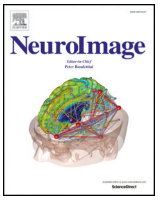
NeuroImage 130 (2016) 48–62

Contents lists available at ScienceDirect

NeuroImage

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



Task complexity and location specific changes of cortical thickness in executive and salience networks after working memory training

Claudia Metzler-Baddeley [a,*], Karen Caeyenberghs [b], Sonya Foley [a], Derek K. Jones [a]

[a] *Cardiff University Brain Research Imaging Centre (CUBRIC), School of Psychology, and Neuroscience and Mental Health Research Institute (NMHRI), Cardiff University, Cardiff CF10 3AT, UK*
[b] *School of Psychology, Australian Catholic University, Melbourne, Australia*

ARTICLE INFO

Article history:
Received 21 September 2015
Accepted 5 January 2016
Available online 13 January 2016

Keywords:
Working memory training
Cortical thickness
Executive network
Salience network
Insula
Parieto-frontal regions
Activity-dependent brain plasticity

ABSTRACT

Novel activities and experiences shape the brain's structure and organisation and, hence, our behaviour. However, evidence from structural plasticity studies remains mixed and the neural correlates of learning and practice are still poorly understood. We conducted a robustly designed study into grey matter plasticity following 2 months of working memory training. We generated a priori hypotheses regarding the location of plastic effects across three cognitive control networks (executive, anterior salience and basal ganglia networks), and compared the effects of adaptive training ($n = 20$) with a well-matched active control group ($n = 20$) which differed in training complexity and included extensive cognitive assessment before and after the training. Adaptive training relative to control activities resulted in a complex pattern of subtle and localised structural changes: Training was associated with *increases* in cortical thickness in right-lateralised executive regions, notably the right caudal middle frontal cortex, as well as *increases* in the volume of the left pallidum. In addition the training group showed *reductions* of thickness in the right insula, which were correlated with training-induced improvements in backward digit span performance. Unexpectedly, control activities were associated with reductions in thickness in the right *pars triangularis*. These results suggest that the direction of activity-induced plastic changes depend on the level of training complexity as well as brain location. These observations are consistent with the view that the brain responds dynamically to environmental demands by focusing resources on task relevant networks and eliminating irrelevant processing for the purpose of energy reduction.

Introduction

The human brain is known to respond adaptively to varying environmental demands (Pascual-Leone et al., 2005). There is general consensus that in addition to our genes, novel activities and experiences may shape the brain's structure and organisation and, hence, our behaviour. However, the neural correlates of learning in the human brain still remain poorly understood. Magnetic resonance imaging (MRI) techniques provide non-invasive tools to investigate training induced brain plasticity *in vivo* and hence may aid our understanding of the neural substrates underpinning learning and practice effects.

Evidence for training-induced brain plasticity remains inconsistent and controversial (Thomas and Baker, 2013). Longitudinal studies into macrostructural brain plasticity have found mixed findings regarding the direction of training-induced alterations in grey matter volume or cortical thickness in task-relevant brain regions (Draganski and May, 2008; Engvig et al., 2010; Mårtensson et al., 2012; Takeuchi et al., 2011; Taubert et al., 2010) (see for review Thomas and Baker, 2013; Valkanova et al., 2014). For instance Draganski et al. (2004) found *increases* in grey matter volume in temporal and parietal regions after 3 months of juggling whilst Takeuchi et al. (2011) reported *reductions* of grey matter volume in parieto-frontal cortical regions after working memory training.

A number of factors may explain these inconsistencies and point to a need for more empirical evidence based on well-controlled studies using a rigorous experimental design (see Thomas and Baker, 2013; Valkanova et al., 2014). For instance, experimental control of the nature of activities undertaken by the comparison groups in previous studies was often weak or not present. Previous studies also varied considerably in terms of activity and length of training interventions as well as the chosen behavioural and imaging outcome measures. Further, the neural mechanisms thought to contribute to the net changes in MRI indices include complex processes of neurogenesis, synaptogenesis, glia cell and myelin formation and selective pruning of nerve fibres (Zatorre et al., 2012). These mechanisms are likely to operate in a dynamic fashion and on different time scales and hence may lead to different effects depending on the precise training conditions and the brain region in which observations are made (Pajevic et al., 2014; Zatorre et al., 2012).

