

Measuring Language Recovery in the Underlying Large-Scale Neural Network: Pulling Together in the Face of Adversity

Language is an essential higher cognitive function. Aphasia following acute or progressive neurological damage always produces significant disability not only for patients' professional lives but also for everyday activities. Aphasia in the context of stroke is relatively common, with estimates suggesting that up to $\frac{1}{3}$ of acute patients present with language impairment, dropping to 20% in the chronic phase.^{1,2} Likewise in recent years there has been an ever-increasing recognition of language impairment in neurodegenerative disorders, not only as the presenting symptom in the context of the primary progressive aphasias,³ but also as a part of the symptom complex in many other types of dementia

As these epidemiological figures would suggest, it is common to find that aphasic patients show at least some degree of language recovery. This is true not only in the very acute phase but also several months after stroke, albeit with the rate of change decreasing over time. This begs the obvious questions of which neural regions support such partial recovery and what the underlying mechanisms are. To answer, we must understand not only the neuroanatomy of normal language function but also how this supports recovery, with the potential of using behavioral and pharmacological interventions² to promote intrinsic recovery processes, thereby achieving maximal language potential and thus minimizing disability.

In the classical, modular view of language function, recovery was assumed to reflect either the return of partial function within the remnants of the affected dominant language region or the uptake of function within other homologous regions.⁴ We are now beginning to see radical changes in this classical view. The emerging contemporary perspective is very different in form and nature, and is a reflection of novel insights that arise from modern neuroscience techniques, with the different methods and analyses that they afford. Three key observations include: (1) that the adult, mature brain is not a fixed, rigid entity but has the

capacity for plasticity-related changes⁵; (2) that higher cognitive function, including language, reflects the joint action of a distributed, neural network^{6,7}; and (3) that recovery of function can reflect altered computation in the remaining nodes within this neural network and also a shift in the division of labor across this yoked set of neural regions.⁸

In their sophisticated investigation, Sharp et al⁹ studied a series of stroke patients with chronic, partially recovered language function using a combination of neuropsychological assessments and functional neuroimaging. Although such dual investigations are still all too rare, Sharp et al included two new elements that advance our understanding of the neural basis and mechanisms of recovered comprehension function. Rather than simply comparing the pattern of activation found in the patients and their matched controls, Sharp and colleagues investigated the changes in cohesion (functional connectivity) between the cortical regions that support language comprehension. Furthermore, they compared these data not only against neurologically intact control participants, but also against results collected from the same people while performing a task under challenging conditions (comprehension of a degraded input). The latter, novel methodology has been used previously in behavioral-only studies (to mimic aspects of patients' performance¹⁰) but, when combined with functional neuroimaging, it licenses a comparison between the changes observed in patients and the intrinsic changes found in neurologically intact brain function under non-optimal conditions.

Two key and important insights arise from this study. The first is that recovery of comprehension in the patients was related to increased, joint activity in the neural network: specifically, recovered comprehension performance aligned with increased functional connectivity between angular gyrus (AG) and the superior frontal gyrus (SFG), as well as between AG and the inferior temporal region. Second, these same functionally related

changes (particularly the increased yoking of AG and SFG) were also observed in the neurologically intact participants during study of degraded speech, suggesting that the changes observed in the patients actually reflect a natural, intrinsic plasticity-related mechanism rather than nonspecific changes resulting from the patients' temporal lobe infarction.

The results from the present study are consistent with those arising in other recent investigations that use a variety of different neuroscience methods. The first is that semantic cognition (including verbal and nonverbal comprehension) is supported by a large-scale network of temporal lobe representational systems (especially anterior, inferior regions^{11–13}) and frontoparietal control mechanisms.¹⁴ The fact that heightened SFG-AG functional connectivity was found in this study fits closely with the emergent observation that both semantic and cognitive control are supported jointly by these two regions.¹⁵ The implication that cognitive control mechanisms are involved in language function also gains further support from the finding that recovery of neuropsychological ability is best predicted by the status of executive cognitive function in patients,¹⁶ and that the outcome of speech pathology intervention can be predicted by a combination of cognitive control and aphasia severity.^{17,18} Together these findings indicate that interventions and clinical management for aphasia should focus not only on the language deficits per se but also on the status of cognitive control mechanisms.

More generally, the results reported by Sharp and colleagues build on previous demonstrations that not only can neural computation be retuned within remaining, language-related areas,¹⁹ but also the interactions across the network can be adjusted to reoptimize performance either in the face of temporary degradation of spoken input or on a more permanent basis after brain damage.⁸ It should be re-emphasized here, perhaps, that such demonstrations have implications for the methods and analyses utilized when exploring recovery of function in neurological groups, promoting the use of correlation and connectivity based-methods in addition to standard subtraction analyses that only detect global changes in neural activity within each region rather than more subtle variation in the underlying computations within and between areas.

Finally, the underpinnings of neural retuning and network reoptimization have been explored in related computational models of cognitive-language function. Mirroring the results reported by Sharp et al and in other functional neuroimaging studies, these models are able to demonstrate partial spontaneous recovery following simulated damage. Careful analyses of these simula-

tions show that such recovery reflects a combination of computational reoptimization not only by the remaining units within the damaged regions, but also by a change in the functional interplay between different regions.⁸ As well as providing a formalism for exploring the basis of recovered function, these models are also potentially interesting because they suggest that the degree of recovery is related not only to lesion size but also to the speed of damage,²⁰ a factor that may explain the sometimes striking contrast in functional outcomes found in stroke versus slow-grade glioma.²¹

Potential Conflicts of Interest

Nothing to report.

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DOI: 10.1002/ana.22213