conditions like dystonia and Parkinson's disease [79,80]. The cerebellum in important for procedural learning [81] and for spatial and verbal aspects of working memory [78]. In patients with cerebellar atrophy there is an impaired capacity for procedural learning, specifically when performing tasks with the hand ipsilateral to the side of the cerebellar lesion [82]. Procedural learning assessed by the serial reaction time test (SRTT) can be improved in healthy adults by cerebellar TDCS [81,83]. Several studies have found the cathodal TDCS to the cerebellum affected the performance of working memory tasks [84-86]. Finally, performance on a visuomotor adaptation task in healthy adults was improved by anodal TDCS [76].

We are interested in whether interventions that target cerebellum for motor learning may affect non-motor function and if promotion of non-motor cerebellar learning may have benefits for motor control. Evidence for cognitive dysfunction in dystonia is still emerging. It is know that aspects of sensory and motor timing related to movement processing and planning are affected are disrupted in people with FHD [87]. There is emerging evidence that motor learning is deficient in people with cervical dystonia using neurophysiological measures of learning [88,89]. People with FHD are slower to adapt to visuomotor perturbations than healthy adults [90]. The only working memory task tested to date to our knowledge is the mental rotation task, a visuospatial working memory task [78]. People with FHD and CD perform poorly on mental rotation tasks involving corporal objects [91,92]. Other aspects of procedural learning and working memory need to be systematically tested in people with dystonia along with the effect of cerebellar NBS on these cognitive processes.

Another interesting aspect arising from a cerebellar contribution to cervical dystonia is that due to lateralisation in cerebellar function [81], there may be an association between deficits and the direction of head turn (i.e. dystonic posture). Lateralisation of the cerebellum is due to the mostly contralateral nature of the connections between cerebellum and cerebral cortex [93], although about 10% of fibres project to the ipsilateral M1. The right cerebellum is concerned with linguistic processes while the left is specific to spatial information [94]. The left cerebellum has a greater role in visuospatial processing and in spatial working memory [78]. The right cerebellum is more associated with verbal working memory particularly when tested using a digit span working memory task [85] or the Paced Auditory Serial Subtraction Task (PASST) evaluating working memory and attention [86]. We have observed a tendency for left cerebellar stimulation to increase the randomness of responses in a random number generation task compared to right cerebellar stimulation and sham stimulation in healthy adults (L. Bradnam, unpublished results). The effect of neck rotation direction on motor and non-motor performance has not been systematically investigated. We have observed a trend in CD for those with right neck rotation to better recognise right neck rotation that was not apparent in those with left neck rotation. We have also observed that people with CD are less likely to verbally generate numbers randomly, but we are yet to elucidate whether the side of neck rotation influences performance in this task (L. Bradnam, unpublished results). Lateralisation of mental performance dependent on head turn requires more systematic investigation as it may provide key information toward individualising interventions in patients based on clinical tests.

Implications for non-invasive brain stimulation to cerebellum

NBS to cerebellum is a safe intervention [95] and early indications is that it may be effective for improving handwriting function in people with CD and FHD [35]. Effects of NBS may be augmented by task-specific motor training [96] and/or non-motor tasks that challenge known cerebellar functions [23]. Together, these therapies may provide an alterantive treatment for the painful muscle spasms and twisted neck postures, and the lesser known cognitive deficits such as sequencing and timing error that are associated with isolated dystonia. In addition to the potential physiological benefit, TDCS is a particularly practical technique for use in people with CD, because it does not require one's head to remain still, thus not applying additional stress to the impaired neck. Furthermore, it is easy to incorporate motor and non-motor training regimes concurrently with TDCS. However, there are still gaps in the knowledge base that impede the translation of TDCS into clinical practice. While it is recognised that repeated sessions of non-invasive brain stimulation are required to promote synaptic plasticity and learning in the human brain [97] many of the parameters of stimulation remain unclear. Issues such as optimum electrode placement and length and frequency of stimulation for best therapeutic effect remain to be elucidated.

Conclusion

We recently found anodal TDCS to cerebellum improved handwriting [35], potentially by modulation of a putative cerebello-red nuclear-rubrospinal tract or a cerebello-brainstem-propriospinal tract. Our results do not seem to be associated with changes in excitability of the cerebello-thalamo-cortical pathway. With the emergence of known non-motor functions of the cerebellum there may be a case for a 'multi-modal approach' to treatment of dystonia. Multi-modal interventions would combine cerebellar TBS with individualised therapy delivered by task practice that challenges motor and non-motor learning and sequencing [23]. The on-going work in our laboratory take this approach to studies using cerebellar NBS in people with cervical dystonia. The aim is to provide evidence for the efficacy of these novel treatment paradigms utilising cerebellar NBS and cognitive and motor training to provide alternative, non-invasive treatments for people with these recalcitrant movement disorders.

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