The contribution of corpus callosum to lateralization of the resting state language network

Olga Dragoy[1], Svetlana Kuptsova[1,2], Nicola Canessa[3], Victoria Zinchenko[1,4], Ekaterina Stupina[1], Aleksey Petrushevsky[2], Oksana Fedina[2], Stefano Cappa[3,5]

[1]National Research University Higher School of Economics, Russia; [2]Center for Speech Pathology and Neurorehabilitation, Russia; [3]IUSS Pavia, Italy; [4]National Research Center "Kurchatov Institute", Russia; [5]IRCCS S. Giovanni di Dio Fatebenefratelli, Italy

Introduction

Language production and comprehension rely on a largely distributed network of brain areas mostly of the left hemisphere (Bishop, 2013). However, such left-lateralized functional asymmetry for language has been found altered in some healthy (e.g., left-handers) and various clinical (people with autism, brain tumors, trauma or stroke) populations (Crosson et al., 2009; Knaus et al., 2010; Tantillo et al., 2016). Recent findings (Josse et al., 2008; Hinckly, 2016) revealed the critical contribution of the corpus callosum (CC) size to language lateralization: counterintuitively, as CC size increased, stronger left lateralization was found, suggesting the inhibitory role of the CC in interhemispheric interactions. We tested this hypothesis measuring lateralization of resting state language networks and the CC size in healthy people and stroke patients with aphasia.

Methods

Participants

Thirty-two left-hemisphere stroke patients with aphasia (9 females; age = 56 ± 10 years; median post-stroke onset = 8 months) and 32 age-matched healthy volunteers (22 females; age = 51 ± 10 years) with no record of neurological or psychiatric disorders participated in the study. All participants were right-handed, monolingual Russian speakers, without premorbid speech or language impairment. Patients were recruited at the Center for Speech Pathology and Neurorehabilitation (Moscow, Russia), where their neuropsychological status was assessed by a certified clinical neuropsychologist. All patients had aphasia diagnosed in terms of A.R. Luria's classification (Luria, 1962/1966) and included non-fluent (efferent motor, afferent motor, dynamic) and fluent (sensory, acoustic-mnestic, semantic) types of aphasia of the whole range of severity scored using the Quantitative Assessment of Speech in Aphasia (Tsvetkova, Akhutina, & Pylaeva, 1981).

MRI data acquisition

The MRI data were obtained at a 1.5T Siemens Magnetom Avanto scanner. High-resolution 3-D structural images were acquired using a T1-weighted MPRAGE sequence (TR/TE/FA=1.9s/2.93ms/15°; spatial resolution 1x1x1 mm; matrix 256x256; 176 slices). Resting-state fMRI whole-brain volumes were acquired with T2*-weighted BOLD imaging (TR/TE/FA = 3s/50ms/90°; spatial resolution 3.9x3.9x3.75 mm; matrix 64x64; 35 slices; 180 volumes). Participants were instructed to stay awake in the scanner, with their eyes closed; no active task was given.

Data analyses

Data preprocessing was performed in SPM8. Following the procedure recommended by Allen et al. (2011), we identified resting state networks using group independent component analysis in GIFT. As a result, in a joint cohort of 64 participants, 29 networks were revealed, including language, default mode, frontal executive, attentional, higher visual and visual functional networks, all classified on the topographical basis.

We used univariate tests corrected for multiple comparisons over all networks to test the difference between people with and without aphasia in the intensity of resting-state spatial maps, related to the connectivity and degree of co-activation within a network (Allen et al., 2011). The effect of group was only found significant in one language network involving the superior and middle temporal gyri, the inferior frontal gyrus and the basal ganglia bilaterally. To establish the direction of the group effect, using SPM8 we compared the intensity of activation between people with aphasia and healthy individuals in binary masks of the two (left and right) components of the found language network. The size of each participant's CC was measured using normalized T1 images. Average white matter volumes of the CC were extracted based on the atlas by Mori et al. (2008).

