

## Introduction

Cortical stimulation mapping (CSM) has provided important insights into the neuroanatomy of language, due to its high spatial and temporal resolution, and the causal relationships that can be inferred from transient disruption of specific functions<sup>[1]</sup>. Almost all CSM studies to date have focused on word level processes such as naming, comprehension and repetition<sup>[2]</sup>. In this study, we used CSM to identify sites where stimulation interfered selectively with syntactic encoding during sentence production<sup>[3]</sup>.

## Methods

Fourteen patients undergoing left hemisphere awake craniotomy (8 men, 6 women, mean age = 46 years, age range = 21 to 70 years) took part in the study. Etiology was epilepsy in 6 cases, glioma in 5 cases, and cavernous malformation in 3 cases. The inclusion criteria were (1) awake craniotomy involving electrocortical stimulation mapping to identify and preserve eloquent cortex; (2) first time brain surgery; (3) significant exposure of left frontal and temporal perisylvian cortex; (4) no significant pre-operative language deficits.

Patients were presented with pictures depicting a boy and a girl engaged in one of seven simple transitive actions (Figure 1) and were asked to describe each picture<sup>[4]</sup> using a simple sentence (e.g. "The boy is pushing the girl") while stimulation was applied to a range of frontal, temporal and parietal sites. No patients had significant aphasia at baseline, and all were readily able to describe the pictures in the absence of cortical stimulation. Patients performed between 14 and 72 trials (mean 36.6 ± 13.7). When sites were found where stimulation interfered with sentence production, the same locations were stimulated again on later trials to establish reproducibility.

Standard language mapping tasks (counting, picture naming, repetition) were also performed.



Figure 1. Examples of the stimulus pictures

## Results

The final cortical stimulation map from a representative patient (P1) is shown in Figure 2.

