A white matter tract mediating awareness of speech

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Supplemental data at Neurology.org

ABSTRACT

Objective: To investigate the effects of extraoperative electrical stimulation of fiber tracts connecting the language territories.

Methods: We describe results of extraoperative electrical stimulation of stereotactic electrodes in 3 patients with epilepsy who underwent presurgical evaluation for epilepsy surgery. Contacts of these electrodes sampled, among other structures, the suprainsular white matter of the left hemisphere.

Results: Aside from speech disturbance and speech arrest, subcortical electrical stimulation of white matter tracts directly superior to the insula representing the anterior part of the arcuate fascicle, reproducibly induced complex verbal auditory phenomena including (1) hearing one’s own voice in the absence of overt speech, and (2) lack of perception of arrest or alteration in ongoing repetition of words.

Conclusion: These results represent direct evidence that the anterior part of the arcuate fascicle is part of a network that is important in the mediation of speech planning and awareness likely by linking the language areas of the inferior parietal and posterior inferior frontal cortices. More specifically, our observations suggest that this structure may be relevant to the pathophysiology of thought disorders and auditory verbal hallucinations.

GLOSSARY

AF = arcuate fascicle.

During auditory verbal hallucinations, it is possible that the speech processing network produces variants of inner speech carrying characteristics of or being perceived as overt external speech. Possibly relevant phenomena may occur when electrical stimulation of the inferior parietal cortex of either hemisphere induces an illusion of a self-motion while stimulation of the lateral prefrontal area eliminates awareness of the subject’s actual movements. These observations indicate that the awareness of one’s motor activity does not solely rely on sensory feedback, but also on a prediction generated before its execution. It is likely that planning and prediction of action involve processing in the inferior parietal lobe, and can thus be elicited by electrical stimulation. Longitudinal fascicles link activities in the parietal and frontal lobes that mediate action planning, execution, and awareness. In particular, the arcuate fascicle (AF) connects the speech centers in the inferior parietal and superior posterior temporal area with those in the posterior inferior frontal region. Intraoperative electrical stimulation of these fiber tracts induces phonemic paraphasias and speech arrest, but no positive speech phenomena. We present evidence that—in a way resembling illusions of movements elicited by inferior parietal cortical stimulation—extraoperative electrical stimulation of the anterior part of the AF can reproducibly induce hallucinations of one’s own speech and thought.

METHODS Three right-handed female patients (aged 21, 38, and 56 years) underwent surgical evaluation for pharmacoresistant focal epilepsy by stereotactic implantation of multicontact depth electrodes into the insular cortex (e-Methods and tables e-1 and

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Go to Neurology.org for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

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e-2 on the Neurology® Web site at Neurology.org). Contacts of these electrodes also sampled the suprasylvian white matter of the left hemisphere. Electrical stimulation mapping of these electrodes was performed as part of routine clinical care. The relation of these electrode contacts to fiber tracts was determined based on superimposition of postoperative CT scans with preoperative volumetric MRI of the brain.

**RESULTS** In subject 1, stimulation of one contact within the frontal opercular white matter above the circum insular sulcus at the junction of anterior insula and frontal operculum (figure 1, P1-AI5; figure e-1 and supplemental protocol 1) reproducibly elicited a verbal auditory hallucination reported as hearing the particular phrase “... so, how do you know ...” in English with an Italian accent—“like an Italian saying that all the time” (supplemental protocol 1).

In subject 2, stimulation of 2 adjacent contacts (figure 1, contacts P2-AI7 and AI8; figure e-2 and supplemental protocol 2) induced a self-speech experience: “talking out loud” and “talking to myself in the head” (supplemental protocol 2). The patient did not report a particular thought, but varying thoughts during stimulation.

In subject 3, more testing was done, as she reported a very similar striking experience repeatedly. The stimulated electrode was more posterior to those in subjects 1 and 2, still lying in the anterior segment of the arcuate fascicle (figure 1, contacts P3-PI8 and P3-PI9; figure e-3, supplemental protocol 3). Similar to the 2 other subjects, she initially reported the impression of having said out loud a spontaneous word and directly after stimulation she said, “That was really weird. I just said ‘ah huu!’ and I did not say it.” She asked, “You did not hear me say it?” and added “I think it was loud, but I don’t think I did say it.” With repeated stimulation sessions, different words were reported (“ah huu,” “lights,” “team,” and “me”) apparently related to the patient’s current experiences being recently spoken or written. Then we asked the patient to constantly repeat a word loudly at her own pace. Overt repetition of the word paused with onset of the stimulation. However, the patient was certain that she continued to repeat the nonword “siat” in one task and the word “me” in another. The duration of stimulation was proportional to the presumed number of repetitions she reported based on her pace of repetition seen at baseline. In other stimulations, the patient continued to repeat the given nonword “blag” or the word “house,” but with dysarthria and very slowly. When asked about the altered pronunciation, she denied any deviations from her baseline speech.

