BRAIN AND LANGUAGE **58,** 427–435 (1997)
ARTICLE NO. BL971809

COMMENTARY

Subcortical Aphasia and the Problem of Attributing Functional Responsibility to Parts of Distributed Brain Processes

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INTRODUCTION

The accompanying article by Nadeau and Crosson (henceforth N&C) is certainly timely, since the notion of subcortical aphasia has been increasingly the subject of case reports and anatomically informed speculation about the systems of the brain mediating language use. The authors bring an enormous and diverse literature to bear on this issue and address it at cognitive, computational, and anatomical levels of analysis. They attempt, in traditional fashion, to explain the symptoms of brain damage by reference to both the cognitive architectures mediating language use and the anatomical mechanisms causally necessary for it. Further, the authors try to bridge these levels of analysis by postulating computational mechanisms that might link physiological activity and cognitive functions.

Broca's discoveries in the middle of the last century introduced a critical tool for the study of language use and the brain. The method derived from this work, the method of clinico-pathological correlation (CPC) (or neuropsychological localization or lesion analysis), has played a central role in the investigation of the brain's participation in language use since that time,

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0093-934X/97 $25.00

with researchers endeavoring to establish criteria for identifying discreet language functions and for pinpointing those brain regions that are necessary for their performance. These projects, in turn, have demanded rigorous descriptive and/or classificatory schemes for the symptoms of patients with brain damage and detailed models of the cognitive functions involved in language use.

While N&C do not intend to build a case for CPC, the problems with that method contribute significantly to the problems in their paper. Our goal is to focus on the extent to which general methodological difficulties involved in CPC create specific difficulties in this essay. Thus, we hope that our comments will shed light not only on the issue of subcortical aphasia but also on the general research program of localizing functions in the brain. Following a short methodological criticism of the authors' interpretation of data, we will focus on the tenability of the assumptions the authors make in defending a theory of thalamic aphasia and rejecting the role of basal ganglionic structures in language use.

DATA PRESENTATION

The paper collates an extraordinary collection of anatomical and neurological data on the subject of subcortical aphasia and for this the authors are to be commended. In particular, their neurobiological discussion addresses elements of anatomy and physiology often ignored in neuroscientific discussions as ''merely supportive,'' rather than integral. Of course, the supportive structures of one scientific generation are the ''central structures'' of the next (e.g., glial cells, neuromodulators), and the authors' attention to such mechanisms as diaschisis, regional cerebral blood flow, and vascular anatomy is both provocative and illuminating.

While we generally appreciate this aspect of the authors' project, their interpretation of these data raises a methodological concern. In particular, the authors selectively discount the results of some studies while failing to explicitly subject the results they accept to the same level of scrutiny. Let us delve into an example.

N&C present four alternative hypotheses to explain non-thalamic subcortical aphasia which frame their evidential discussion. These explanations include (a) diaschisis, (b) infarction of structures *directly* involved in language processes (our italics), (c) disconnection and cortical ischemia, and (d) deregulation of the output of cortically generated language. N&C conclude that radiographically silent ischemic damage to white matter (c) is responsible for basal ganglionic aphasia, and that direct infarction of a particular functional anatomical system (b) is responsible for thalamic aphasia.

A major problem with the presentation of these arguments is that while they consider all of the alternative explanations for basal ganglionic aphasia (in order to reject it), they do not give these same possibilities any weight

at all in the discussion of thalamic aphasia (in order not to reject it). Certainly, infarctions in the distribution of the paramedian or tuberothalamic arteries are not likely to lead to ischemia in perisylvian cortical structures commonly thought necessary for language use, as might infarctions in the distribution of the lenticulostriate arteries. However, the authors fail to dismiss the possible role of such infarcts in cortico-cortical disconnection, diaschisis, or compression of areas or pathways necessary for language use. Ischemia is merely one of a number of alternative explanations proposed to explain basal ganglionic aphasia that are not addressed in the discussion of thalamic aphasia.

Furthermore, the same methodology used (but discounted) in research studies supporting basal ganglionic aphasia is used (without comment) in studies supporting thalamic aphasia. For example, evidence of the absence of aphasia accompanying damage to the caudate and putamen are accepted with little fanfare, while similar evidence that surgical lesions of the pulvinar have typically failed to result in aphasic syndromes are rejected because (a) the lesions were not confirmed histologically, (b) the lesions might have been too small, or (c) the language disturbances might have been too subtle to detect. Similarly, we wonder whether the homogeneity of symptoms in victims of thalamic infarct is susceptible to the same sort of critical analysis that the authors bring to cases of basal ganglionic damage. In short, the authors, at times, seem to apply their standards of evidence inconsistently in such a way as to preserve evidence that is favorable and reject evidence that is not.

