NeuroImage: Clinical 8 (2015) 180–192

Contents lists available at ScienceDirect

NeuroImage: Clinical

journal homepage: www.elsevier.com/locate/ynicl

Increased cortico-striatal connectivity during motor practice contributes to the consolidation of motor memory in writer's cramp patients

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ARTICLE INFO

Article history:
Received 2 March 2015
Received in revised form 15 April 2015
Accepted 16 April 2015
Available online 22 April 2015

Keywords:
Focal dystonia
Striatum
Hippocampus
Motor cortex
MRI

ABSTRACT

Sensorimotor representations of movements are created in the sensorimotor network through repeated practice to support successful and effortless performance. Writer's cramp (WC) is a disorder acquired through extensive practice of finger movements, and it is likely associated with the abnormal acquisition of sensorimotor representations. We investigated (i) the activation and connectivity changes in the brain network supporting the acquisition of sensorimotor representations of finger sequences in patients with WC and (ii) the link between these changes and consolidation of motor performance 24 h after the initial practice. Twenty-two patients with WC and 22 age-matched healthy volunteers practiced a complex sequence with the right (pathological) hand during functional MRI recording. Speed and accuracy were measured immediately before and after practice (day 1) and 24 h after practice (day 2). The two groups reached equivalent motor performance on day 1 and day 2. During motor practice, patients with WC had (i) reduced hippocampal activation and hippocampal–striatal functional connectivity; and (ii) overactivation of premotor–striatal areas, whose connectivity correlated with motor performance after consolidation. These results suggest that patients with WC use alternative networks to reach equiperformance in the acquisition of new motor memories.

1. Introduction

Writer's cramp (WC) is a task-specific form of focal hand dystonia (FHD) characterized by disruption in motor performance specifically occurring during overlearned handwriting. Retraining of sensorimotor subroutines is one of the main approaches for the rehabilitation of this movement disorder. Therefore, understanding the mechanisms by which new motor programs are acquired and consolidated in patients with WC is crucial for improving therapeutic strategies. For now, it is not known how brain processes related to the acquisition of sensorimotor representation during motor practice are altered in patients with WC or how dysfunction in these processes would influence the consolidation of sensorimotor representation.

WC patients have impaired sensorimotor integration and maladaptive neural plasticity (Hallett, 2006; Quartarone et al., 2003; Rothwell and Huang, 2003; Tinazzi et al., 2009), which are brain processes playing a key role in the acquisition of sensorimotor representations. These deficits might be caused by structural and functional impairments of the striatum and sensorimotor cortical areas (Berardelli et al., 1998; Blood et al., 2004; Delmaire et al., 2005; Hallett, 2006; Mink, 1996; Peller et al., 2006; Vitek et al., 1999; Wu et al., 2010). However, to our knowledge, how the striatal network is involved in the acquisition of sensorimotor representations during motor practice has never been

Abbreviations: WC, writer's cramp; FHD, focal hand dystonia; HV, healthy volunteers; DT1, dual task 1; DT2, dual task 2; PD, practice dependent; CD, consolidation dependent; CV-RT, coefficient of variation for reaction time; PPI, psychophysiological interaction; FA, fractional anisotropy; RD, radial diffusivity; LD, longitudinal diffusivity; PMd, dorsal premotor cortex; PMv, ventral premotor cortex; BA, Brodmann area.

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http://dx.doi.org/10.1016/j.nicl.2015.04.013

studied in patients with WC. Motor learning has been studied in genetic forms of dystonia, which revealed abnormal activation and structural changes in the frontal and cerebellar areas (Argyelan et al., 2009; Carbon et al., 2008). In contrast to WC, genetic dystonia develops at early age independently from intensive motor practice. In FHD patients, previous studies have reported abnormal brain activation and functional connectivity during the execution of complex finger sequences and complex finger coordination (Moore et al., 2012; Wu et al., 2010), without looking at time-dependent changes during motor practice. Time-dependent changes in brain connectivity were found during simple finger sequences with EEG, but the spatial resolution did not allow the investigation of the striatal impairments precisely (Jin et al., 2011a, 2011b). The present study aimed to investigate (i) the activation and connectivity changes in striatal and sensorimotor networks associated with the acquisition of sequential finger movements by the affected hand in patients with WC; and (ii) how these changes influence the performance of sequential finger movements after consolidation 24 h after the initial practice.

