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Note

Motor correlates of phantom limb pain

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ABSTRACT

Following amputation, individuals ubiquitously report experiencing lingering sensations of their missing limb. While phantom sensations can be innocuous, they are often manifested as painful. Phantom limb pain (PLP) is notorious for being difficult to monitor and treat. A major challenge in PLP management is the difficulty in assessing PLP symptoms, given the physical absence of the affected body part. Here, we offer a means of quantifying chronic PLP by harnessing the known ability of amputees to voluntarily move their phantom limbs. Upper-limb amputees suffering from chronic PLP performed a simple finger-tapping task with their phantom hand. We confirm that amputees suffering from worse chronic PLP had worse motor control over their phantom hand. We further demonstrate that task performance was consistent over weeks and did not relate to transient PLP or non-painful phantom sensations. Finally, we explore the neural basis of these behavioural correlates of PLP. Using neuroimaging, we reveal that slower phantom hand movements were coupled with stronger activity in the primary sensorimotor phantom hand cortex, previously shown to associate with chronic PLP. By demonstrating a specific link between phantom hand motor control and chronic PLP, our findings open up new avenues for PLP management and improvement of existing PLP treatments.

1. Introduction

Following arm amputation individuals generally perceive vivid sensations of the amputated limb as if it is still present, with varying ability to voluntarily move this phantom hand. In up to 80% of arm amputees these phantom sensations are experienced as painful and can manifest as an intractable chronic neuropathic pain syndrome (Weeks, Anderson-Barnes, & Tsao, 2010). Phantom limb pain (PLP) often does not respond to conventional analgesic therapies and poses a

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significant medical problem (Knotkova, Cruciani, Tronnier, & Rasche, 2012).

A large number of studies have associated PLP with plastic changes in the sensorimotor nervous system (Flor et al., 1995; Makin et al., 2013; Mercier & Leonard, 2011; Raffin, Richard, Giraux, & Reilly, 2016; Reilly & Sirigu, 2008). Following this, a surge of behavioural therapies that aim to normalise the representation of the phantom hand have been developed in recent years (MacLachlan, McDonald, & Waloch, 2004; Moseley, 2006; Moseley & Flor, 2012; Ramachandran & Rogers-Ramachandran, 1996). The overarching objective of these behavioural therapies is to relieve PLP by improving the ability to move the phantom limb [e.g., mirror therapy (Chan et al., 2007; Rothgangel Stefan, Braun, Beurskens, Seitz, & Wade, 2011) and graded motor imagery (Moseley, 2006; Thieme, Morkisch, Rietz, Dohle, & Borgetto, 2016)]. The assumption behind these therapies is that increased motor control (or motor imagery) over the phantom hand would cause PLP relief. Despite the large number of PLP therapies relying on this notion, the link between PLP and phantom hand motor control is only recently starting to be uncovered behaviourally (Gagné, Reilly, Hétu, & Mercier, 2009; Raffin, Giraux, & Reilly, 2012), or using neuroimaging (Makin et al., 2013; Yanagisawa et al., 2016). Systematic evidence for the role of phantom hand motor control in predicting (let alone modulating) PLP is lacking.

The current study aimed at characterising the assumed link between PLP and phantom hand motor control in fourteen upper-limb amputees suffering from chronic PLP. Functional magnetic resonance imaging (fMRI) was used to further examine the neural correlates of deteriorated phantom hand motor control. Specifically, we investigated the relationship between deteriorated motor control and the representation of the phantom hand in primary sensorimotor cortex.

2. Materials and methods

2.1. Participants

Fifteen unilateral upper-limb amputees who experienced PLP episodes more than once a week in the month preceding recruitment (mean age ± s.e.m. = 47 ± 3, mean years since amputation ± s.e.m. = 16 ± 3, 6 right arm amputees, 4 females; see Table 1 for demographic and clinical details) and fifteen age- and sex-matched controls (2-handers, age = 46 ± 3, 7 with a dominant left hand, 4 females) were recruited through the Oxford Centre for Enablement and Opcare. In this study, we specifically targeted amputees suffering from relatively high chronic PLP. As such, the variance and range of chronic PLP sampled was reduced in the current study (variance: 670, range: 82) compared to our previous study that demonstrated a relationship between chronic PLP and primary sensorimotor phantom hand representation (variance: 754, range: 94; Kikkert, Johansen-Berg, Tracey, & Makin, 2017). However, we note that this difference in chronic PLP variance was not significant, as assessed using Levene's Test of Equality of Variances [$F_{(1,29)} = .03$, $p = .86$]. Ethical approval was granted by the NHS National Research Ethics service (10/H0707/29) and written informed consent was obtained from all participants prior to the study. Data from one amputee was discarded due to inability to perform the motor task with the phantom hand.

Amputees participated in four consecutive testing sessions that were separated by at least one week, as part of a larger study (see https://osf.io/4a5zg/ for full protocol). Here, only methods related to results reported in the current paper are detailed. One amputee completed only three testing sessions. Control participants took part in a single session. To compare between the amputees and controls, the phantom hand was matched to the non-dominant hand of controls, and the intact hand was matched to the dominant hand of controls.

2.2. Pain ratings

At the start of the first testing session, amputees rated the frequency of PLP, as experienced within the last year, as well as the intensity of worst PLP experienced during the last week (or in a typical week involving PLP). Chronic PLP was calculated by dividing worst PLP intensity (scale 0–100: ranging from no pain to worst pain imaginable) by PLP frequency (1 – all the time, 2 – daily, 3 – weekly, 4 – several times per month, and 5 – once or less per month). This approach reflects the chronic aspect of PLP as it combines both frequency and intensity (Makin, Filippini, et al., 2015; Makin et al., 2013; Makin, Scholz, Henderson Slater, Johansen-Berg, & Tracey, 2015; see Appendix A: Supplementary materials for further details on this measure's consistency over years). A similar measure was obtained for non-painful phantom sensation vividness and stump pain. Ratings of transient PLP intensity (scale 0–100, as above) were obtained in each testing session prior to the finger-tapping test.

2.3. Finger-tapping test

Motor control was assessed using the 'finger-to-thumb opposition task' (hereafter finger-tapping task). In this task, participants sequentially opposed each of the four fingertips to the tip of their thumb, starting with the index finger. Participants were instructed to repeat this movement cycle five times, and verbally indicated the ending of each cycle. Participants first performed the finger-tapping task with their intact hand and then repeated the task using their phantom hand. Importantly, phantom hand movements are distinguishable from imagined movements, as is supported by empirical evidence demonstrating that phantom limb movements elicit both central and peripheral motor signals that are different from those found during movement imagery (Makin et al., 2013; Raffin, Mattout, Reilly, & Giraux, 2012; Reilly, Mercier, Schieber, & Sirigu, 2006; Raffin, Giraux, et al., 2012). As such, emphasis was given to making "actual" instead of imagined phantom hand movements. Participants were encouraged to perform the finger-tapping task as well as possible, given their volitional motor control over the fingers. If it was impossible to make the full finger-to-thumb movements with the phantom fingers, participants were asked to attempt to perform the instructed movement. During the task, participants were requested to keep their eyes closed, their intact hand relaxed in their lap and all other body parts still. Note that this task has no spatial components (e.g., Makin, Wilf, Schwartz, & Zohary, 2010; Wilf, Holmes, Schwartz, &