IS BROCA'S AREA PART OF A BASAL GANGLIA THALAMOCORTICAL CIRCUIT?

Michael T. Ullman

(Departments of Neuroscience, Linguistics, Neurology and Psychology, Georgetown University, Washington, D.C., USA)

ABSTRACT

The cortex constituting Broca's area does not exist in isolation. Rather, like other cortical regions, Broca's area is connected to other brain structures, which likely play closely related functional roles. This paper focuses on the basal ganglia, a set of subcortical structures that project through topographically organized "channels" via the thalamus to different frontal regions. It is hypothesized that the basal ganglia project to Broca's area. This circuitry is further posited to encompass at least two channels. One channel can be characterized as subserving procedural memory, while the other underlies the retrieval of knowledge from declarative memory. These hypotheses are supported by both anatomical and functional evidence. Implications and issues for further investigation are discussed.

Key words: Broca's area, basal ganglia, BA 45, BA 44, language, lexicon, grammar, syntax, morphology, phonology, declarative memory, procedural memory

INTRODUCTION

Broca's area is often investigated and discussed in isolation, as though it existed alone and unattached in the universe of brain structures. However, like other areas of cortex, it is likely to be highly interconnected with both cortical and sub-cortical structures. This interconnectivity may be expected to have important anatomical and functional consequences for Broca's area. Here I examine the hypothesis that Broca's area is part of a larger circuit that involves the basal ganglia, a set of subcortical structures that have traditionally been implicated in motor functions. First, I provide a brief overview of the basal ganglia and their connectivity to frontal cortex. Second, I outline specific predictions regarding the relation between Broca's area and the basal ganglia. Third, the empirical evidence related to these predictions is summarized. Finally, I conclude with a brief discussion of implications and further issues to be examined.

THE BASAL GANGLIA

The basal ganglia are a collection of highly interconnected subcortical structures, including the neostriatum (composed largely of the putamen and the caudate nucleus in primates), the globus pallidus (internal and external segments), the substantia nigra (pars compacta and pars reticulata), and the sub-thalamic nucleus (Cote and Crutcher, 1991; Wise et al., 1996). Studies of non-human primates have revealed much about the internal and external connectivity of the basal ganglia, with important implications for their function. The basal ganglia are closely linked to cortical regions, particularly in the frontal lobes, via parallel and largely anatomically and functionally segregated "channels", also referred to as "circuits" or "loops" (Alexander and Crutcher, 1990; Alexander et al., 1986; Middleton and Strick, 2000a, 2000b). Each channel receives cortical projections at the neostriatum, which constitutes the main input structure of the basal ganglia. The various channels follow parallel routes within the basal ganglia (e.g., through the external segment of the globus pallidus and the subthalamic nucleus). The channels then project from the basal ganglia – specifically, from the internal segment of the globus pallidus and the pars reticulata of the substantia nigra, which together constitute the primary output structures of the basal ganglia – to the thalamus, and thence to specific cortical regions, primarily in frontal cortex. Each cortical region then projects back to the neostriatum, thus forming a closed loop circuit.

The channels are topographically organized at each level of the circuit. That is, the parallel channels have a topographic organization that is maintained from the neostriatum throughout the basal ganglia and to the thalamus and frontal cortex. The various channels project to a heterogeneous set of frontal regions (as well as to certain temporal and parietal regions). Thus apparently distinct channels project to, and receive input from, not only primary motor cortex, but also

a variety of premotor and prefrontal regions, including the frontal eye fields, ventral premotor cortex, the supplementary motor area, dorsolateral prefrontal cortex, and lateral orbitofrontal cortex (Alexander et al., 1986; Clower et al., 2004; Middleton and Strick, 2000a, 2000b).

Each channel underlies the functions that are associated with the cortical region to which it projects (Middleton and Strick, 2000b). Channels passing through the putamen play a particularly important role in movement (hence the prominent motor dysfunction in Parkinson's disease, which affects the putamen more than the caudate nucleus), whereas those passing through the caudate nucleus seem to be especially important for aspects of cognition – although it should be emphasized that both neostriatal structures likely play at least some sort of role in both motor and cognitive functions (Middleton and Strick, 2000b; Wise et al., 1996).

