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# Diffusion tensor MRI tractography reveals increased fractional anisotropy (FA) in arcuate fasciculus following music-cued motor training

Emma Moore[a], Rebecca S. Schaefer[b,c], Mark E. Bastin[d], Neil Roberts[e], Katie Overy[a,f,*]

[a] Institute for Music in Human and Social Development (IMHSD), Reid School of Music, University of Edinburgh, Edinburgh, UK
[b] Health, Medical and Neuropsychology Unit, Institute of Psychology, Faculty of Social and Behavioural Sciences, Leiden University, Leiden, The Netherlands
[c] Leiden Institute for Brain and Cognition (LIBC), Leiden University, Leiden, The Netherlands
[d] Centre for Clinical Brain Sciences, University of Edinburgh, Edinburgh, UK
[e] Clinical Research Imaging Centre (CRIC), University of Edinburgh, Edinburgh, UK
[f] Department of Music Education, Don Wright Faculty of Music, University of Western Ontario, London, Canada

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ABSTRACT

Auditory cues are frequently used to support movement learning and rehabilitation, but the neural basis of this behavioural effect is not yet clear. We investigated the microstructural neuroplasticity effects of adding musical cues to a motor learning task. We hypothesised that music-cued, left-handed motor training would increase fractional anisotropy (FA) in the contralateral arcuate fasciculus, a fibre tract connecting auditory, pre-motor and motor regions. Thirty right-handed participants were assigned to a motor learning condition either with (Music Group) or without (Control Group) musical cues. Participants completed 20 minutes of training three times per week over four weeks. Diffusion tensor MRI and probabilistic neighbourhood tractography identified FA, axial (AD) and radial (RD) diffusivity before and after training. Results revealed that FA increased significantly in the right arcuate fasciculus of the Music group only, as hypothesised, with trends for AD to increase and RD to decrease, a pattern of results consistent with activity-dependent increases in myelination. No significant changes were found in the left ipsilateral arcuate fasciculus of either group. This is the first evidence that adding musical cues to movement learning can induce rapid microstructural change in white matter pathways in adults, with potential implications for therapeutic clinical practice.

## 1. Introduction

Moving physically to a steady beat is a universal human phenomenon, often occurring spontaneously and enjoyably in a musical context (Chen, Zatorre, & Penhune, 2006; Schaefer & Overy, 2015). Accordingly, auditory cues are increasingly used to support movement learning and rehabilitation (Schaefer, 2014), with evidence suggesting that musical stimuli can support physical exercise (Karageorghis & Priest, 2012), movement rehabilitation after stroke (Thaut, 2005) and improve gait in patients with Parkinson's disease (Benoit et al., 2014; Thaut et al., 1996; Dalla Bella, Benoit, Farrugia, Schwartz, & Kotz, 2015). However, the neural basis of effective auditory-cued motor training is not yet fully understood (Schaefer, Morcom, Roberts, & Overy, 2014).

A range of evidence suggests that high levels of musical training are associated with neural differences in motor circuitry, including corticospinal tracts (Imfeld, Oechslin, Meyer, Loenneker, & Jancke, 2009), pyramidal tracts (Rüber, Lindenberg, & Schlaug, 2013), corpus callosum (Schlaug, Jäncke, Huang, Staiger, & Steinmetz, 1995; Schmithorst & Wilke 2002; Steele, Bailey, Zatorre, & Penhune, 2013), and internal capsule (Bengtsson et al., 2005; Han et al., 2009) (for a review see Moore, Schaefer, Bastin, Roberts, & Overy, 2014). Further evidence suggests that musical training can specifically affect auditory-motor circuitry (Bangert et al., 2006; Baumann et al., 2007; Chen, Penhune, & Zatorre, 2008; Herholz, Coffey, Pantev, & Zatorre, 2016; Palomar-Garcia, Zatorre, Ventura-Campos, Bueicheku, & Avila, 2016; Zatorre, Chen, & Penhune, 2007). For example, short-term piano training has been shown to lead to co-activation of auditory and motor regions during music listening tasks (Bangert & Altenmüller, 2003; Lahav, Saltzman, & Schlaug, 2007) and enhanced activation in premotor cortex and brain areas associated with sensorimotor integration (Herholz et al., 2016). In individual patient case studies, Melodic Intonation Therapy (MIT) (Albert, Sparks, & Helm, 1973), a speech therapy method involving synchronised singing and tapping, has been found to lead to an increased number of fibres and increased tract volume of the arcuate fasciculus, a major fibre tract connecting auditory

