volunteers [mean age (years) = 23.7 SD = 3.2; mean education(years) = 15.1 SD = 2.0 (9 males, 23 females)] and 32 healthy older individuals [mean age (years) = 67.9 SD = 4.7; mean education (years) = 10.8 SD = 4.6 (15 males, 17 females)] took part in the experiment. All of the subjects had normal or corrected-to-normal vision, were native Italian speakers and were right-handed [42] young volunteers: 85.6 SD = 14; elderly individuals: 87.0 SD = 13]. See Table 1 for demographic details.

Participants reported being free of neurological disorders and had no history of seizures. All participants were informed about the procedures and the possible risks of tDCS, and written informed consent was obtained after a safety screening. The experimental methods got ethical approval from the local Human Ethics Committee (Ethics Committee of the IRCCS Centro San Giovanni di Dio Fatebenefratelli, Brescia, Italy).

Prior to being enrolled in the experiment, subjects completed a Mini Mental State Examination (MMSE) [43] and a detailed neuropsychological evaluation to verify the absence of any cognitive deficit. A pathological score in one or more of the tests was an exclusion criterion. The neuropsychological test battery included measures used to assess non-verbal reasoning (Raven's Colored Progressive Matrices), verbal fluency (phonemic and semantic), visuo-spatial capacity (Rey–Osterrieth complex figure, copy), attention and executive functions (Trail Making Test A and B). In addition, memory was assessed in depth (Story Recall, Rey–Osterrieth complex figure recall, digit span, auditory verbal learning test immediate and delayed recall). All of the tests were administered and scored according to standard procedures [44]. In addition, older subjects completed the Cognitive Reserve Index questionnaire (CRIq), which provides a standardized measure of the cognitive reserve accumulated by individuals through their lifespan. The CRIq includes demographic data and items grouped into three sections: education, working activity and leisure time, each of which returns a subscore and composes the total score [45]. The results of the cognitive assessments and CRI are presented in Table 1.

2.2. Experimental verbal episodic memory task

2.2.1. Stimuli

The experimental procedure was structured in a first encoding phase followed by a retrieval phase. For the encoding phase we selected 51 abstract and 51 concrete words (3 abstract and 3 concrete words for a practice list) from the "Corpus e Lessico di Frequenza dell'Italiano Scritto (CoLFIS)" [46]. For the retrieval phase, we selected an additional pool of 51 abstract and 51 concrete "new" words (3 abstract and 3 concrete words for a practice list). Thus, the retrieval word list consisted of the original encoding or "old" words (48 concrete, 48 abstract) and 96 new words (48 concrete, 48 abstract). On average, the words were 6.8 (SD = 1.7) letters long with 2.9 (SD = 0.7) syllables. Abstract and concrete words were balanced according to word length and to variables known to influence memory performance. There were significant differences between the two word categories with respect to "concreteness" (concrete = 6.3 SD = 0.7; abstract = 3.9 SD = 0.8; $p < 0.05$) and "imageability" (concrete = 5.9 SD = 0.5; abstract = 3.3 SD = 0.6; $p < 0.05$) based on CoLFIS. The frequencies and lengths of the selected words were counterbalanced in the three experimental blocks.

2.2.2. Task procedure

Subjects were seated in a dimly lit room, facing a computer monitor that was placed 60 cm from the subject. The stimuli were presented using Presentation software (Version 14.9, www.neurobs.com) running on a personal computer with a 17-inch screen. Before starting the experiment, subjects completed a practice run. Both the encoding and the retrieval phases consisted of three separate blocks of 32 (16 concrete and 16 abstract) tri-