Representations of finger sequences are stored in the brain and subsequently used for successful performance (Doyon et al., 2009; Wolpert et al., 2011). Brain regions that are involved include the sensorimotor system, specifically the striatum (Doyon et al., 2009; Lehéricy et al., 2005; Ungerleider et al., 2002). In the early phase of motor practice, during which sensorimotor representations are built within a single practice session, activation decreases in the associative striatal territory (Floyer-Lea and Matthews, 2004; Jueptner et al., 1997; Laforce and Doyon, 2002; Lehéricy et al., 2005; Toni et al., 1998) and increases in the sensorimotor striatal territory (Doyon et al., 2009; Floyer-Lea and Matthews, 2004; Lehéricy et al., 2005). This functional remapping is associated with the reorganization of functional interactions in the striato-cortical networks (Coynel et al., 2010). After sleep or the simple passage of time, a consolidation phase occurs, during which sensorimotor representations are maintained or strengthened (Albouy et al., 2013a, 2013b; Dayan and Cohen, 2011; Doyon et al., 2009; Ungerleider et al., 2002). The striatum and the hippocampus are involved during the early phase of learning (Dickerson et al., 2011; Mattfeld and Stark, 2011; Schendan et al., 2003). Functional interaction between the hippocampus and the striatum during motor practice predicts the behavioral consolidation of the trained motor task performed 24 h later (Albouy et al., 2013a, 2013b, 2008). This suggests that motor skill consolidation is a continuous process relying on mechanisms that occur as early as the practice phase of motor sequence learning (Censor et al., 2014; Dayan and Cohen, 2011). Changes in striatal activation level and functional connectivity with the cortex or the hippocampus may therefore contribute to abnormal motor learning in patients with WC.

In addition to functional changes, motor practice is also associated with local structural changes of white matter fiber bundles (Dayan and Cohen, 2011; Zatorre et al., 2012). In healthy volunteers, activity in and the gray-matter volume of sensorimotor cortices predict individual learning abilities (Bueti et al., 2012). Training of patients with motor impairments induces gray matter changes within the non-affected secondary motor cortex (Burciu et al., 2013). Subcortical structural changes also affect behavioral performance in patients with hippocampal sclerosis; for instance, gray matter volume reduction in the hippocampus is correlated with decreased behavioral performance and working memory deficits (Winston et al., 2013). Altogether, functional basal ganglia impairments in patients with WC could be associated with structural changes in brain networks that usually support practice-related improvement of performance and consolidation processes.

In the present neuroimaging study, we investigated changes in the activation and functional connectivity of brain networks involved in the acquisition of sensorimotor representations of a complex finger sequence within a single practice session on day 1. We controlled for the factor of motor repetition by using a simple finger sequence. We assessed the structural integrity of the networks involved in the practice of the finger sequences using diffusion tensor imaging and tractography. Lastly, we looked at functional and structural mechanisms that support motor performance after consolidation in patients with WC on day 2 (24 h after the initial practice). We specifically studied three main hypotheses: During motor practice, WC patients would have altered striatal activation (hypothesis 1), abnormal striatal connectivity (hypothesis 2) and an abnormal link between striatal connectivity and the consolidation of motor performance (hypothesis 3).

2. Materials and methods

2.1. Participants

Twenty-two patients with WC (mean age ± standard deviation = 45.1 ± 15.5 years, 8 females) and 22 aged-matched healthy volunteers (HV, mean age 48.0 ± 14.9, 8 females) participated in the study. All subjects were right-handed (i.e., had positive scores on the Edinburgh Handedness Questionnaire). The patients were recruited from the movement disorders clinic of the Fédération de Neurologie (Hôpital Pitié-Salpêtrière, Paris, France) and were diagnosed with pure WC of the right dominant hand by a neurologist (i.e., focal symptoms on fingers and/or wrist). None of the patients showed any additional neurological deficits. The duration of dystonia ranged between 3 and 34 years (mean 13.0 ± 8.9 years). The patients did not receive botulinum toxin (BTox) injections for at least 6 months preceding the study, and 2 patients were never treated with BTox. The HVs had no history of neurological or psychiatric diseases, no known learning disability, and no medical conditions that could impair fine motor performance. None of the HVs or patients was a musical instrument player or professional typist and none frequently played computer games, all conditions that do affect the level of manual dexterity. Informed consent was obtained from all participants. The experimental protocol was approved by the local Ethics Committee, Groupe Hospitalier Pitié-Salpêtrière, Paris, France.

2.2. Behavioral tasks

Participants performed two motor tasks with their right dominant hand (which was the impaired hand for all patients): a complex motor sequence, which consisted of an 8-digit sequence (complex condition), and a simple fixed sequence (simple condition involving taping with consecutive fingers 5–4–3–2, where the index finger is "2" and the middle finger is "3"). Apart from the thumb, all fingers were equally involved in the task performance. In the complex sequence, the order of finger movements was pseudo-randomly generated using Matlab® (The Mathworks, Inc.) such that each complex sequence included two occurrences of each finger and did not include two consecutive taps with the same finger (e.g., 3–2–5–2–4–3–5–4). A given complex sequence was randomly assigned to each participant, and each participant performed the same complex sequence throughout the course of the experiment. The simple sequence was used to control for the factor of motor repetition. The simple finger sequence involved the movement of consecutive fingers, which was already represented in the brain before the beginning of motor practice, as confirmed by the lack of performance improvement in this sequence after practice (see the Results section).

2.3. Procedures (Fig. 1)

A behavioral session preceded and followed the fMRI recordings to provide a baseline before motor practice and to measure the behavioral improvement after motor practice (Fig. 1). Before scanning, subjects practiced the simple and complex conditions without metronome pacing. This familiarization phase ended when participants could perform