While we were disturbed by this general approach to the interpretation of data, we have more serious questions about the localizational assumptions that underlie many of the arguments leading up to and supporting the overall theory.

UNCOVERING THE LESION'S MODUS OPERANDI

It is a well-known truism that the inferential bridge between the loss of a behavioral capacity subsequent to brain damage and the function of a particular brain region in the absence of such damage is perilous indeed. N&C are extremely careful to avoid such dangers, and their detailed consideration of hemodynamic changes and possible diaschisis resulting from basal ganglionic damage is both interesting and instructive. Obviously, the fact that highly visible damage to one area of the brain is often attended by less conspicuous degradation of some functionally distinct brain region complicates our search for the anatomical systems that are causally necessary for the performance of a particular behavioral task.

Given the central role of such indirect damage in N&C's discussion of basal ganglionic infarct, we find it puzzling that the authors fail to dismiss diaschisis as a possible explanation of the aphasic syndrome resulting from damage to the frontal-ITP-NR-CM (henceforth, FINC) system. Diaschisis, as they define it, is an indirect effect of brain damage in one region on the

physiological integrity of another functionally distinct system elsewhere. Thus, damage to a system which plays no ''direct'' role in language use might, secondarily, produce a language disturbance by degrading the activity of a brain region that is directly involved.

How might one distinguish diaschisis from direct damage? As a partial answer, N&C suggest two necessary criteria for invoking diaschisis as the mechanism:

> . . . if diaschisis [is] the mechanism [by which brain damage causes the language impairment], a lesion confined to a given structure or set of structures should produce a consistent pattern of physiologic dysfunction in connected regions, and therefore a consistent pattern of behavioral impairment. (p.7)

Thus by their account, the area must (1) be connected to an area directly involved in language use and (2) be connected in such a way that whenever it is damaged, a coherent syndrome results.

These criteria are inadequate for the purpose at hand. All of the anatomical regions currently hypothesized to be involved in language processing satisfy these requirements, and so, ipso facto, does the FINC system. The list of criteria must include some factor that distinguishes those areas that are directly involved in language use from those that are not.

One possibility arises from the assumption that only damage to an area directly involved in language use would produce a unique complex of symptoms; symptoms resulting from diaschisis would more or less mimic those resulting from a lesion in a primary language area. Unique symptomology might, then, be a criterion for distinguishing direct disruption from diaschisis.

As we will discuss in the next section, the criterion of a well-defined unique complex of symptoms is arguably not satisfied by the classical aphasias, suggesting that it is extremely difficult to demarcate new syndromes from old. Be that as it may, this criterion still fails to adequately distinguish direct and indirect causation of language impairments. First, damage to an area directly involved in language use can produce behavioral symptoms that mimic classical aphasias. In the easiest case, the lesioned area may be functionally connected with one and only one of the so-called ''primary language areas.'' Further, our cognitive vocabulary likely fails to match up one to one with the processing mechanisms in the brain, and it is certainly possible (indeed likely) that multiple functionally independent regions of the brain each perform subcomponents of the larger task represented in that cognitive vocabulary. Thus ''speech production'' is likely not unitary from the brain's perspective but involves several independent causally necessary processing components, damage to any one of which would produce the same impairment in behavior (as described in our cognitive vocabulary). Second, indirect damage can produce unique clusters of symptoms by, for instance, uniquely degrading the performance of a particular module or more than one module at once.

Our point is not to be picky about these issues. Instead, we intend to highlight a general difficulty in parsing off structures as ''directly'' vs. ''indirectly'' involved in language processing. Language is a complex phenomenon even as described at the cognitive level. When we recognize the wealth of background knowledge required to disambiguate the sentence, ''The man eating shrimp was swimming,'' or the importance of emotive intonation in assigning meaning to a sentence, or the effects of somatic discomfort on an aphasic's word fluency score, we begin to realize that the ability to use language is not neatly separable from a whole host of other faculties. Likewise, there are a number of areas of the brain which, when damaged, produce language disturbances by virtue of neural connectivity (and not, for instance, swelling or hemodynamic changes), and the distinction between those that are ''directly'' and ''indirectly'' involved in language processing is difficult to make unless we make some strong a priori assumptions about the types of functions that are instantiated in the brain.