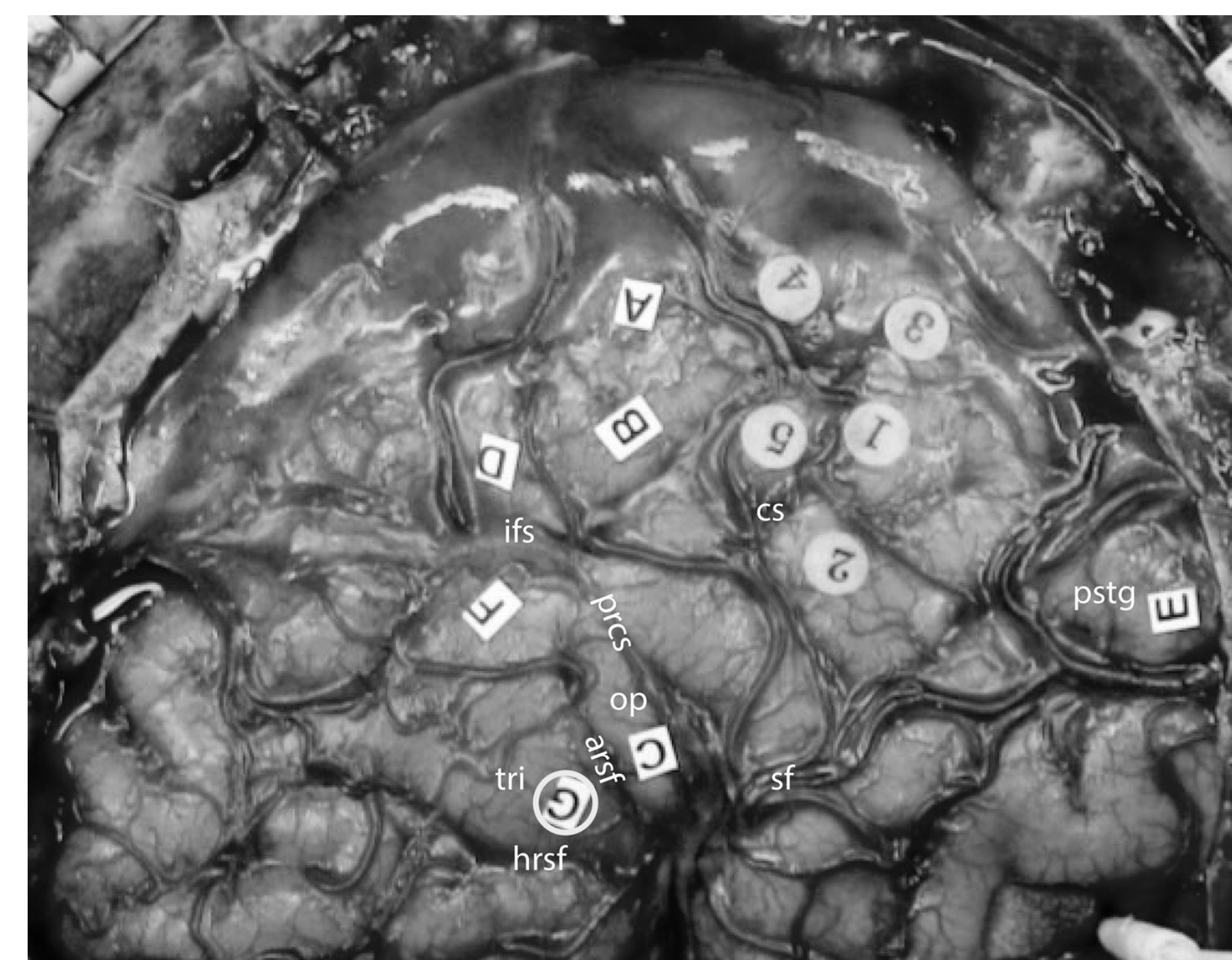


Figure 2. Final cortical stimulation in patient P1. One syntactic encoding site was observed in this patient (label G, circled). Six other language sites were documented (A-F). Sites 1-5 were sensorimotor sites.

In 7 out of 14 patients, we found a total of nine syntactic encoding sites where stimulation interfered with syntactic encoding in a reproducible manner, but did not disrupt word-level language functions or automatic speech (Figure 3). All nine sites were localized to the IFG: five to the pars triangularis, three to the pars opercularis, and one to the pars orbitalis.

