EC NEUROLOGY
Short Communication

Brain Functional Reorganization after Stroke: What has Recovery from Aphasia Taught Us?

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Received: May 14, 2018; **Published:** June 22, 2018

Stroke is one of the most common serious diseases and the second leading cause of death and disability in developed countries (globally in 2013 there were 6.5 million deaths from stroke). Approximately 795,000 strokes occur in the United States each year [1]. It remains the leading cause of serious, long-term disability in the United States.

Human speech, the most complex of higher-level brain functions, is based on widespread and multimodal networks. As we recently reported [2] the classical Broca-Wernicke-Lichtheim-Geschwind model of speech processing has been outdated and a new, dual-stream model by Hickok and Poeppel is now in use [3], with a bilaterally, mainly temporal organized, ventral stream processing speech signals for comprehension, and a strongly left-hemisphere dominant, fronto-parietal, dorsal stream mapping acoustic speech signals to parietal and frontal-lobe articulatory networks. Fridriksson., *et al*. using lesion data from aphasic patients due to stroke offered additional support to this model, showing that language functions rely on a broader cortical network and on interactions between the two streams, and this explains why patients with different lesion locations often experience similar language impairments [4]. Furthermore Mirman., *et al*. [5] revealed two major divisions within the language system, a peri-Sylvian (meaning versus form), and an extra-Sylvian (recognition versus production), illuminating the importance of tracts beyond the arcuate fasciculus, i.e. the uncinate fasciculus, the inferior fronto-occipital fasciculus, and the anterior thalamic radiations.

When these networks are disrupted by brain lesions, most commonly from a stroke, aphasia occurs. Aphasia due to stroke accounts for negative features such as prolonged stay in rehabilitation settings, poorer overall outcome prognosis, reduced participation in daily activities and influenced quality of life. Each year approximately 100,000 new stroke survivors are diagnosed with aphasia [6].

Traditionally speech and language therapy is applied to these patients in order to improve their language and communication abilities, allowing them to re-participate in everyday life activities. What varies in these speech and language therapy approaches is mainly the intervention methodology, its duration, intensity and frequency [7]. However, purely linguistic approaches are not fair neither for the patients, nor for aphasia. In their excellent book titled “Redefining recovery from aphasia”, Cahana-Amitay and Albert focus on the “nonlinguistic factors that participate in reshaping the neural networks supporting recovery of language functions in aphasia” ([8], pp. ix-x). They had previously defined the term language’s “neural multifunctionality” i.e. “the incorporation of nonlinguistic functions into language models of the intact brain, reflecting a multifunctional perspective whereby a constant and dynamic interaction exists among neural networks subserving cognitive, affective, and praxic functions with neural networks specialized for lexical retrieval, sentence comprehension, and discourse processing, giving rise to language as we know it” [9]. This neural multifunctionality is beneficial not only for the diseased, but also for the aging brain: successful language ability among older adults has been linked to the sparing of cognitive abilities, where "the combined contribution of preserved cognitive functions reflects a compensatory mechanism recruited to support a given compromised linguistic function" [10]. In other words, language functions in the elderly increasingly rely on supportive (ancillary) networks outside traditional core language networks. These ancillary networks are also present of course in younger individuals, but there is no need for them to become involved in linguistic functions.

The brain's functional reorganization actually relies on the availability of supportive networks and neurorehabilitation is the science of enhancing their recruitment in order to serve different functions than those they were originally used for. Availability of supportive networks after stroke depends on the localization and the extent of tissue damage. Prediction measures of outcome after ischemic stroke can be improved by a combination of morphological imaging including DTI of fiber tracts and activation (functional) studies revealing residual functions, reserve capacity, and prospects for recovery [11]. With simple words, when brain regions involved in recovery remain intact, the outcome is more favorable, and vice versa. With this in mind a database was created, in order to "Predict Language Outcome and Recovery After Stroke (PLORAS)" on the basis of a single structural brain scan that indexes the stereotactic location and extent of brain damage. The PLORAS database can also be used to predict recovery of other cognitive abilities on the basis of anatomical brain scans [12].

Saur., *et al*. [13] studied the dynamics of reorganization in the language system by repeated functional MRI (fMRI) examinations with parallel language testing from the acute to the chronic stage in patients with aphasia after stroke. They found that brain reorganization during language recovery proceeds in three phases: a strongly reduced activation of remaining left language areas in the acute phase, followed by an up regulation with recruitment of homologue language zones, which correlates with language improvement, and later, a normalization of activation possibly reflecting consolidation in the language system. Turkeltaub., *et al*. [14] performed a meta-analysis of functional neuroimaging studies of chronic aphasia after stroke, addressing the question "if networks for residual language function and recovery are consistent across aphasic patients". The answer was "yes", areas included some spared left hemisphere language nodes, new left hemisphere areas, and right hemisphere areas homotopic to the control subjects' language network and this consistency in network recruitment is critical in formulating better rehabilitation protocols targeting these networks. Several recruitment mechanisms are postulated, including persistent function in spared nodes, compensatory recruitment of alternate nodes, and recruitment of areas that may hinder recovery.

Activation of areas (mainly in the unaffected hemisphere) that actually hinder recovery by inhibiting recruitment of functional networks ipsilateral to the lesion (transcallosal inhibition) can be reduced by non-invasive brain stimulation techniques, and this can be visualized by neuroimaging [15]. Targeting these areas (and more specifically the triangular part of the right inferior frontal gyrus-IFG) with low-frequency, inhibitory rTMS has a positive effect on language recovery in patients with aphasia following stroke [16].

What have we learned to take with us in our everyday clinical practice through this short journey on brain functional reorganization underlying recovery from aphasia after stroke? Firstly, lesions that cause aphasia interrupt "multifunctional" networks, so aphasic patients do not only suffer from aphasia. Secondly, aphasic patients need a holistic cognitive neurorehabilitation approach, in order to improve their communication skills and their quality of life. Thirdly, neuroimaging should play a protagonistic role both in predicting outcome and designing therapeutic protocols, including neuromodulation procedures. The multidisciplinary team that is called upon to rehabilitate these patients should therefore include a specialized neurologist, clinical neuropsychologist, neuroradiologist and speech – language pathologist to comprehensively deal with this multifunctional problem/situation.

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Volume 10 Issue 7 July 2018