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PROMINENT 5–18 HZ OSCILLATIONS IN THE PALLIDAL-THALAMIC CIRCUIT IN SECONDARY DYSTONIA

Previous studies in primary dystonia suggested that abnormal oscillations of 5–18 Hz in the bilateral internal globus pallidus (GPi) may be a specific feature of dystonia.^{1–3} Moreover, voluntary movements were associated with bilateral desynchronization of β (<30 Hz) and contralateral synchronization of γ (~70 Hz) frequencies in the GPi.^{2–4} We recorded local field potentials (LFPs) from the GPi and motor thalamus in a patient with severe hemidystonia to test the following hypotheses. First, the 5–18 Hz synchronization is present in the basal ganglia (BG)–thalamic circuit in patients with secondary dystonia. Second, the bilaterally coherent 5–18 Hz activity may be transmitted between the hemispheres through the motor thalamus. Finally, if the 5–18 Hz rhythm is related to dystonia, attempted movements of dystonic muscles would result in less attenuation of this 5–18 Hz oscillation compared to normal movements.

Methods. We studied a 43-year-old woman with severe left hemidystonia secondary to a cryptogenic stroke in the right putamen and the external globus pallidus 5 years earlier (figure e-1 on the *Neurology*[®] Web site at www.neurology.org). She received unilateral right GPi and ventral intermediate nucleus of the thalamus (Vim) deep brain stimulation (DBS) implants (table e-1).

GPi/Vim LFPs were recorded from the quadripolar DBS electrodes using linked-ears reference 2 days after electrode implantations. EMG were recorded from the extensor and flexor carpi radialis muscles. The patient made brisk self-initiated right wrist extension and attempted left wrist extension approximately once every 10 seconds. Each side was studied for ~10–15 minutes. See appendix e-1 for further details.

Results. Attempted movements of the left wrist produced barely perceptible movements but was associated with discrete EMG bursts that were of much lower amplitude than the normal right wrist (figure 1, A and B). Left wrist movement led to a diffuse

~6–25 Hz event-related desynchronization (ERD) and a high amplitude 64–68 Hz event-related synchronization (ERS) in the right GPi and Vim (figure 1, C and E). This γ activity showed coherence between the GPi and Vim (figure 1G). Right wrist movements were associated with 6–25 Hz ERD but no γ ERS at the right GPi and Vim (figure 1, B, D, and F). A strong resting 5–18 Hz coherence with strength of ~0.8 was observed between the right GPi and Vim, which attenuated during movements of the unaffected ipsilateral right wrist (figure 1H), but not during attempted movements of the dystonic left wrist (figure 1G).

Discussion. Coherence between GPi and motor thalamus in dystonia has not been reported. Several observations here are consistent with the hypothesis^{1–3,5} that 5–18 Hz rhythm is related to dystonia. First, the 5–18 Hz GPi-Vim coherence in our patient with severe hemidystonia (figure 1, G and H) is much stronger than the bilateral GPi coherence in patients with cervical dystonia (CD),² suggesting its amplitude may be related to the severity of dystonia. Second, this 5–18 Hz oscillation is present in our patient with secondary dystonia in addition to primary dystonia demonstrated in previous studies,^{2,3} suggesting that the 5–18 Hz oscillation in the pallidal-thalamic circuit may be a general feature of dystonia. Third, we observed the attenuation of the 5–18 Hz GPi-Vim coherence only during ipsilateral normal arm movements (figure 1H) but not during attempted movement of the contralateral dystonic arm (figure 1G). Since previous studies found that unilateral wrist movements of unaffected hands in CD patients led to the attenuation of the resting 5–18 Hz coherence between the bilateral GPi,² the present findings support the notion that excessive 5–18 Hz oscillation is related to dystonia. However, the failure to attenuate the 5–18 Hz coherence may also be related to the low movement amplitudes of the dystonic left hand.