* Corresponding author at: Institute for Music in Human and Social Development, Reid School of Music, University of Edinburgh, Alison House, 12 Nicolson Square, Edinburgh EH8 9DF, UK.
*E-mail address:* K.Overy@ed.ac.uk (K. Overy).

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and motor brain regions (Schlaug, Marchina, & Norton, 2009; Zipse, Norton, Marchina, & Schlaug, 2012). Highly trained musicians have also been found to show higher fractional anisotropy (FA) values and increased tract volume in the arcuate fasciculus, when compared with non-musicians (Halwani, Loui, Rüber, & Schlaug, 2011). Recent research confirms a posterior termination of the arcuate fasciculus in the superior temporal gyrus, containing primary auditory cortex (Maffei, Soria, Prats-Galino, & Catani, 2015), and anterior termination in the inferior precentral gyrus, containing both primary and premotor regions (Brown et al., 2014). The arcuate fasciculus thus presents a strong candidate tract for the potential neuroplasticity effects of auditory-cued motor training. Despite this, to our knowledge, no controlled, longitudinal studies have yet investigated this possibility (Moore et al., 2014).

The aim of the present study was to use diffusion tensor MRI (DT-MRI) and probabilistic neighbourhood tractography (PNT; Clayden et al., 2011) to investigate whether a short period of left-handed, music-cued motor training would induce increased FA in the contralateral but not ipsilateral arcuate fasciculus. DT-MRI and tractography allow for detailed exploration of the white matter structure of the brain via measurement of the direction and magnitude of water molecule diffusion in segmented tracts-of-interest (Clayden, Storkey, Maniega, & Bastin, 2009). In white matter, water molecule motion is restricted such that diffusion is greater along than perpendicular to the principal fibre direction. FA measures the directionality coherence of water molecule diffusion and is frequently used to infer information about white matter structure and connectivity (Basser, 1995), while mean (MD), axial (AD) and radial (RD) diffusivity measure the total magnitude of water diffusion and its components parallel and perpendicular to the principal fibre direction, respectively (Song et al., 2002). Together these parameters can provide an indication of levels of myelination, axonal membrane integrity and other underlying biological structures (Beaulieu, 2002; Beaulieu, 2014; Song et al., 2002; Wheeler-Kingshott & Cercignani, 2009). PNT has several advantages over region-of-interest, voxel-based and deterministic tractography methods, including automatic tract segmentation rather than manual seed-point placement (thus reducing observer bias) and tract segmentation in native space rather than standard space, thereby allowing subtler changes in white matter microstructure to be detected (Clayden et al., 2011).

We designed a novel training paradigm in which participants learned four sequences of eight finger-to-thumb opposition movements with their left, non-dominant hand, using a visual display either with (Music group) or without (Control group) musical cues. To explore changes in the microstructural properties of the arcuate fasciculus we compared FA, AD and RD biomarkers, obtained using PNT, in bilateral arcuate fasciculi of both groups before and after training. We predicted that left-handed, music-cued motor training would lead to increased FA specifically in the right arcuate fasciculus of the Music group only.

