Anterior Disconnection Syndrome Revisited using Modern Technologies

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ANTERIOR DISCONNECTION SYNDROME REVISITED USING MODERN TECHNOLOGIES

An anterior disconnection syndrome was first described over 100 years ago by Liepmann and Maas[1] and brought back to clinical awareness 50 years ago by Geschwind and Kaplan.[2] Damage to the corpus callosum has been confirmed by postmortem analysis but precise anatomic along with its functional characterization has not been accomplished. We report a patient with the anterior disconnection syndrome after stroke. Diffusion tensor imaging (DTI) tractography and transcallosal neurophysiologic recordings confirmed the exact transcallosal disconnection.

Case report. A 60-year-old right-handed woman presented to the emergency room with a 1-day history of unsteadiness and loss of urinary control. Her past medical history was notable for type II diabetes mellitus, hypertension, and dyslipidemia.

On neurologic examination she was alert and oriented. She had decreased spontaneity and prolonged latencies to respond to questions or commands. When she spoke, language was fluent and grammatical. Confrontation naming, repetition, and oral reading were intact. She could do no writing movements with the left hand, even copying print, and she had severe apraxia of the left hand to command, imitation, and even holding an object. She could not cross-replicate hand postures or cross-localize stimulation of finger tips. When objects were placed in her left hand (but not the right) without visualization, she could not name them, but she could subsequently select the correct object from among several objects placed in front of her. This was performed normally with the right hand. She had only mild upper motor neuron pattern weakness in the right leg.

Methods. Stroke localization was documented by diffusion-weighted images (DWI) on the clinical MRI obtained on admission. DTI images were acquired and analyzed (see details in e-Methods on the *Neurology*® Web site at www.neurology.org).

Transcranial magnetic stimulation (TMS) performed 2 weeks after the stroke measured 1) interhemispheric inhibition (IHI) and 2) propagation of TMS-generated brain activity to contralateral areas (see e-Methods). After the baseline measurements, conditioned responses were measured at different interpulse intervals (IPIs) for both the hemispheres with the conditioning stimuli delivered at 120% of resting motor threshold (RMT) (figure, D).

During another TMS study (TMS-EEG), 2 batches of 30–32 single pulses of TMS were delivered on both sides, 120% of RMT, while EEG was recorded simultaneously with a 60-channel TMS-compatible EEG system. EEG topographic maps, averaged over periods showing similar activity, from 25 to 53 msec after TMS pulse, were plotted (figure, E).

Results. ***MRI.*** DWI demonstrated an acute infarct in the left anterior cerebral artery territory (ACA), involving the corpus callosum (figure, A and B).

The volume of corpus callosal fibers between motor cortices in the corpus callosum was reduced. Measures for corticospinal tract (CST) of leg fibers indicated injury on the left, consistent with the mild leg weakness and the distribution of the infarct (figure, C).

TMS. The right hemisphere RMT was 33% of the maximum stimulator output (MSO); the left 40%. The mean MEP amplitude for the unconditioned responses (baseline) was 0.366 mV and 0.244 mV for right and left M1, respectively (figure, D). Conditioning stimuli at all the tested IPIs failed to cause statistically significant reduction in the MEP amplitude of the test pulses (figure, D). The IHI results consistently showed no transcallosal inhibition when the conditioning stimuli were delivered on either right or left hemispheres.

TMS-EEG demonstrated that right M1 stimulation provoked a larger local response than left M1 stimulation. Propagation of TMS-generated brain activity to the homologous contralateral area was greater after left stimulation than after right stimulation. The most prominent contralateral activity was recorded at 25–29 msec and then around 50 msec (figure, E).

Discussion. Liepmann and Maas[1] in 1907 were the first to recognize that a callosal lesion disconnects the motor area in the right hemisphere from the language-dominant left hemisphere most commonly producing unilateral left hand apraxia and agraphia. Other neuropsychological findings later investigated can include tactile anomia, difficulty in copying drawings, abnormalities of somesthetic transfer, and the alien hand sign, depending on the location of the lesion.

