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Research report

Compensatory networks to counteract the effects of ageing on language

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HIGHLIGHTS

- rTMS was used to influence the function of the prefrontal cortex.
- TMS effects on naming ability differed according to the subject's performance.
- Less prefrontal asymmetry is a strategy to counteract age-related naming decline.

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ABSTRACT

Background: Word-retrieval difficulties are a common consequence of healthy ageing and are associated with a reduction in asymmetrical recruitment of the dorsolateral prefrontal cortex (DLPFC), although the significance of this reduction has not yet been clarified. Using repetitive transcranial magnetic stimulation (rTMS) it has been demonstrated that an asymmetrical involvement of the DLPFC during action naming in young subjects, whereas bilateral involvement was shown in elderly participants. By using rTMS during a naming task in a group of elderly subjects, the aim of the present work was to investigate whether the magnitude of DLPFC asymmetry (left–right rTMS effect) during action naming correlates with task performance, proving the presence of a compensation strategy in some but not all elderly participants.
Methods: We aimed to test if there was a correlation between DLPFC asymmetry (left–right rTMS effect) and naming performance in a group of elderly subjects.
Results: The results show that rTMS affects action naming differently according to individual naming ability. In particular, the predominance of a left vs. right DLPFC effect was observed only in the low-performing older adults, while an asymmetric reduction was selectively shown in the high-performing group. Interestingly, high-performing older adults also displayed better performances on a phonemic fluency test.
Conclusion: The present data suggest that successful ageing is linked to less prefrontal asymmetry, an efficient strategy for counteracting age-related declines in cognitive function.

1. Introduction

Ample evidence has illustrated the relationship between age-related changes in the brain and alterations in cognitive performance [1]. Studies at the neuronal level have demonstrated that during physiological ageing, dopaminergic decline as well as grey and white matter atrophy are both correlated with specific cognitive changes [2,3]. A recent review [4] concluded that the brain shrinks in volume and that the ventricular system expands in the ageing brain (with high heterogeneity). The volumetric reductions are likely related, to a minor extent, to neural loss because the shrinkage of neurons, reduction of synaptic spines and lower numbers of synapses probably account for the reduction in grey matter [4]. However, reductions in processing speed, memory, executive functions and language production have been shown during physiological ageing. Such reductions are mediated by neuroanatomical changes, with increased age often associated with lower performance on a wide variety of cognitive tasks [4,5]. Accordingly, it is clear that ageing is influenced by a large number of factors that vary from individual to individual, and, to date, it is unclear how differences in brain activity relate to cognitive performance in elderly participants [5,6]. Because the mean age of the population increases the number of people that will experience an age-related reduction in cognitive abilities will increase; despite this, although some individuals will show pronounced cognitive deficits, others will not.

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Understanding the basis of minor vs. major age-related cognitive decline is of great interest, and some investigations have assessed the predictive value of several factors for successful ageing [7,8], and non-pharmacological interventions for cognitive difficulties in healthy older adults have gained much attention in recent years [9–11]. Relevant studies have suggested that cerebral plasticity and cognitive reserve play important roles in physiological ageing [9,10,12,13].

One method used to investigate age-related modifications in cognition is neuroimaging, and neuroimaging data from some cognitive models on ageing have been acquired. A recent review highlights that the application of functional neuroimaging to healthy ageing participants suggests functional age-related changes during the execution of several cognitive tasks, despite the many discrepancies in this literature [14]. Alterations in hemispheric asymmetry have been reported in studies of physiological and pathological ageing [15–17]. Frontal asymmetry was significantly reduced during a cognitive task in healthy elderly participants as compared to young participants [16]. As one of the major cognitive declines in both healthy and pathological ageing is a reduction in memory performance, most of the neuroimaging studies on healthy ageing participants have investigated memory processes and suggest the presence of functional age-related reductions in the left prefrontal cortex (PFC) and temporo-occipital regions and increases in activity in the insular regions. Generally, these studies have shown a reduction in functional asymmetry in the prefrontal cortex [18] and have led to development of the hemispheric asymmetry reduction in older adults (HAROLD) model [16], subsequently confirmed by rTMS [16,19–24]. Additionally, over-activation of the PFC in older adults represents the starting point of the posterior–anterior shift in ageing (PASA) model, which implicates age-related increases in frontal activity and decreases in occipital lobe activity [25].

