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White matter and Reaction Time: Reply to Commentaries[1]

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Abstract

We appreciate the many comments we received on our discussion paper, and believe that they reflect a recognition of the importance of this topic worldwide. We point out in this reply that there appears to be a confusion between the role of oscillations in creating white matter and other functions of oscillations in communicating between neural areas during task performance or at rest. We also discuss some mechanisms other than the enhancement of white matter that must influence reaction time. We recognize the limited understanding we have of transfer, and outline some future directions designed to improve our understanding of transfer.

Keywords

Diffusion Tensor Imaging; Oligodendrocytes; Oscillations; Transfer; White Matter

We agree with the commentators that the evidence on which our discussion is based is both incomplete and subject to revision, and appreciate their efforts to caution readers against premature conclusions. We also support the possible extension of our ideas in directions we did not deal with in our original paper. Below we group the comments into major categories, seeking to clarify our views and to encourage additional research.

The Dual Role of Oscillations

Several papers (Hopfinger; Kepinska & Schiller; and Slagter, Vissers, Talsma & Ridderinkhof) suggest that the theta rhythm is just one of the many oscillations that occur during cognitive tasks. They correctly indicate that alpha, beta and gamma oscillations play important roles in cognitive tasks. This provides an opportunity to clarify a central issue of our argument. We believe there is an important distinction between the oscillations related to communication between areas during task performance or in the resting state and those oscillations that influence changes in white matter. Our unpublished mouse data suggests that low frequency stimulation results in changes in oligodendrocytes from a dormant to an active form with the capacity to increase white matter efficiency. We used biochemical methods to mark the changes in oligodendrocytes that occurred during the experiment

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(McKenzie et al 2014). We are now using electron microscopy to test whether and how white matter is changed. High frequency (in our case 40 Hz) stimulation does not increase changes in oligodendrocytes to an active form and may even result in their reduction, even though gamma oscillations (40 Hz and higher frequency) are important in communication between neural areas (Canolty et al 2006). We believe that the changes in white matter that occur with low frequency stimulation or with learning can improve communication in ALL frequencies, not merely at low frequencies. This distinction may help reconcile the importance of many different frequencies involved in task performance with the more restricted activity that results in white matter change.

Mechanisms of RT Change

Our views do not require that white matter change be positively correlated with BOLD signal changes, an issue raised by Farrar & Budson, who point out that BOLD change may or may not correlate with DTI findings. We comment on the more general issue of whether both grey and white matter contribute to reaction time (Kuang; Williams) below.

We agree with the many comments pointing out that white matter change may be only one of the mechanisms that account for changes in RT (Aisenberg, Cohen and Linkovsky; Kuang; Williams). It is clear that white matter change cannot be involved in all RT changes. For example, in repetition and semantic priming there is clearly no time for white matter to change within the short time between prime and target presentation, since priming effects can be seen on the very first occasion. Even in skill learning the change in RT with practice may only involve white matter in the later stages of practice.

RT often improves after a single trial. We assume that cellular processes and changes in micro-circuitry are associated with some of these rapid behavioral phenomena. However, we do not see white and gray matter changes as being incompatible (Williams). Indeed, long term potentiation, one of the chief learning mechanisms of neurons, can also be induced by theta (Larson, Wong & Lynch, 1986) and we believe that change in gray and white matter are linked. It seems likely that cellular changes are first induced by new learning and as more cells are involved these result in changes in axon density and/or myelination changes in the white matter.

As outlined by Roy & Pammi, there are many difficulties in interpreting DTI studies of white matter. There are difficulties in tracing overlapping pathways and in interpretation of DTI parameters. These are among the many reasons we have worked with a mouse model to determine more directly whether and how white matter undergoes the changes suggested by the DTI results in our meditation training studies (Tang et al 2010; 2012). If rhythmic illumination can alter axonal density and/or myelination, we can establish closer relations between the statistical parameters measured by DTI (such as radial and axial diffusivity) and physical changes observed with electron microscopy.

Aisenberg and colleagues suggest that improvements in strategy may be involved in RT change. This is certainly one of the psychological explanations for improvement in RT with learning. However, a strategy is a summary of processes at the psychological level, whereas

we argue that strategic changes are related to structural improvement of neural networks. If new neural pathways undergo cellular or axonal changes during practice on the task we will have an understanding of the physical basis for a change in strategy.

Does Transfer Involve Overlap of Pathways?