The present study followed recent recommendations (Thomas and Baker, 2013) and addressed many of the problems above to shed further light on the nature of training-induced cortical plasticity. An established

---

* Corresponding author. Fax: +44 29 208 70339.
E-mail address: Metzler-BaddeleyC@cardiff.ac.uk (C. Metzler-Baddeley).

http://dx.doi.org/10.1016/j.neuroimage.2016.01.007
1053-8119/

working memory training (Cogmed, 2012) targeting the ability to maintain and manipulate information temporarily (Baddeley, 1996) was chosen because of its demonstrated efficacy in terms of improving working memory span capacity (Holmes et al., 2009; Klingberg, 2010).

Participants were asked to train their working memory using computerised verbal and spatial working memory span tasks for 2 months (Cogmed, 2012). To ensure that participants trained at an optimally challenging level, task difficulty was increased or decreased adaptively depending on a trainee's performance levels (adaptive training). Importantly, the effects of adaptive training on cognition and brain structure were compared to an active control condition in which the same working memory tasks were performed for the same number of sessions (40 in total) but at a constant low level of difficulty (non-adaptive control). Thus the two groups were exposed to the same number and order of learning activities in the same computer environment but differed in terms of the level of training complexity.

Working memory training was also chosen because of evidence from neuroimaging studies of localised structural and functional alterations in parieto-frontal regions: Reduced grey matter volume in dorsolateral prefrontal and parietal cortices (Takeuchi et al., 2011), increased diffusion MRI derived fractional anisotropy around the intraparietal sulcus (Takeuchi et al., 2010), increased functional MRI activity in right middle frontal gyrus, inferior parietal and intraparietal cortices (Olesen et al., 2004) and changes in D1 receptor binding potential in right dorsal and ventral frontal and posterior cortices (McNab et al., 2009).

In addition there is a large body of evidence based on imaging and lesion studies that parieto-frontal regions, notably the dorsolateral prefrontal cortex and posterior parietal cortex, form part of a central executive network important for the control of goal-directed actions in working memory (Duncan and Owen, 2000; Owen et al., 1990). The executive network is thought to interact with anterior salience and basal ganglia regions to support efficient working memory processes (Dosenbach et al., 2008; Dosenbach et al., 2006; Menon and Uddin, 2010). Anterior insula and anterior cingulate cortex detect salient stimuli and initiate executive control (Menon and Uddin, 2010) whilst the basal ganglia regulate the information flow into working memory and the selection of goal-directed responses via inhibitory feedback loops (Gurney et al., 2001a, 2001b; McNab and Klingberg, 2008; McNab et al., 2008; Redgrave et al., 2010; Redgrave et al., 2011). Temporal dynamic changes in the striatum have also been observed after working memory-updating training (7 versus 50 days) suggesting a potential role of the basal ganglia in mediating working memory function (Kühn et al., 2013).

Thus based on ample evidence regarding brain regions involved in working memory functions combined with the results from previous working memory plasticity studies, it was possible to formulate hypothesis-driven predictions regarding the localisation of the expected structural alterations, hence yielding anatomical specificity (Thomas and Baker, 2013). We utilised the known anatomy of the central executive, anterior salience, and basal ganglia networks as well as the results by Olesen et al. (2004) to guide the selection of cortical and subcortical regions of interest (ROI) from the Desikan–Killiany parcellation scheme (2006) (see Fig. 1).

An ROI approach was chosen because it is already known that training may lead to localised changes in brain networks that support the trained activity and that such plastic changes are usually small in effect size (Thomas and Baker, 2013; Valkanova et al., 2013). For instance, memory training in older people was found previously to increase cortical thickness by around 0.05 mm (Engvig et al., 2010). Thus the rationale for focusing on the selected ROIs was to increase the power of our study to detect localised and subtle training effects across different cognitive control networks.

