Voice-based singing is a fascinating ability broadly shared between ancient and modern human cultures. Cognitive neuroscientists have been interested in this function, but its precise neural implementation remains unclear. Current data suggest that the neural network subserving singing partly overlaps with those involved in speech production per se (left-lateralized), however with some degree of difference.8,11,16 Specifically, singing would recruit a far more distributed neural network in both hemispheres, suggesting the additional involvement of a dedicated neural subcircuit. 8,11 Famous dissociations observed in some aphasic patients who remain able to some extent to sing lyrics despite severe expressive disturbances fit well with these findings derived from activation functional MRI paradigms.5,15 However, to date, whether the brain has an evolved and relatively independent neural system for singing is still matter of controversy. Here, we present a strikingly unusual case of behavioral alteration induced by intraoperative electrical stimulations that appear to substantially contribute to this debate.

Case Report

History and Examination

This 36-year-old right-handed male, with no previous medical history, a well-trained singer, underwent brain MRI because of seizures. This MRI study revealed a right fronto-temporo-insular lesion highly suggestive of a low-grade glioma (nonenhancing hypointense lesion on T1-
weighted MRI, hyperintense lesion on FLAIR MRI) (Fig. 1). Findings from the preoperative neurological examination and neuropsychological assessment were normal. An antiepileptic drug (levetiracetam) was administered and surgery was proposed in the awake condition to perform intrasurgical functional mapping (movement, language, cognition, and mentalizing).

Operation
The patient was surgically treated after administration of local anesthesia (asleep-awake-asleep protocol using propofol and remifentanil). A frontotemporal craniotomy was performed, and intraoperative ultrasonography was used to delineate the lesion. Then, functional mapping with direct electrical stimulation (DES) was achieved just before resection. DES is a surgical technique allowing real-time anatomo-functional correlations with a high spatial resolution, by functionally inactivating a small cerebral territory for a few seconds. This common procedure in neurosurgical practice gives the surgeon mapping the eloquent structures a set of basic cognitive processes. If responsive anatomical sites are identified, they will not be removed (even despite lesion infiltration). Here, a bipolar electrode with 5-mm spaced tips delivering a biphasic current (pulse frequency 60 Hz, single pulse phase duration 1 msec, amplitude 2 mA, time of stimulation, ~4 seconds; Nimbus, Hemodia) was applied to the patient’s brain. In agreement with a well-validated method, the same site was not stimulated twice consecutively. During DES, the patient was asked to perform a set of tasks, including movement, counting, naming, line bisection, spontaneous language, and mentalizing (i.e., a complex emotional recognition task).

Whereas classic neuropsychological and neurological disturbances were elicited when stimulating the ventral part of the precentral cortex (anarthria and speech arrest) and the motor cortex (left facial deviation) (Fig. 2, blue labels 1, 2, and 3; Video 1), DES of the anteroposterior part of the pars opercularis of the right inferior frontal gyrus (IFGop), a noninfiltrated brain area, was identified to elicit in a reproducible manner an automatic switch from a speaking to a singing mode of language production (Fig. 2, red label 4; Fig. 3).

VIDEO 1. This video shows a classic functional mapping of the precentral cortex. As shown in Fig. 1, whereas stimulation of the ventral premotor cortex elicited an anarthria or a speech arrest, stimulation of the motor cortex of the face induced a facial deviation. Copyright Hugues Duffau. Published with permission. Click here to view with Media Player. Click here to view with Quicktime.

This acute neuropsychological manifestation was first evoked during the naming task (Video 2) and then during the mentalizing task.

VIDEO 2. This video shows the DES-induced singing manifestation. This behavioral alteration was induced 3 times during the naming task and was specifically related to the stimulation of the ventral sector of the right inferior frontal gyrus. Copyright Hugues Duffau. Published with permission. Click here to view with Media Player. Click here to view with Quicktime.

Finally, it was reproduced at the end of the surgery during spontaneous speech. No neighboring or more distant anatomical sites, covering frontal, temporal, and parietal cortices, were found to induce the same behavioral alteration at the cortical level (Fig. 2 green crosses). The patient was hardly aware of the switch and justified it by the fact that he likes singing, generally. The resection was achieved according to these functional boundaries.