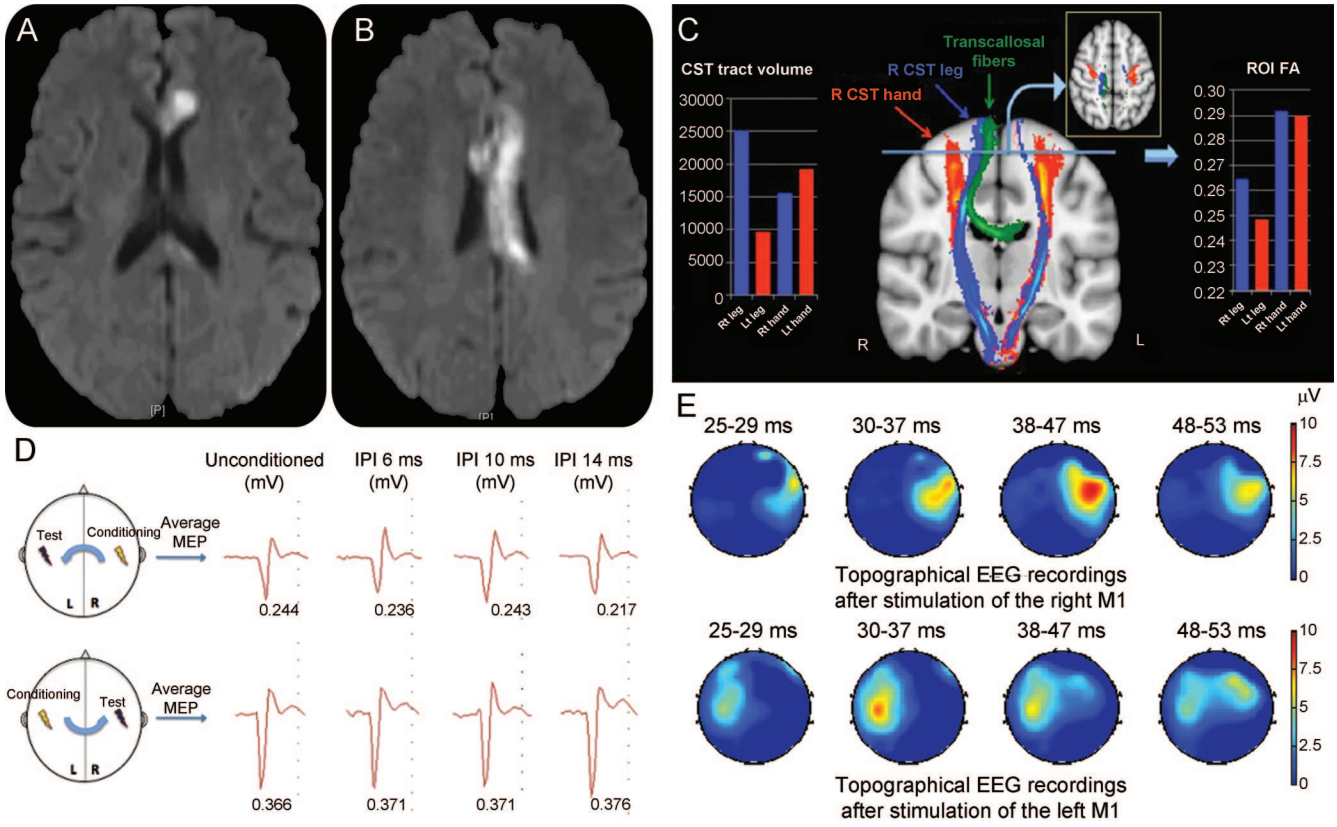
Demonstration of damaged pathway in a disconnection syndrome with tractography has been accomplished,[3] but without a physiologic parallel. With modern technologies, we were able to demonstrate the structural connectivity consequences of callosal damage (DTI/FA) and the physiologic consequences (TMS/TMS-EEG) of that loss of connectivity, i.e., demonstrate the meaning of disconnection. The

Supplemental data at www.neurology.org

Supplemental Data

Podcast

Figure Neuroanatomic images and neurophysiological experiments in a patient with anterior disconnection syndrome



(A, B) Diffusion-weighted images (DWI) of infarction in the anterior cerebral artery territory. (C) Diffusion tensor imaging (DTI) shows interruption of transcallosal fibers; corticospinal tract (CST) and fractional anisotropy (FA) analysis. (D) Motor evoked potentials (MEP) of the hand muscles recorded with EMG electrodes at interpulse intervals (IPI) of 6 msec, 10 msec, and 14 msec when stimulated right-to-left and left-to-right hemispheres. Compared to unconditioned responses, conditioned responses measured at all tested IPIs failed to cause statistically significant reduction in mean amplitude showing no transcallosal inhibition from either right or left hemispheres. (E) TMS-EEG study showed asymmetric response after right and left M1 stimulation.

same methodologies will continue to be just as informative studying the less transparent connectivities critical for language, memory, and many other cognitive and emotional functions.[4,5]

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Disclosures deemed relevant by the authors, if any, are provided at the end of this article. ***Go to Neurology.org for full disclosures.***

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