HYPOTHESES

Two hypotheses are proposed. First, the existence of basal ganglia thalamocortical circuitry that projects to (and loops back from) Broca's area is predicted. As is appropriate when discussing both structural and cytoarchitectonic evidence, Broca's area is defined broadly here: structurally, it corresponds closely to the pars triangularis and the pars opercularis of the inferior frontal gyrus; cytoarchitectonically, it consists of Brodmann's Area (BA) 45 and BA 44.

Second, the basal ganglia thalamocortical circuitry passing through Broca's area is expected to be topographically organized into at least two parallel and largely functionally segregated channels. Within Broca's area, one channel is predicted to encompass anterior/ventral cortical regions, corresponding largely to the pars triangularis and BA 45, while the other channel encompasses posterior/dorsal regions, corresponding largely to the pars opercularis and BA 44. Each of these channels is hypothesized to subserve functions that cut across language and non-language domains. The "anterior" channel may be characterized as subserving the retrieval of lexical and semantic information stored in declarative memory. This memory system has been implicated in the learning and use of both conceptual-semantic and lexical knowledge (Eichenbaum and Cohen, 2001; Schacter and Tulving, 1994; Squire and Knowlton, 2000; Ullman, 2001, 2004; Ullman et al., 1997). The "posterior" channel may be profitably viewed as subserving aspects of procedural memory. This system underlies the acquisition and real-time expression of motor and cognitive skills, especially those involving sequential knowledge (Eichenbaum and Cohen, 2001; Schacter and Tulving, 1994; Squire and Knowlton, 2000). The procedural memory system has also been implicated

in grammar, in particular in aspects of the acquisition of grammar and in rule-governed grammatical composition (Ullman, 2001, 2004; Ullman et al., 1997).

EVIDENCE

Both anatomical and functional evidence support the existence of basal ganglia thalamocortical circuits that project to Broca's area. First, although there seem to be no anatomical data that directly demonstrate such circuitry in humans, indirect anatomical evidence supports its presence. In anatomical investigations of non-human primates, all frontal regions examined thus far have been found to receive inputs from basal ganglia thalamocortical circuits (Middleton and Strick, 2002), suggesting that other frontal regions also receive such inputs. Importantly, the frontal regions that have been shown to receive basal ganglia projections comprise portions of ventral premotor cortex (Middleton and Strick, 2000b), including region F5 (Strick, personal communication), which has been claimed – though this is controversial – to be homologous to Broca's area, and to BA 44 in particular (Rizzolatti and Arbib, 1998; Rizzolatti et al., 2001).

The existence of close links between the basal ganglia and Broca's area is further strengthened by evidence suggesting that the two structures underlie a common set of functions. In the domain of language, both structures have been implicated in lexical selection or retrieval (Alexander, 1997; Crosson et al., 2003; Desmond et al., 1998), in aspects of grammar across both morphology and syntax (Embick et al., 2000; Fabbro et al., 1996; Friederici, 2002; Moro et al., 2001; Ni et al., 2000; Pickett et al., 1998; Stromswold et al., 1996; Ullman, 2001, 2004; Ullman et al., 1997), and in phonology (Crosson et al., 2003; Poldrack et al., 1999; Zurowski et al., 2002). A number of other functions and domains also appear to be subserved by both structures, including the selection or retrieval of conceptual/semantic knowledge (Buckner and Wheeler, 2001; Fabbro et al., 1996; Poldrack et al., 1999; Thompson-Schill et al., 1997); working memory (Braver et al., 2001; Cabeza and Nyberg, 2000; D'Esposito et al., 1998; Jahanshahi et al., 2002; Menon et al., 2000; Smith and Jonides, 1999); sequencing (Gelfand and Bookheimer, 2003; Menon et al., 2000; Pickett et al., 1998); musical syntax (Maess et al., 2001; Tillmann et al., 2003); motor imagery (Binkofski et al., 2000; Gerardin et al., 2000); action control and motor function (Albin et al., 1995; Fox et al., 1988, 2001; Graybiel, 1998; Iacoboni et al., 1999; Rizzolatti and Arbib, 1998); learning in procedural memory (Conway and Christiansen, 2001; Dominey et al., 2003; Eichenbaum and Cohen, 2001; Goschke et al., 2001; Schacter and Tulving, 1994; Squire and Knowlton,