Postoperative Course
The patient’s postoperative course was uneventful, with no neurological worsening. Language processes were fully preserved. We did not notice any disruption of prosody or tonality during spontaneous speech or language tests (including the naming task used during surgery). The patient was still able to sing following surgery. There were no local or general complications. There were no seizures. The patient returned home 4 days after surgery and resumed a normal life. Neuropathological examination led to a diagnosis of WHO Grade II astrocytoma. Postsurgical MRI revealed a subtotal resection, and no adjuvant treatment was given (no chemotherapy or radiotherapy).

Discussion
A long-standing issue in the neuroscience of language is to know whether the human brain has a dedicated neural network sustaining our capacity to sing. Whereas several functional MRI and patient studies have begun to ascertain this possibility, no clear-cut evidence has been provided to support this hypothesis. The results reported here suggest the existence of a neurocognitive mechanism allowing an individual to flexibly pass from a speaking to a singing mode of speech production. This assumes the existence of 2 independent neural networks relatively specialized in either one or the other expressive mode of language.

Pathological language switching (e.g., from English to Dutch) has been described in bilingual patients after injury of the left frontal lobe or electrical stimulations of
different anatomical structures, including classic language areas and their underlying subcortical connectivity as well as other brain regions classically involved in cognitive control. Consequently, it has been hypothesized that this involuntary language switching might reflect not a disturbance of language processing per se, but a more general impairment of executive control processes. Indeed, voluntary switching from one language to another presupposes the involvement of some executive processes, such as selection and inhibition.

Given the high similarity between bilingual language switching and the observation reported here, it is likely that stimulating IFGop might have transiently disrupted inhibitory control processes leading to an involuntary switch in a singing mode of speech production. This interpretation is broadly supported by the acknowledged role of the right pars opercularis in response inhibition and, more specifically, in the inhibition of speech acts. It is also strengthened by the automatic nature of the switch induced (Video 2).

Surprisingly, this kind of switching has never been described in the literature despite functional mapping of the right frontal cortex. The explanation is likely to be related to patient competence. Indeed, although with no musical education, the patient reported that he sang very often (between 1 and 2 hours a day). Accordingly, it is reasonable to assume that he has developed a specialized subnetwork for singing and, a fortiori, specific speech-related inhibition processes. This is in agreement with current hypotheses that state that development of expertise may induce a progressive decoupling of the normal language and singing neural networks through time.

Given the well-established involvement of the right hemisphere in prosody, one could correctly argue that the switch observed during stimulation is more related to a transitory disruption of prosody-related processes. However, although it is clear that prosody had been modified (more exactly, a switch from linguistic to musical prosody), no disruption of prosody per se had been observed. Indeed, given the stimulation parameters used and the structure stimulated, a negative effect (e.g., monochord phrasing) rather than a positive effect (generation of a musical phrasing) would have been expected. Simulation is thought to disrupt the function of the area being stimulated (e.g., stimulating the left pars opercularis may lead to anomia). At another level, if we suppose that prosody is a process common to all humans, one would expect that the manifestation described here would be also commonly observed during functional mapping of patients with right-sided lesions. However, this is the first time we have observed this kind of switching despite the tens of functional mapping procedures of the right pars opercularis achieved, most notably in our center, clearly mitigating this alternative hypothesis.
Conclusions

It seems that, in certain situations, the brain selects concurrent modes of speech production, which become competitive with specialization. As bilingual people, proficient singers may develop a dedicated neural subnetwork specialized in the sustenance of the melodically intoned articulation of words, parallel to and in competition with the neural network devoted to the classic speaking-based language. To maintain one or the other over time, an inhibitory pressure has to be exerted to avoid aberrant mixing. We propose that the right $\text{IFG}_{\text{op}}$, previously identified as a crucial cortical area in the response inhibition and task switching networks, may play this role. Further work is needed to confirm this interpretation, however, as it remains speculative and is based on an isolated case report.

From a more clinical perspective, we consider that this finding has clinical implications for awake neurosurgery, especially to preserve quality of life in singers.

References


Author Contributions
Conception and design: Duffau, Herbet. Acquisition of data: Duffau, Herbet. Analysis and interpretation of data: all authors. Drafting the article: all authors. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Duffau. Study supervision: Duffau.

Videos


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