Writing and function of facial muscles were fully preserved during stimulation, as was the production of simple repetitive guttural, lingual, and labial sounds. Reading remained intact, albeit at a slower pace and aprosodically. Naming was associated with semantic paraphasias (supplemental protocol 3).

**DISCUSSION** Our current observation indicates that the perisylvian AF mediates awareness of speech. The AF consists of 1 direct (long segment) and 2 indirect parts (posterior and anterior segment). In our study, the electrode contacts were all located within the anterior segment of the AF. This anterior segment likely connects the Geschwind territory, which consists of the angular and supramarginal gyri, with the Broca territory. The Geschwind territory has been associated with phonologic short-term memory processing. Its late myelination suggests evolutionary recency and has supported theories relating it to the evolution of language. Our data do not directly allow determination of the cortical area or areas that were primarily activated by the subcortical stimulation. However, since our subjects’ symptoms resemble those produced by posterior parietal cortex stimulation, it is possible that the fibers we stimulated are of parietal origin.

Neuroanatomically, theories on motor awareness converge on emphasizing the importance of the parietal cortex for awareness and conception of movements and the premotor cortex in execution of
movement plans. von Helmholtz reported in the 19th century that a priori internal knowledge of the eyes’ oculomotor system is required for realistic interpretation of visual impressions. In this regard, formation of efference copies of movement plans generated ahead of execution may be essential for aligning inner predictions with actual performance even prompting concepts stating that every voluntary movement includes the generation of at least 2 different streams of impulses, one targeting the effector and the other directed to a central structure preparing the brain for the consequences of the action. Apparently, coherence or comparison between feed-forward plans of an action and control via a feedback signal is altered in disorders of self-agency and action control, and, thus, verbal auditory hallucinations possibly represent abnormalities in prediction processing. Indeed, lesions of the inferior parietal cortex can affect the awareness of the intention to perform a voluntary movement and delay the Bereitschaftspotential by up to 1 second. Moreover, studies in nonhuman primates suggest that motor execution includes the generation of a forward model of the predicted state of the limb or body part. In addition, phenomena of autoscopy (e.g., seeing one’s own body) have been induced by stimulation of the posterior parietal cortex and thus may relate to the impression of hearing one’s own voice as reported by our patients. In line with the results of our stimulation, disrupting the connectivity between planning and execution centers that are generally sensory and motor areas of the brain and de-correlating plans and perceptions may explain autoperceptive phenomena including auditory verbal hallucinations as supported by reduced fractional anisotropy in the left AF in subjects with schizophrenia who experience auditory verbal hallucinations. In addition, the semantic complexity, context sensitivity, attributing the speech to one’s own, and uncertainty about one’s having uttered any words clearly indicate the difference between these phenomena and ones induced by electrical stimulation of auditory cortex.

Our findings suggest that the left anterior AF is part of the network that subserves intentionality and awareness of language production, probably sharing a common mechanism with general motor awareness subserved by other parts of the superior longitudinal fascicle.

**AUTHOR CONTRIBUTIONS**
M.Z.K. contributed to conception, conduction, analysis, and review. G.F.-B.V. contributed to conduction, analysis, and review. R.M. contributed to conception and conduction. C.S. contributed to conception, conduction, analysis, writing of the first draft, and review.

**ACKNOWLEDGMENT**
The authors thank Prof. Ugur Türe for providing the photograph used in figure 1.

**STUDY FUNDING**
This work was supported by educational grant S134-10.044 of the “Stifterverband für die Deutsche Wissenschaft” to author C.S.

**DISCLOSURE**
The authors report no disclosures relevant to the manuscript. Robert Maciunas is deceased; disclosures are not included for this author. Go to Neurology.org for full disclosures.

Received May 1, 2015. Accepted in final form September 1, 2015.

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