Language represents another example of a cognitive ability that dramatically changes during ageing. Evidence from both lesion and imaging studies suggests a central role for the left prefrontal, temporal and parietal areas during naming, although some differences exist for object (noun) vs. action (verb) naming [26–28]. A progressive reduction in lexical retrieval has been well-documented in older adults [29–31]. Unlike word-meaning retrieval, which appears to be preserved or even enhanced with ageing [32,33], the ability to retrieve the sound or phonology of words seems to decline in older adults. Moreover, the frequency of tip-of-the-tongue experiences significantly increases with ageing, and older adults report an inability to produce well-known words as one of the most annoying cognitive "symptoms" that they experience [34,35]. A few imaging studies have reported on a neural age-related change that correlates with the increase of this disturbance in healthy ageing. The results of these studies support a neural cause of word retrieval difficulties (tip-of-tongue effect) in physiological ageing, highlighting the effects of ageing on the activity of the insula [36] and in the white matter integrity of the posterior aspect of the superior longitudinal fasciculus [37].

Even if naming is an ability that shows adaptation during ageing, only a few studies have investigated how age-related changes in activity relate to performance during naming tasks in older adults.

Different hypotheses have been considered to explain the significance of these age-related changes. First, the compensation hypothesis [25,38–41] proposes that increased functional hemispheric symmetry in older adults is counteracted by age-related neurocognitive deficits. Second, the dedifferentiation hypothesis explains the reduced asymmetry as a difficulty in recruiting specialised neural networks [42,43]. Last, the default network theory postulates that the major components of the default mode network remain stable in healthy, older individuals, whereas the activity in a number of discrete cortical areas located in the prefrontal, temporal, and occipital regions changes over time [44]. There is a large degree of overlap among these hypotheses, but all of them at least partially underline the ability of cerebral tissue to change its structure and function continuously in response to environmental demands. To compare these hypotheses, several studies have investigated whether PFC functional symmetry is linked to a reduction or enhancement of memory performance, but the results are still inconclusive. Regarding naming tasks, only a few neuroimaging studies have shown age-induced increases in cortical activation in the brain areas typically associated with language processing (Broca's and Wernicke's areas) [45,46]. Interestingly, only one fMRI study has examined the role of functional age-related changes in naming abilities and found a positive correlation between BOLD responses, naming accuracy and response latencies in the frontal areas of older adults [46], verifying the presence of compensatory mechanisms in the frontal cortex that are invoked to maintain performance in healthy ageing. A recent review of the functional brain imaging correlates of successful cognitive ageing found frontal cortex responses in older, as compared to younger, individuals, independent of task [41].

However, functional neuroimaging data cannot prove the necessity of an area during a cognitive task because an activated area may simply be correlated with, rather than responsible for, task performance. In contrast, repetitive transcranial magnetic stimulation (rTMS) can induce a temporary impairment in performance only if the stimulated area is causally engaged in the task [47]. Based on this assumption, TMS has been used in many different cognitive domains to establish causality in brain–behaviour relationships and, specifically, to verify asymmetrical involvement of the PFC during selected tasks. Hemispheric specialisations of the dorsolateral PFC (DLPFC) during episodic memory have previously been demonstrated using rTMS in young subjects [19,21–23,48–52] and in elderly adults [20,53]. For an extensive review of this literature, please refer to Manenti et al. [24]. Regarding naming, an rTMS study of young participants showed a left predominance of the DLPFC during action naming [54]. A unique study that investigated the effects of physiological ageing on DLPFC asymmetry during action and object naming showed a selective bilateral facilitatory effect during action naming, namely a decrease in vocal reaction time, in a group of older adults [55].

The purpose of this study was to examine if the magnitude of DLPFC lateralisation (left–right rTMS effect) during action naming was correlated with task performance, proving the presence of a compensation strategy in some but not all elderly participants. In the present report, we re-analysed data acquired in our previous study [55] to thoroughly investigate this issue. Based on previous studies [20,46,56], we predicted that DLPFC hemispherical symmetry during action naming would only be present in high-performing older adults. If identified, this result would prove that a reduction in DLPFC asymmetry in some but not all elderly participants represents a compensation strategy used to counteract age-related changes, resulting in better task performance.

2. Materials and methods

2.1. Participants

Prior to being enrolled in the experiment, participants were administered a standard health history questionnaire and completed a Mini Mental State Examination (MMSE) [57]. Potential participants were excluded if they reported a history of neurological disease, cardiovascular disease, psychiatric disorders or alcohol or other substance abuse. Individuals who reported subjective memory complaints or scored below 27 out of 30 on the MMSE were also excluded. In addition, a neuropsychological battery was applied, and a pathological score in at least one of the tests was a further exclusion criterion. Thirteen (4 male, 9 female) healthy older adults (age: 65–78 years, mean = 70.2 years, education: mean = 13.8 years) participated in the rTMS experiment. All participants were native Italian speakers and had normal or corrected-to-normal vision. All participants were right-handed [58] and had no contraindications for rTMS [59]. This study was approved by the local ethics