Results

The left part of the revealed language network (specifically, left superior temporal gyrus, see Fig. 1 left) displayed stronger intensity of spontaneous activity in healthy individuals than in people with aphasia, while the right part of the network (right superior temporal gyrus and basal ganglia, see Fig. 1 right) was more strongly activated in people with aphasia. This difference in lateralization was not affected by the aphasia type, nor by severity.
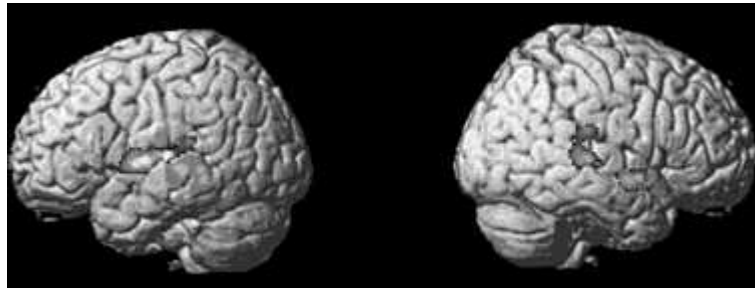

Fig. 1. Components of the resting state language network with stronger intensity of spontaneous activity in healthy individuals (left) than in people with aphasia (right).

Overall, the CC volume was found reduced in patients as compared to healthy individuals ($p < .001$). Critically, in a joint group of patients and healthy people, significant positive correlation ($r = .34$, $p < .01$) was found between the CC volume and the left-lateralized intensity in the language network. In turn, the correlation between the CC volume and the right-lateralized intensity was found negative ($r = -.26$, $p < .05$).

Discussion

A clear asymmetry has been found between healthy individuals and brain-damaged people with aphasia, regarding the revealed resting state language network. The left-lateralized component of this network was stronger in healthy people, in contrast to its right components, which was more strongly recruited in people with aphasia. More intense engagement of the right hemisphere language-related homologues under the condition of a left-hemisphere damage was suggested underling this asymmetry (Saur, 2006). However, we found a significant contribution of the CC size to the language network asymmetry. As the size of the CC increased, the left lateralization of the network increased. With decrease of the CC size, in contrast, the right lateralization increased. Overall, the CC was smaller in patients with aphasia, which explains their altered left-hemisphere asymmetry for language. This is the first evidence from the resting state functional data regarding language lateralization in people with aphasia and it structural determinants.

References

Allen, E. A., Erhardt, E. B., Damaraju, E., Gruner, W., Segall, J. M., Silva, R. F., …. Calhoun, V. D. (2011). A baseline for the multivariate comparison of resting-state networks. *Frontiers in Systems Neuroscience, 5,* 2.
Bishop, D. V. (2013). Cerebral asymmetry and language development: cause, correlate or consequence? *Science, 340*(6138), 1230531

Crosson B., Moore A. B., McGregor K. M., Chang Y. L., Benjamin M., Gopinath K., ... White, K. D. (2009). Regional changes in word-production laterality after a naming treatment designed to produce a rightward shift in frontal activity. *Brain and Language, 111,* 73-85.

Hinkley, L. B, Marco, E. J., Brown, E. G., Bukshpun, P., Gold, J., Hill, S., ... Nagarajan, S. S. (2016). The contribution of corpus callosum to language lateralization. *Journal of Neuroscience, 36(16),* 4522-4533.

Josse, G., Seghier, M. L., Kherif, F. & Price, C. J. (2008). Explaining function with anatomy: language lateralization and corpus callosum size. *Journal of Neuroscience, 28*(52), 14132-14139.

Knaus, T. A., Silver, A. M., Kennedy, M., Lindgren, K. A., Dominick, K. C., Siegel, J., & Tager-Flusberg, H. (2010). Language laterality in autism spectrum disorder and typical controls: a functional, volumetric, and diffusion tensor MRI study. *Brain and Language, 112,* 113-120.

Luria, A. R. (1962). *Higher cortical functions in man.* Moscow: Moscow University Publishing House (in Russian); New York: Basic Books (1966) (English Edition).

Mori, S., Oishi, K., Jiang, H., Jiang, L., Li, X., Akhter, K., ... Mazziotta, J. (2008). Stereotaxic white matter atlas based on diffusion tensor imaging in an ICBM template. *Neuroimage, 40*(2), 570-582.

Saur, D., Lange, R., Baumgaertner, A., Schraknepper, V., Willmes, K., Rijntjes, M., & Weiller, C. (2006). Dynamics of language reorganization after stroke. *Brain, 129,* 1371-1384.

Tantillo, G., Peck, K. K., Arevalo-Perez, J., Lyo, J. K., Chou, J. F., Young, R. J., ... Holodny, A. I. (2016). Corpus callosum diffusion and language lateralization in patients with brain tumors: a DTI and fMRI study. *Journal of Neuroimaging, 26*(2), 224-231.

Tsvetkova, L. S., Akhutina, T. V., & Pylaeva, N. M. (1981). *Kolichestvennaya otsenka rechi u bolnyx s aphasiej* [Quantitative assessment of speech in aphasia]. Moscow: Izdatelstvo Moskovskogo Gosudarstvennogo Universiteta.