Even if white matter change improves RT for a given task, many commentators, for example, Aisenberg, Cohen & Linkovsky question whether this implies transfer to remote tasks. Bilinguals activate mechanisms used to resolve conflict as they switch between languages. This should predict that they would show improved executive attention and some studies do show this (Wisehart & Bialystok, 2016). While these observations remain controversial (Papp & Greenberg, 2013), they are a good example of where we would predict far transfer, based on the general proposition that exercising control of conflict between languages would involve the anterior cingulate and over time improve its ability to monitor and control conflict in many tasks involving the executive attention network in the control of conflict.

On the other hand, working memory training generally activates lateral brain areas and we would think it less likely that they would transfer to conflict tasks that involve medial regions such as the anterior cingulate and insula. We believe that the effort to examine such predictions could be useful in guiding future research.

As Aisenberg et al point out, transfer may depend on many factors, including age, and to incorporate these many factors it is important to construct computational models based on principles of transfer between tasks.

Computational Models

Several authors suggest that computational models might be a better way to examine reaction time change (Siettos & Smyrnis; Williams). For example Siettos & Smyrnis argue that stochastic models of eye movements account for RT without the inclusion of brain mechanisms. It should be pointed out that even shifts of eye movements involve a coordination of many brain areas including the frontal eye field, parietal lobe and superior colliculus. Coordinating these areas involves long pathways which might be important in accounting for RT differences in the task. Moreover, tasks such as problem solving, involving complex mental processes, would recruit additional brain areas not activated by simple eye movements and would thus represent an increased opportunity for white matter to influence RT.

It is our intention to develop a computational model related to our studies of skill learning. We believe that new findings concerning the mechanisms that influence response speed need to be expressed in new computational models.

During normal development from childhood to adulthood, RT to perform a cognitive task is reduced (Voelker, Rothbart &Posner, 2016) and studies indicate that improved white matter change in long connections is an important reason (Fjell et al 2012). In our studies of children (Voelker, Sheese, Rothbart & Posner 2016) and adults (Voelker, Rothbart & Posner,

2016) we found a gene related to the efficiency of methylation that influences improvement in RT. However, in some children and adults, RT actually increased later in practice. A different gene related to sustained attention appeared to be involved in this increase. An increase in RT violated most current models of the relation between practice and speed of performance. Our results were more consistent with the classic rat models of performance in which each trial produced both facilitatory and inhibitory effects on speed (Hull, 1943). An important goal is to develop models that take account of both behavioral and brain mechanisms involved in changes in RT with learning.

Future Studies

Our future efforts using the mouse model are designed to replicate the finding that low frequency stimulation (1 and 8 Hz) increases active oligodendrocytes (also see work cited by Bujalka & Emery). In addition, we are using electron microscopy to determine if this change in active oligodendrocytes leads to increases in axon density and myelination.

As suggested by Bujalka & Emery, we also hope to compare human and mouse studies in more detail by examining human white matter changes with DTI and comparing this with mouse axonal changes using electron microscopy. This could help with the difficulties of interpreting statistical parameters of DTI raised by Roy & Pammi.

There will be several other opportunities to compare mouse and human data at different levels. We have obtained mouse behavioral data on duration of time spent in the light versus in the dark following the month of low frequency stimulation. Our finding that mice opt for greater time in the light after 1 and 8 Hz stimulation may be related to the anxiety reduction we see in people after meditation training.

In human DTI studies, we found increases in white matter in connections to and from the anterior cingulate following meditation training. After two weeks of training these changes were in axon density as measured by axial diffusivity using DTI. After four weeks of training the changes involved both axial and radial diffusivity indicating changes in axon density and myelination (Tang et al 2012). We can compare this human result with the time course of changes due to low frequency stimulation in mice. For more direct comparison it may be possible to use low frequency stimulation in humans from the scalp by transcranial electrical or magnetic stimulation to compare against the mouse data obtained by optogenetics. We also plan to examine mouse brain tissue and blood following stimulation to compare changes in gene expression to those in human blood following meditation training. However, most of these efforts are still less direct than comparing the increase in oligodendrocytes suggested by Bujalka & Emery. The many issues involved in direct comparisons of mice and humans remain difficult to resolve.

We thank all for their helpful comments. We know that a completely satisfactory account of how changes in the brain support the behavioral observations found with many forms of training remains a difficult problem Even more complex are issues surrounding the identification of changes that could support transfer to other tasks. We hope that our paper

and our current studies, together with the work of others mentioned in the commentaries, can make a contribution to the solution of these difficult issues.