Instead of classifying systems as ''directly or indirectly'' involved in language processing, we suggest the following: a system is involved in language use if language disturbances are the causal consequences of impaired function in that system. This statement is meant both to exclude such indirect effects as swelling and vascular occlusion (only impaired function of that system can be the relevant causal influence) and to include systems outside the standard bounds of ''language processing'' (temporal monitoring, rate analysis, etc). By thus conceiving of the language system broadly, we would eliminate the question of direct and indirect involvement and focus attention on the potentially counter-intuitive complexity of the brain's role in language use.

Such an orientation to the project of CPC focuses our attention away from correlations between cognitive phenomena and brain regions and toward correlations between behavioral phenomena and the causal mechanisms in the brain which make them possible. With this in mind, investigation the causal mechanisms operative in the FINC system and thalamocortical projections is far more experimentally tractable and, in the long run, potentially more theoretically fruitful than correlating them with hypothesized cognitive functions. The latter pursuit is simply far more inferentially perilous.

PURE CASES AND COHERENT SYNDROMES

Reproducible anatomically circumscribed lesions, loss of single elementary functions and coherent clinical syndromes in patients with damage to identical brain regions head the list in the clinical neurobiologist's wishbook of dreams. Individual variation in brain structure, heterogeneity in brain damage, and differences in cognitive-level processing from one subject to another are no longer considered exceptions, but are acknowledged to be the rule in cognitive neurobiology.

There is a temptation, however, to treat ''pure cases'' and ''coherent syndromes'' as ideals toward which actual clinical cases converge (like an object with no forces acting on it in Newtonian mechanics). Thus, while terms such as ''Wernicke's aphasia,'' ''conduction aphasia,'' or ''Broca's aphasia'' have been reified, they constitute a convenient illusion, since they carry neither unambiguous behavioral nor unique anatomical definitions. There is no such thing as a ''pure case'' of one of these aphasia types, and the vast majority of patients with aphasia manifest clusters of symptoms that span all of the classificatory units. The point, simply, is this: cases of aphasia generally do not conform to the idealized classificatory schemes that have been used to describe them, and therefore the notion of a ''coherent syndrome'' fails even as applied to the more classical disorders.

N&C show that ''every possible degree of impairment in these various aspects of language has been reported'' in ''nonthalamic subcortical aphasia,'' thereby contradicting the concept that this represents a ''coherent syndrome.'' Of course, this is similar (perhaps to a lesser degree) to the cortical situation, where patients with the most classical of aphasia syndromes have been shown to manifest language impairments thought characteristic of some contrasting syndrome (e.g., comprehension problems in Broca's aphasia). While the presence of some stereotypic subset of aphasia symptoms would provide strong support for a role of some area in a *particular* task, the consistent presence of some aphasia symptoms implies that the area has some role to play in language use, without supporting a role on particular subtasks. We are not in accord with N&C's belief that the former situation holds with respect to cortical aphasia, i.e., that specific cognitive subtasks are specifically impaired in specific syndromes, and are thus not distressed by their finding that the same situation holds with respect to subcortical aphasia. Furthermore, since the cognitive subtasks have often been characterized in the context of cortical aphasias, there are solely poorly motivated reasons to apply them to the study of these different syndromes.

The absence of homogeneity and sharp boundaries at the level of symptom descriptions is matched by a lack of clarity at the anatomical level. There is tremendous anatomical heterogeneity in the location of the cortical patches that produce language dysfunction under direct electrical stimulation, and it is interesting to note that there is little agreement in the anatomical literature as to the exact topographic boundaries of such widely discussed structures as ''Wernicke's area,'' ''Broca's area,'' or the ''angular gyrus.'' These considerations make it difficult to define syndromes the locus of the lesion. The classical aphasias are homogeneous neither at the level of symptomology nor at the level of anatomy, and can therefore not be considered paradigm cases of coherent syndromes.

Against this backdrop, we find it odd that N&C rely repeatedly on the assumption that coherent syndromes must manifest themselves in individual cases of damage to similar brain regions. For example, they reject the possi-

bility that the head of the caudate, the putamen, or the ICal are directly involved in language processing on the grounds that if aphasia following damage in these areas were directly due to their dysfunction, then ''a coherent syndrome should have arisen'' (p.6). Why, we wonder, should one expect lesions of subcortical areas to eventuate in coherent syndromes when cortical damage also fails in that regard?

Given the authors' commitment to this principle, however, it is also surprising that they did not subject the syndromes observed after thalamic damage to the same sort of critical scrutiny applied to those observed after damage to the basal ganglionic structures. N&C's compilation of cases of putamenal hemorrhage reveals a wide range of symptomologies from essentially *no* impairment (following surgical lesion) to typically productive impairment (Rousseaux's cases) to joint productive and receptive impairment (Tuszyinski and Pitito's cases). Further, individual cases of aphasia following tuberothalamic and paramedian territory infarcts are described en masse, without attention to individual differences in pathology. Variance within these cases (particularly the impaired comprehension in some) is reminiscent of the sort of heterogeneity evident in cases of basal ganglionic infarction. We are left wondering what constitutes a sufficiently coherent syndrome to warrant the postulation of a new organ of language.