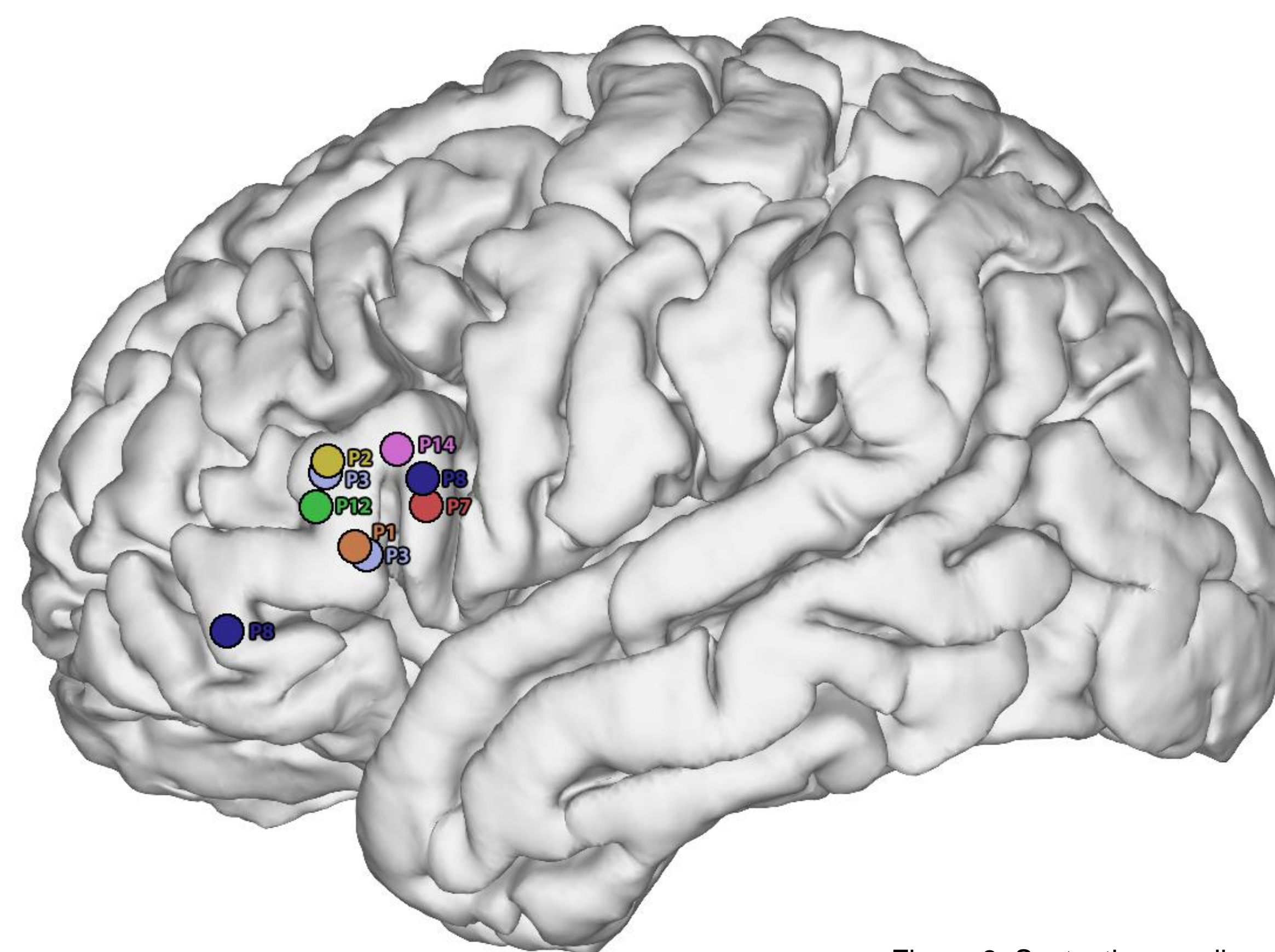


Figure 3. Syntactic encoding sites

Disruptions of syntactic encoding took several different forms, including mis-assignment of arguments to grammatical roles, mis-assignment of nouns to verb slots, omission of function words and/or inflectional morphology, and various paragrammatic constructions (Table 1).

Patient	Site	Stimulus	Response
P1	tri	girl chasing boy	(.) the girl is boying (...) uh the girl is kicking, the girl is chasing the boy
		girl pushing boy	(...) the girl is boying (.) is uh (.) pushing the boy
P2	tri	boy washing girl	(.....) the girl is (...) bathing (...) bathing the girl (.) the boy is bathing the girl
P3	tri (ventral)	girl kicking boy	the um girl is kicking the (...) the boy is kicking the girl
	tri (dorsal)	boy kissing girl	the girl is kissing the (.) the boy is kissing the the girl
P7	op	girl kissing boy	the girl is being kissed by the girl
P8	op	girl kissing boy	girl is (.) kiss a (.) kiss a boy
		girl kicking boy	girl (.) kick boy
	boy pushing girl	um (.) sh- uh he's p- p- uh s- sw- swinging him (.) on a little swing (.) he's pushing her	
	boy kissing girl	the girl is k- k- kissing the boy ah is kiss- I mean the boy is kissing the girl	
	boy washing girl	the girl's (.) kiss- is kiss- kissing (.) the boy is kissing the girl	
orb	girl washing boy	ah (.) the girl (.) is (.) is (.) um (.) it was bathed she bathed him	
	girl kicking girl	(.) um (.) the (.) uh boy is uh um (.) uh um (.) kick girl	
	girl pushing boy	same thing um (.) boy a- are um (.) oh switcheroos ok xxx a girl (.) pushin' a boy (.) in a swing	
P12	tri	boy washing girl	boy is (.) is uh um (.) is uh uh (.) um (.) washing (.) uh (.) wash girl in the tub
		girl chasing boy	the boy is chasing the boy ... er sorry did i say that wrong? the girl is chasing the boy
P14	op	boy pushing girl	the girl is (.) s- swinging the girl
		boy pulling girl	(...) boy (.) i- is chase of girl in th- um (.) trailer

## Discussion

Our results indicate that the left IFG is critically important for syntactic encoding during sentence production. We observed clear evidence that direct electrocortical stimulation of the IFG resulted in reproducible and selective disturbances of sentence production. The frequency with which syntactic encoding sites were identified (50%) is comparable to the frequency at which speech arrest sites are identified during standard CSM<sup>[1]</sup>. All but one of the syntactic encoding sites were localized to the pars triangularis or pars opercularis of the IFG, which together make up Broca's area. None of the syntactic encoding sites were identified during routine cortical stimulation mapping tasks of counting, naming, or repetition, suggesting that these sites are selectively involved in sentence production<sup>[3]</sup>.

## Acknowledgements

We thank the patients for their participation in this research. This work was supported by the National Institutes of Health (NS065120, NS098971, DC013270, DC016080, DC012379), the New York Stem Cell Foundation, the Howard Hughes Medical Institute, the McKnight Foundation, the Shurl and Kay Curci Foundation, and the William K. Bowes Foundation. EFC is a New York Stem Cell Foundation Robertson Investigator.

## References

- [1] Ojemann, G., Ojemann, J., Lettich, E., & Berger, M. (1989). Cortical language localization in left, dominant hemisphere. *Journal of Neurosurgery*, 71, 316-326.
- [2] Rofes, A., & Miceli, G. (2014). Language mapping with verbs and sentences in awake surgery: a review. *Neuropsychology Review*, 24, 185-199.
- [3] Indefrey, P., Brown, C.M., Hellwig, F., Amunts, K., Herzog, H., Seitz, R.J., & Hagoort, P. (2011). A neural correlate of syntactic encoding during speech production. *Proceedings of the National Academy of Sciences of the United States of America*, 98, 5933-5936.
- [4] Wilson, S.M., Dronkers, N.F., Ogar, J.M., Jang, J., Growdon, M.E., Agosta, F., ... Gorno-Tempini, M.L. (2010). Neural correlates of syntactic processing in the nonfluent variant of primary progressive aphasia. *Journal of Neuroscience*, 30, 16845-16854.