Investigating the neural basis of healthy cognitive ageing using functional imaging and neruostimulation: Are two hemispheres better than one?

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Background:

It is generally accepted that some cognitive tasks preferentially engage activity in one side of the brain (Walker, 1980). For example, it has been consistently demonstrated that speech production relies heavily on regions of the left frontal lobe (Pujol et al., 1999). On the other hand, the right frontal lobe has been repeatedly linked with aspects of behavioural control and inhibitory processing (Mostofsky et al., 2008). Interestingly, as the human brain ages, this lateralization of function appears to be gradually replaced by a more distributed pattern of neural activity involving both cerebral hemispheres (Cabeza, 2002). The exact reason for age-related shifts to bilateral processing is unclear, however it has been proposed that it may reflect dedifferentiation of neural activity or functional reorganisation.

According to the dedifferentiation account, additional neural activity reflects the loss of specialisation in previously sensitive neural populations and is indicative of age induced pathology (Li et al., 2001). This account is primarily based on evidence showing that age related overactivation is observed in conjunction with poorer behavioural performance (Colcombe et al., 2005; Duverne et al., 2009). Importantly, this approach proposes that the ageing brain recruits general task irrelevant neural activity that does not aid cognitive performance. Indeed, Spreng et al. (2010) have reported that increased activation of the right frontal lobe in older adults is associated with poor task performance.

In contrast, the functional reorganisation account stresses that additional activity serves a compensatory role, supporting previously dominant neural networks that have become less efficient with age, with the epicentre of compensatory activity will be localised in the identical neural structure on the opposite side (Cabeza et al., 2002). In many of the studies reviewed by Eyler et al. (2011), additional activity in the opposite but identical structure appears to be crucial in supporting efficient task performance. These results have led to development of the hemispheric asymmetry reduction in older adults model (HAROLD), which suggests functional lateralization breaks down with ageing in an attempt to maintain a high level of cognitive ability (Cabeza, 2002).

Research concerning the mental ability of older adults has consistently demonstrated that the normal ageing process is associated with deficits in multiple cognitive operations (Park et al., 2009). Interestingly, these deficits appear to be most severe on tasks that usually engage unilateral activity in younger adults, such as speech production and response inhibition (Burke & Shafto, 2004; Gazzaley & D'Esposito, 2007). These deficits can undermine social interaction, confidence and general wellbeing (Ryan et al., 1995). Given that past research has delivered mixed results concerning the neural mechanisms that support good performance during normal aging, this project aims to determine the role of age-related bilateral processing through a unique combination of functional imaging and neuromodulation.

Research Plan:

Firstly two groups of 20 younger adults (aged 18-25) and 20 older adults (aged 65+) will perform a speech production and behavioural inhibition task whilst undergoing functional magnetic resonance imaging (fMRI). These tasks have been chosen because research suggests they induce unilateral frontal activity in younger adults and more bilateral frontal activity in older adults (Wierenga et al., 2008). By including an imaging component it is possible to confirm age related areas of overactivation that can then be selectively targeted for neuromodulation. According to the HAROLD model, it is expected that high functioning older adults will engage in more bilateral frontal activity in both tasks, while younger participants are expected to exhibit predominately left frontal activity during speech production and right during behavioural inhibition.

The second stage of the study will involve applying Transcranial Direct Current Stimulation (tDCS) to the same 40 participants. tDCS involves the application of a weak electrical current to the cerebral cortex delivered via two electrodes placed on the scalp. Excitability can be increased by anodal stimulation or decreased by cathodal stimulation relative to a sham baseline. Participants will perform the same behavioural tasks used previously while receiving anodal stimulation to the lateralized frontal lobe (left for speech production and right for response inhibition), cathodal to the contralateral frontal lobe and sham stimulation to both sites. It is anticipated that excitatory stimulation of the lateralised structure will improve task performance in young and older adults, however the effect will be more pronounced for older adults due to the relative weakness of this region. If older adults are relying on activity of the non-dominant hemisphere to compensate for this weakness, then inhibitory stimulation of the contralateral frontal lobe (right for speech production and left for response inhibition) should impair performance, an effect that will be not be observed in younger adults. Such an approach will determine whether overactivation is indeed compensatory by experimentally modulating neural activity, a technique that has not been previously utilised in the cognitive ageing literature. Clarification of this issue is essential if we are to exploit the potential of neurostimulation to help offset the detrimental effects of normal cognitive ageing in the future.

References:

Burke, D. M., & Shafto, M. A. (2004). Ageing and language production. *Current Directions in Psychological Science*, *13(1)*, 21-24.

Cabeza, R. (2002). Hemispheric asymmetry reduction in older adults: The HAROLD model. *Psychology and Ageing*, 17(1), 85-100.

Cabeza, R., Anderson, N. D., Locantore, J. K., & McIntosh, A. R. (2002). Ageing gracefully: Compensatory brain activity in high-performing older adults. *Neuroimage*, *17(3)*, 1394-1402.

Colcombe, S.J., Kramer, A.F., Erickson, K.I, & Scalf, P. (2005). The implications of cortical recruitment and brain morophology for individual differences in inhibitory function in ageing humans. *Psychology of ageing, 20*, 363-375.

Duverne, S., Motamedinia, S., & Rugg, M.D. (2009). The relationship between ageing, performance , and neural correlates of successful memory encoding. *Cerebral cortex, 19*, 733-744.

Eyler, L.T., Sherzai, A., Kaup, A.R., & Jeste, D.V. (2011). A review of function brain imaging correlates of successful cognitive ageing. *Biological psychiatry, 70*, 115-122.

Gazzaley, A., & D'Esposito, M. (2007). Top-down modulation and normal ageing. *Annals of the New York Academy of Sciences, 1097*, 67-83.

Mostofsky, S. H., Simmonds, D. J., & Pekar, J. J. (2008). Meta-analysis of Go/No-go tasks, demonstrating that fMRI activation associated with response inhibition is task-dependent. *Neuropsychologia, 46(1)*, 224-232.

Park, D. C., & Reuter-Lorenz, P. (2009). The Adaptive Brain: Ageing and Neurocognitive Scaffolding. *Annual Review of Psychology, 60*, 173-196.

Pujol, J., Deus, J., Losilla, J. M., & Capdevila, A. (1999). Cerebral lateralization of language in normal left-handed people studied by functional MRI. *Neurology, 52(5)*, 1038-1043.

Ryan, E.B., Hummert, M.L., & Boich, L.H. (1995). Communication predicaments of ageing: Patronizing behaviour toward older adults. *Journal of Language and Social Psychology, 14*, 144-166.

Spreng, R.N., Wojtowicz, M., & Grady, C.L. (2010). Reliable differences in brain activity between young and old adults: A quantitative meta-analysis across multiple cognitive domains.

Walker, S. F. (1980). Lateralization of Functions in the Vertebrate Brain - a Review. *British Journal of Psychology, 71*, 329-367.

Wierenga, C. E., Benjamin, M., Gopinath, K., Perlstein, W. M., Leonard, C. M., Rothi, L. J. G., et al. (2008). Age-related changes in word retrieval: Role of bilateral frontal and subcortical networks. *Neurobiology of Ageing, 29(3)*, 436-451.