With this question in mind, we now turn our attention to the evidential basis for a thalamic role in selective engagement.

HOW DOES SELECTIVE ENGAGEMENT FIT THE FACTS?

The evidence in favor of a role for the FINC-pulv-LP system in ''selective engagement'' boils down to two points: (1) there is considerable evidence for the role of the thalamus in external attention, and it is therefore possible that it has a role in internal attention (see p.32); and (2) disruption of ''selective engagement'' following damage to the FINC-pulvinar-LP system adequately explains the subsequent symptoms.

The first line of evidence relies entirely on the degree of functional analogy between internal and external attention. While we find intriguing the notion that the same neural mechanisms might, by virtue of differences in anatomical connectivity, serve two distinct (albeit related) functions, we are not convinced that there is sufficient evidence to suggest that they might in this case. The authors admit that there is no neurophysiological evidence in humans to support a ''motoric gating'' role for the thalamus, and evidence of hemineglect syndrome following thalamic damage seems easily explainable as the result of damage to a system involved in sensory gating. Perhaps it would be helpful for the authors to consider other syndromes resulting from thalamic infarct. Are there syndromes that are not explainable on the assumption of a sensory-gating-only role for the thalamus? This form of argument from analogy is useful for generating hypotheses, but not particularly useful for testing them.

The second argument in favor of the selective engagement hypothesis appears even less convincing for two reasons. First, the notion of selective engagement, as currently fleshed out, is simply too vague to allow rigorous empirical investigation. As the authors define it, selective engagement is the ''selective temporary enlistment of specific neural nets to carry out a particular behavior or maintain a particular mental state.'' What sort of predictions would such a hypothesis make that, for instance, the alternative hypothesis that pulvinar-LP connections with the cortex serve the function of general tonic excitation would not? Again, what sorts of predictions for patient syndromes would distinguish loss of selective engagement from diaschisis? Further, why is the notion of ''motoric gating'' a better fit to the facts than the traditional role of the thalamus in sensory gating? Without some discussion of either the relative virtues of, or the experimental work that could uncover the relative virtues of, the selective engagement hypothesis relative to other competing alternatives, we are left without a reason to entertain it.

This second line of evidence (accounting for the symptoms of thalamic aphasia) is questionable precisely because of the lack of guidance afforded by the hypothesis of selective engagement. The authors do not explicitly discuss how the symptoms of thalamic aphasia (e.g., problems with naming to confrontation) are entailed by the selective engagement hypothesis. Instead, the role of the pulvinar-LP projections to temporal and parietal cortex is built up out of the symptoms that it was designed to explain, and its ability to explain them is therefore probatively irrelevant. Why, on this hypothesis, would we expect patients with thalamic lesions to have spared repetition and comprehension (certainly these also require motoric gating)? Why would the thalamus be involved in regulating merely the lexical semantic aspects of selective engagement and not more syntactic and automatic processes? Surely, for instance, repetition (especially after some delay) requires attentional focus at least to some degree.

Once again, were there other evidence that damage to the thalamus produces similar symptoms in other motor processes or other cognitive capacities, and were there evidence that these functional aberrations could not be accounted for by reference to the role of the thalamus in sensory gating or general arousal, then the argument for its involvement in ''selective engagement'' would be more compelling.

SUMMARY AND CONCLUSION

N&C's discussion is, in places, an exemplar of the sort of rigor and attention to detail that will bring us closer to an understanding of the functional organization of the brain. Indeed, it is this level of work that pushes us to reflect on the assumptions that undergird our research efforts.

Our criticisms have developed four main points. First, the level of rigor applied to the consideration of basal ganglionic aphasia should extend to

each application of the CPC method (thalamic aphasia included). Second, in our haste to identify specific brain systems with distinct cognitive functions we should not neglect the more basic question of the causal mechanisms by which the brain organizes behavior. Questions of ''direct'' versus ''indirect'' involvement of a particular organ in a cognitive function are only likely to distract our attention from this more basic and less inferentially perilous issue. Third, pure cases should no longer be considered touchstones against which all behavioral disturbances are measured. Reifying such ideals is more likely to shroud than reveal the brain's true complexity. Finally, the functions that we enshrine in particular brain regions should explain the particular character of the symptoms observed when they are damaged and should admit of independent verification.