## 2. Materials and methods

### 2.1. Participants

Thirty healthy volunteers aged 18–30 years were recruited using an online student recruitment website at the University of Edinburgh, UK. All participants were right-handed according to the Edinburgh Handedness Inventory (Oldfield, 1971; mean = 81.90, SD = 17.26) and had no history of neurological or psychiatric disorders. None of the participants had more than six years (mean = 1.41, SD = 1.56 years) of musical training and none were currently practising or learning to play a musical instrument. The participants were quasi-randomly assigned (according to the order of recruitment) to either the Music (n = 15; mean age = 21.27, SD = 1.98 years; 4 male) or Control (n = 15; mean age = 21.33, SD = 2.38 years; 5 male) groups. All participants gave informed written consent of their willingness to participate and were reimbursed for their practice time and travel expenses for attending the two MRI scans. The study was carried out in accordance with the Declaration of Helsinki and was approved by the local ethics committee of the University of Edinburgh and the West of Scotland Research Ethics Committee, UK (REC reference number 12/WS/0229).

**Table 1**
The four motor sequences of eight finger-to-thumb opposition movements.

| | |
|---|---|
| Sequence 1 | 1, 3, 2, 4, 3, 1, 3, 2 |
| Sequence 2 | 2, 4, 3, 4, 1, 1, 2, 3 |
| Sequence 3 | 3, 4, 1, 2, 4, 4, 2, 1 |
| Sequence 4 | 4, 2, 1, 3, 2, 3, 1, 4 |

### 2.2. Stimuli

The training paradigm involved learning four sequences of eight finger-to-thumb opposition movements (shown in Table 1) with the left (non-dominant) hand (in order to allow greater potential for improvement). For the purposes of the study, the second to fifth digits (i.e. index to pinkie fingers) of the left hand were labelled from 1 to 4, respectively. All participants were asked to practice the four sequences with their left hand for 20 min, three times per week over a four-week period.

For each sequence, an animated visual display was created consisting of four vertical lines, one to represent each finger. Circles descended the vertical lines onto a horizontal line near the bottom of the screen, at which point participants touched the appropriate finger to their thumb (Fig. 1), synchronising with the visual display. For the Music group there was an additional soundtrack providing temporal cues for each finger movement and pitch cues to indicate the correct finger to move, thus establishing an auditory-motor relationship between the musical cues and corresponding finger movements. To ensure that the four digits were equally involved during training, each individual finger was used at the start of one sequence, at the end of another sequence and appeared a total of eight times overall within the four sequences.

### 2.3. Procedure

Following recruitment and confirmation of inclusion criteria, participants underwent an initial MRI scanning session and behavioural assessment. Training then consisted of watching the videos online and practising the appropriate motor sequences, followed by logging progress. Each video sequence was identified by the starting finger and had

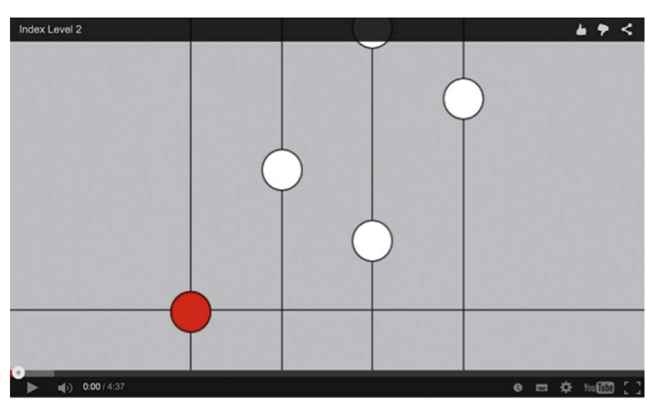


**Fig. 1.** A snap-shot ‘still’ from one of the training videos. From left to right the four vertical lines represent the index to pinkie fingers of the left hand. As the video plays, the circles move down the screen and when they reach the horizontal line the participant moves the appropriate finger to touch the thumb; in the auditory-motor condition this corresponds with an appropriate pitch cue and a steady beat. The red circle denotes the start of the sequence.