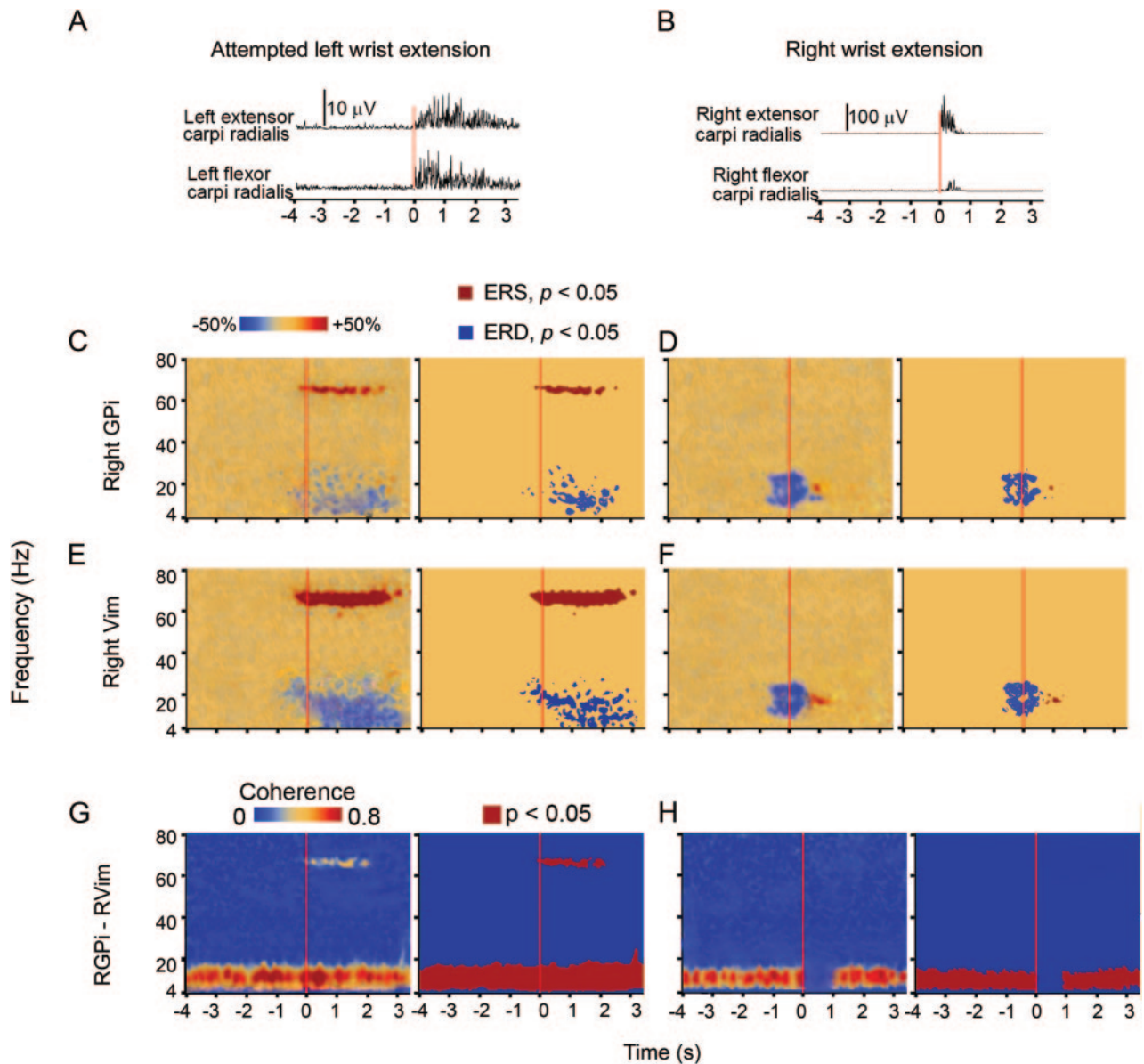
Our findings also suggest that the motor thalamus may be part of the circuit mediating the coherence between bilateral GPi in dystonia.^{2,5} Although the DBS was targeted to the Vim, the cerebellar receiving thalamus, some of the activities recorded likely originated from the adjacent pallidal receiving thalamus.⁶

Supplemental data at
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Supplemental Data



Figure 1 Movement-related event-related desynchronization (ERD) and event-related synchronization (ERS) and coherence in the right internal globus pallidus (GPi) and ventral intermediate nucleus of the thalamus (Vim)



(A) Rectified averaged EMG recordings of the extensor carpi radialis (top) and flexor carpi radialis (bottom) muscles during attempted self-initiated extension movements of the dystonic left wrist and (B) extension movements of the unaffected right wrist. From C to F, movement-related ERD/ERS in the right GPi and Vim are shown. The baseline period comprised of recordings from -4 to -3 seconds. ERD/ERS power changes (left) are color coded in percentage relative to the mean of the baseline period. Blue represents ERD while red represents ERS. The abscissa denotes time in seconds, where the red marker at time 0 represents movement onset, and the ordinate denotes frequency from 4 to 100 Hz. In the corresponding permutation tests (right), blue areas indicate significant ERD while red areas indicate significant ERS. (C) ERD/ERS of the right GPi during attempted self-initiated extension movements of the dystonic left wrist and (D) self-initiated extension movements of the unaffected right wrist. (E) ERD/ERS of the right Vim during attempted self-initiated extension movements of the dystonic left wrist and (F) self-initiated extension movements of the unaffected right wrist. For G and H, coherences are shown on the left and the corresponding permutation tests on the right. The abscissa denotes time in seconds, where the red marker at time 0 represents movement onset, and the ordinate denotes frequency from 4 to 100 Hz. In the permutation tests, red areas indicate significant coherences. (G) Coherence between the right GPi and right Vim during attempted movements of the contralateral dystonic left wrist and (H) during movements of the unaffected ipsilateral right wrist.

Anatomically, $\sim 20\%$ of pallidal-thalamic fibers cross over to the contralateral motor thalamus,⁶ which projects to the cortex and to the centromedian nucleus, which in turn projects to other BG nuclei such as the putamen, subthalamic nucleus, and GPi.⁶

The finding for the γ band was opposite to that of the β band with a 64–68 Hz GPi/Vim ERS and coherence contralateral to the movements of the dystonic arm (figure 1, C, E, and G) but no change with movements of the normal ipsilateral right wrist

(figure 1, D, F, and H). The strictly contralateral modulation of the γ frequency is consistent with the previous finding in the cortex and GPi during normal wrist movements.^{2,4} Moreover, the moderately high amplitude γ coherence observed during attempted movements of severely dystonic left wrist (figure 1G) suggests that this γ oscillation in the pallidal-thalamic circuit may be related to the effort involved in movement execution and is not attenuated by the presence of dystonia.

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