2000); and aspects of temporal processing (Fiez et al., 1995; Harrington et al., 1998; Meck and Benson, 2002; Rammsayer and Classen, 1997; Schubotz and von Cramon, 2001).

Similarly, both anatomical and functional evidence suggest the existence of at least two functionally distinct basal ganglia thalamocortical channels running through Broca's area. Anatomically, the cytoarchitectonic distinction between BA 45 and BA 44 suggests at least somewhat distinct neural circuitry for these two cortical regions. Importantly, cytoarchitectonically distinctive frontal regions have been associated with distinct basal ganglia thalamocortical channels (Middleton and Strick, 2000b), suggesting that separate channels pass through BA 44 and 45.

Functional data also support such a dichotomy. The functions listed above do not appear to be distributed randomly across Broca's area. Rather, anterior portions of Broca's area seem to be particularly important in the retrieval of lexical/semantic knowledge (Amunts et al., 2004; Binder et al., 1996; Price et al., 1996). In contrast, posterior portions have been more heavily implicated in syntax (Friederici, 2002, 2004), phonology (McDermott et al., 2003), working memory (Cabeza and Nyberg, 2000; Chein et al., 2002), sequencing (Gelfand and Bookheimer, 2003), musical syntax (Maess et al., 2001; Tillmann et al., 2003), motor imagery (Binkofski et al., 2000; Gerardin et al., 2000), action control and other motor functions (Fincham et al., 2002; Iacoboni et al., 1999; Rizzolatti et al., 2001), and temporal processing (Schubotz et al., 2000; Schubotz and von Cramon, 2001).

The co-occurrence of these apparently disparate functions within posterior Broca's area, as well as within the basal ganglia, is consistent with two views. On the one hand, there may be *functional* sub-specialization within the basal ganglia thalamocortical circuitry passing through posterior Broca's area, such that distinct portions of this circuit (i.e., 'sub-channels') subserve each of these functions (e.g., temporal processing, working memory, etc.). On the other hand, some or all of these apparently distinct functions may in fact represent different aspects of the same underlying function, analogous to the blind men touching different parts of the elephant, and falsely inducing the presence of a snake, a rope, a wall, and so on. This underlying function may profitably be characterized as procedural memory (Ullman, 2004; Ullman and Pierpont, 2005). On this view, procedural memory is a brain system specialized for the acquisition and processing of sequences across domains (including motor, music and language), whose function is integrally bound up both in the timing of the sequences it subserves, and in the maintenance and manipulation of these sequences in working memory (Ullman, 2004; Ullman and Pierpont, 2005).

The existence of such a procedural system does *not* imply that all its *parts* have the same functional roles. Indeed, the basal ganglia and Broca's area seem to have at least somewhat distinct functions. The basal ganglia may play a particularly important role in the *acquisition* of grammatical and other procedural knowledge, whose *use* eventually depends largely on the posterior portion of Broca's area. This hypothesis is consistent with extensive evidence suggesting that the basal ganglia are involved in learning (Packard and Knowlton, 2002; Schultz, 2001), and a relative dearth of evidence (e.g., Goschke et al., 2001) implicating inferior frontal cortex in a similar role. Additionally, grammatical deficits appear to be more reliable following adult-onset damage of Broca's area than of the basal ganglia (Alexander, 1997; Fabbro et al., 1996; Ullman, 2004). In contrast, basal ganglia abnormalities seem to be reliably found in at least certain developmental disorders linked to grammatical dysfunction, consistent with a role for the basal ganglia in learning (Ullman, 2004; Ullman and Pierpont, 2005). Note that although grammatical processing impairments have been observed in adult-onset disorders of the basal ganglia such as Parkinson's or Huntington's disease (Gordon and Illes, 1987; Lieberman et al., 1992; Ullman et al., 1997), such impairments may be at least partly explained by the *anomalous* (inhibitory or disinhibitory) output from the basal ganglia to frontal cortex in these disorders, thereby affecting frontal processing. In this case, other basal ganglia disorders with anomalous output, such as hemiballismus or levodopa-induced hyperkinesia, should also result in such grammatical impairments.

