Letter to the Editor

Re: 'Failure of spinal paired associative stimulation to induce neuroplasticity in the human corticospinal tract.'

McGie and colleagues¹ describe the use of paired stimulus protocols to induce corticospinal pathway plasticity in the human spinal cord. In some aspects, techniques used were similar to previous reports^{2–5}; however, previously reported findings were not replicated.

We would like to raise several concerns regarding the methodology of the recent article in context of the relevant literature.

The most critical concern is that the article states that methods were very similar to previous reports, with methods most likened to Bunday and Perez,² which implemented a protocol of paired stimuli to corticospinal axons and motoneurons to induce facilitation of corticospinal-motoneuronal synapses, a technique first described in 2009 by Taylor and Martin.⁵ There are key differences between this previously described technique, and that reported by McGie *et al.*, including differences in stimulus timing and intensity.

Previous work describes pairing transcranial magnetic stimuli (TMS) and electrical peripheral nerve stimuli (PNS) to elicit descending corticospinal volleys timed to arrive at corticospinal-motoneuronal synapses 1–2 ms prior to antidromic potentials in postsynaptic motoneurons.^{2,5} The specific timing of pre- and postsynaptic volleys is critical for the resulting direction of plasticity. The arrival of presynaptic volleys at the synapse before postsynaptic volleys favours facilitation, whereas the reverse favours depression, comparable to the well-known phenomenon of spike-timing-dependent-plasticity.⁶ In contrast, McGie *et al.* timed volleys to arrive simultaneously. This may be problematic because small latency differences could cause facilitation or depression depending on the precise order of volley arrival.

In addition, McGie *et al.* discuss a possible 'mismatch between muscle fibres targeted' by paired stimuli, which is true in their case, as they used PNS intensities of 1.2 times motor threshold, thereby activating only a portion of the motoneuron pool. They state that higher stimulation intensities may provide better matching of volleys and that existing literature does not address this; however Taylor and Martin, and subsequently Bunday and Perez, directly addressed this issue by using PNS to elicit maximal responses, thus antidromically activating the entire motoneurone pool and ensuring a match with corticospinal volleys.^{2,5} Perhaps the technique used by McGie and colleagues is more consistent with other studies^{3,4}; however in these, TMS was paired with low intensity PNS to activate Ia afferents, rather than antidromically activating motoneurons, and spinal changes were tested with conditioned H-reflexes, not TMS-elicited responses as was the case for McGie *et al.*

Given these methodological differences, it is unsurprising that McGie *et al.* could not replicate previous results. Although there are other methodological inconsistencies, such as the questionable use of grip force and adduction to test the abductor pollicis brevis, the key points made here are sufficient to say that the technique used by McGie *et al.* is not comparable to previous reports, and is not evidence against the use of paired corticospinal, motoneuronal stimulation. Treating it as such would be detrimental to the emerging body of work describing the use of the technique for producing functionally relevant improvements in corticospinal transmission in able-bodied and spinal cord injured humans.

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References

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