Reference List

Aisenberg D, Cohen Z, Linkovsky O. Training and transfer in aging – Is pathways overlap really necessary? Cognitive Neuroscience. (this issue).

Bujalka H, Emery B. Cellular mechanisms of adaptive myelination: Bridging the gap between animal studies and human cognition. Cognitive Neuroscience. (this issue).

Canolty RT, Edward E, Dalal SS, Soltani M, Nagarajan SS, Kirsch HE, Berger MS, Barbaro NM, Knight RT. High gamma power Is phase-locked to theta oscillations in human neocortex. Science. 2006; 313(5793):1626–1628. [PubMed: 16973878]

Farrar D, Budson A. The relationship between functional magnetic resonance Imaging activation, diffusion tensor imaging, and training effects. Cognitive Neuroscience. (this issue).

Fjell AM, Walhovd KB, Brown TT, Kuperman JM, Chung Y, Hagler DJ Jr, Dale AM. Multimodal imaging of the self-regulating developing brain. Proceedings of the National Academy of Sciences. 2012; 109(48):19620–19625.

Hopfinger JB. Relation of higher frequency oscillatory activity to white matter changes and to core mechanisms of attention. Cognitive Neuroscience. (this issue).

Kepinska O, Schiller NO. Possible neural oscillatory mechanisms underlying learning. Cognitive Neuroscience. (this issue).

Hull, CL. Principles of behavior, an introduction to behavior theory. New York, NY: Appleton-Century Company; 1943.

Kuang S. Is reaction time an index of white matter connectivity during training? Cognitive Neuroscience. (this issue).

Larson J, Wong D, Lynch G. Patterned stimulation at the theta frequency is optimal for the induction of hippocampal long-term potentiation. Brain Research. 1986; 368:347–350. [PubMed: 3697730]

McKenzie IA, Ohayon D, Li H, De Faria JP, Emery B, Tohyama K, Richardson WD. Motor skill learning requires active central myelination. Science. 2014; 346(6207):318–322. DOI: 10.1126/science.1254960 [PubMed: 25324381]

Papp KR, Greenberg Z. There is no coherent evidence for a bilingual advantage in executive processing. Cognitive Psychology. 2013; 66(2):232–258. [PubMed: 23370226]

Roy D, Pammi VSC. Promises and pitfalls of relating alteration of white matter pathways causing improvement in cognitive performance. Cognitive Neuroscience. (this issue).

Siettos CI, Smyrnis N. Reaction Time as a stochastic process implemented by functional brain networks. Cognitive Neuroscience. (this issue).

Slagter HA, Vissers ME, Talsma LJ, Ridderinkhof KR. Cognitive enhancement: it's about time. Cognitive Neuroscience. (this issue).

Tang YY, Lu Q, Fan M, Yang Y, Posner MI. Mechanisms of White Matter Changes Induced by Meditation. Proceedings of the National Academy of Sciences. 2012; 109(26):10570–10574. DOI: 10.1073/pnas.1207817109

Tang Y, Lu Q, Geng X, Stein EA, Yang Y, Posner MI. Short term mental training induces white-matter changes in the anterior cingulate. Proceedings of the National Academy of Sciences. 2010; 107:16649–16652.

Vanderklish P, Saido TC, Galll C, Aral A, Lynch G. Proteolysis of spectrin by calpain accompanies theta burst stimulation in cultured hippocampal slices. Brain Research. 1995; 32:25–35. [PubMed: 7494460]

Voelker P, Piscopo D, Weible A, Lynch G, Rothbart MK, Posner MI, Niell CM. How changes in white matter might underlie improvement in reaction time with practice. Cognitive Neuroscience. 2016; doi: 10.1080/17588928.2016.1173664

Voelker P, Rothbart MK, Posner MI. A polymorphism related to methylation influences attention during performance of speeded skills. AIMS Neuroscience. 2016; 3(1):40–55.

Voelker P, Sheese BE, Rothbart MK, Posner MI. Methylation polymorphism influences practice effects in children during attention tasks. Cognitive Neuroscience. 2016; doi: 10.1080/17588928.2016.1170006

Williams JM. Complex models of white and gray matter integration following training. Cognitive Neuroscience. (this issue).

Wiseheart M, Viswanathan M, Bialystok E. Flexibility in task switching by monolinguals and bilinguals. Bilingualism (Cambridge, England). 2016; 19(1):141–146.