However, learning does not appear to be the only function of the basal ganglia, which, as we have seen above, have also been implicated in aspects of selection, timing, working memory, and other functions. One or more of these functions seem to be involved in lexical/semantic retrieval (e.g., in selecting the item to be retrieved), and may explain the findings of neuroimaging and ERP studies that have implicated the basal ganglia in aspects of sentence processing – such as in rapidly presented speech (Peelle et al., 2004), or in the processing of errors that require reanalysis, and hence impose a high working memory load (Friederici et al., 1999, 2003; Moro et al., 2001). It remains to be seen whether and how these functions are related to the basal ganglia's role in learning.

FURTHER PREDICTIONS AND IMPLICATIONS

A number of other predictions and implications also remain to be investigated. First, the two hypothesized basal ganglia thalamocortical channels are expected to show topographic and

functional separability in every structure through which they pass, including within each structure of the basal ganglia. For example, different portions of the neostriatum should be associated with lexical/semantic retrieval and procedural memory, and thus should be differentially activated in high-resolution neuroimaging studies.

Second, the two putative channels may not be restricted exactly to classical Broca's area. Evidence suggests that the anterior/ventral region extends ventrally from the pars triangularis to portions of the pars orbitalis of the inferior frontal gyrus (which may include part of BA 45; Duvernoy, 1991), while the posterior/dorsal region may extend from the pars orbitalis to the precentral gyrus, and include portions of the frontal operculum (Friederici, 2002, 2004; Poldrack et al., 1999).

Third, the existence of the two channels does not preclude further topographic and functional sub-segregation *within* each channel, even if the two channels are dedicated to declarative and procedural memory. On this view, specialized parallel sub-circuits subserve different *domains*, or possibly different types of representations, within one or both channels. For example, motor, music, and grammar, or possibly hierchical and linear sequences, may each be subserved by distinct parallel sub-circuits within procedural memory (Ullman, 2001, 2004). Importantly, these sub-circuits are expected to share common computational underpinnings and basic functional roles (e.g., timing-related sequencing), with each structure at a given level of the circuitry making a similar functional contribution (e.g., learning within the basal ganglia) across the sub-circuits.

Finally, it should be emphasized that the functions of declarative and procedural memory are by no means limited to these two hypothesized basal ganglia thalamocortical channels. Declarative memory is in fact rooted in temporal lobe structures, which underlie the consolidation and storage of linguistic and non-linguistic declarative knowledge (Eichenbaum and Cohen, 2001; Squire and Knowlton, 2000; Ullman, 2004). The inclusion of frontal/basal-ganglia circuitry in this system is somewhat unconventional, and is consistent with a more holistic view that brings together the learning of declarative knowledge with its eventual use (Ullman, 2004). Similarly, procedural memory functions are subserved not only by the basal ganglia and posterior Broca's area, but also by a number of other interconnected structures, including portions of the cerebellum, inferior parietal cortex, and superior temporal cortex, as well as other frontal regions such as the supplementary motor area (Eichenbaum and Cohen, 2001; Ullman, 2004). An important goal of future studies will be to tease apart the specific computational and functional roles of each of these structures to the procedural memory system.

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Michael Ullman, Department of Neuroscience, Georgetown University, Box 571464, Washington, D.C., 20057-1464, USA. e-mail: michael@georgetown.edu