For each ROI we measured average cortical thickness or subcortical volume respectively at baseline and outcome time points. Cortical thickness measures were derived from the FreeSurfer longitudinal analysis pipeline (Reuter et al., 2012) which was chosen due to the demonstrated precision (Lerch and Evans, 2005), reproducibility (Reuter et al., 2012), sensitivity to longitudinal changes (Engvig et al., 2010; Sabuncu et al., 2011) and consistency with post mortem data (Fischl and Dale, 2000).

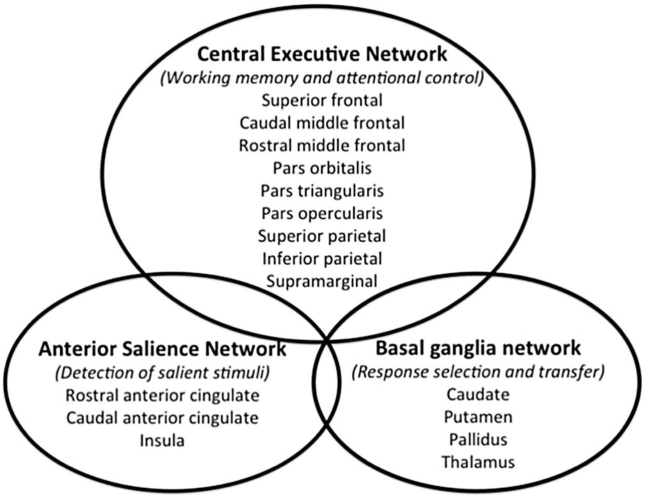


Fig. 1. Schematic representation of cortical and sub-cortical regions of cognitive control networks and their proposed function. Target regions of the central executive, anterior salience and basal ganglia networks were selected from the Desikan–Killiany atlas (Desikan et al., 2006). Executive parieto-frontal regions selected were the inferior parietal cortex, superior parietal cortex, supramarginal gyrus encompassing intraparietal sulcus, caudal middle frontal gyrus, rostral middle frontal gyrus, superior frontal cortex as well as *pars opercularis*, *pars triangularis*, and *pars orbitalis* of the inferior ventrolateral prefrontal cortex. Anterior salience network regions selected were the insula and caudal and rostral anterior cingulate cortices. Sub-cortical regions of the basal ganglia, i.e., caudate, putamen, and *globus pallidum* and the thalamus were also included in the analyses. All regions were included from both hemispheres.

We hypothesised that 2 months of adaptive working memory training would lead to alterations in cortical thickness in parieto-frontal executive network regions notably in the middle frontal gyrus, inferior parietal and intra-parietal cortices of the right hemisphere (e.g. Olesen et al., 2004). Although previous studies provided guidance with regard to which brain regions were expected to alter their thickness, it was more difficult to generate hypotheses regarding the direction of change. Based on findings of increased receptor density we expected to observe an increase in cortical thickness in parieto-frontal regions likely due to an increase in neural activity and hence an increase in synapses, receptors and myelin-forming glia cells. However, Takeuchi et al. (2011) reported reductions of grey matter volume in parieto-frontal regions suggesting that training effects are more complex and may depend on the precise training schedule and location in the brain.

Similarly, working memory training has been associated both with a decrease of fMRI BOLD activity (Olesen et al., 2004) and an increase in functional resting state connectivity of the anterior cingulate, a region of the anterior salience network (Jolles et al., 2013). Although structural and functional MRI measures are not directly comparable, we utilised these findings to hypothesise that adaptive training would result in changes in anterior salience network regions, i.e., in the anterior cingulate and the insula; however, the direction of plastic changes to be expected remained unclear (Jolles et al., 2013; Olesen et al., 2004).

Participants were tested before and after the training in a number of near- and far-transfer working memory and executive function benchmark tasks (Owen et al., 2010). We assumed that training-induced plastic alterations would be relevant for working memory functions and hence hypothesised any potential structural changes to correlate with training specific cognitive improvements. Finally, the question of whether reasoning and executive function abilities can be improved by working memory training remains controversial (Melby-Lervåg and Hulme, 2013; Shipstead et al., 2012; von Bastian and Oberauer,