

Section A Introduction

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1 Subcortical involvement in speech and language: an introduction and historical perspective

Introduction

Recent advances in our understanding of the connectivity of subcortical structures such as the basal ganglia and cerebellum with the cerebral cortex, combined with the development and introduction of advanced neuroimaging techniques, has, over the past two decades, forced a re-think of our concepts of the contribution of subcortical structures to speech and language function. In particular, there has been a growing realization that subcortical structures such as the thalamus, caudate nucleus, globus pallidus, subthalamic nucleus, substantia nigra and cerebellum, among others, not only contribute to the regulation and coordination of the motor aspects of speech production but also are important components of the neural circuits that regulate cognitive and linguistic function. Consequently, there is now much greater acceptance that subcortical structures participate in the regulation of language to a greater extent than proposed by various localizationist models of language function (e.g. Wernicke–Lichtheim model) that had their origins in phrenological theory in the early 1800s and the post-mortem studies of Broca (1861), Wernicke (1874) and Lichtheim (1885), each of which dominated our thinking in relation to language function throughout the twentieth century.

Gall (1809), through his introduction of the concept of phrenology, was the first person to propose a systematic relationship between specific psychological components of human behaviour and specific cerebral regions. According to phrenological theory, complex behaviours such as language, mathematical ability, musical ability and various aspects of human character (e.g. ambition, charity, etc.) were regulated in specific locations in the cerebral cortex. These specific cortical locations were thought to correspond to surface regions of the skull and accordingly the exterior of the skull was partitioned into regions that were believed to be the 'seat' of a 'faculty', with the size of these seats and the areas of the protuberances and lumps of the skull being innately determined in a given individual. Further, the area of each region was considered to be a measure of the complex behaviour or particular aspect of character regulated by that region. Although phrenology fell into disfavour, the underlying premise of phrenological theory, that all aspects of a complex behaviour (e.g. language) are regulated in an anatomically discrete, separable, area of the cerebral cortex, remained as an important component of influential models and theories of speech and language function (e.g. Wernicke–Lichtheim model) that dominated this field throughout the majority of the twentieth century. For example, Broca (1861) adhered to phrenological theory when he concluded that speech production was regulated in the anterior cortical region of the left cerebral hemisphere on the basis of his

observation of a patient with a lesion in this region who was unable to speak except for production of a single monosyllable.

Unfortunately Broca overlooked the fact that his patient also had extensive subcortical damage and extensive non-linguistic motor impairment. Likewise, on the basis of his observation that patients who had suffered lesions in the second temporal gyrus of the cortex in the posterior left hemisphere had difficulty comprehending speech, Wernicke (1874) concluded that receptive linguistic ability was located in the posterior region of the left temporal gyrus. Lichtheim (1885) proposed a hypothetical pathway connecting Broca's and Wernicke's areas of the cerebral cortex, his revision of the Broca–Wernicke model, later recognized as the Wernicke–Lichtheim model persisting in textbooks and research literature to the present day. Importantly, the Wernicke–Lichtheim model plays down the importance of subcortical structures in language function, and implies that subcortical lesions only disrupt language if they cause disconnection between the major language centres of the cerebral cortex, as occurs for instance with disruption to the arcuate fasciculus in conduction aphasia.

More recently, localizationist models such as the Wernicke–Lichtheim model that neglect the contribution of subcortical structures to speech and language have been challenged, primarily because of their failure to account for emerging knowledge of the computational architecture of the human brain. Clinical evidence is now available to show that permanent loss of language does not occur without subcortical damage, even when Broca's and Wernicke's areas have been destroyed by lesions. For example, patients with extensive damage to Broca's area generally recover linguistic ability, unless subcortical damage also occurs (Stuss and Benson, 1986; Dronkers *et al.*, 1992; D'Esposito and Alexander, 1995). Patients suffering brain damage that involves subcortical structures but that leaves Broca's area alone can also manifest the signs and symptoms of Broca's aphasia (Alexander *et al.*, 1987; Mega and Alexander, 1994). The case for Wernicke's aphasia appears to be similar, with reports of premorbid linguistic skills being recovered after complete destruction of Wernicke's area (Lieberman, 2000). Also, although the locus for brain damage associated with Wernicke's aphasia includes the posterior region of the left temporal gyrus (Wernicke's area) it often extends to the supramarginal and angular gyrus including involvement of the white matter below. As stated by D'Esposito and Alexander (1995) a purely cortical lesion that can produce Broca's or Wernicke's aphasia has never been documented. In contrast, numerous cliniconeuroradiological correlation studies reported in recent years have documented the occurrence of aphasic syndromes in association with subcortical lesions that apparently spare the cerebral cortex. Further details of the latter studies are outlined below.

Rather than being regulated by specific cortical sites, it is now recognized that complex behaviours such as talking and walking are mediated by neural circuits that link anatomically segregated populations of neurones in both subcortical and cortical regions of the human brain. In other words, complex behaviours such as talking and walking are regulated by neural circuits that constitute networks linking activity in many parts of the brain at both the cortical and subcortical levels, these networks therefore constituting the neural basis of complex behaviours. As Mesulam (1990) states 'complex behaviour is mapped at the level of multifocal neural systems rather than specific anatomical sites, giving rise to brain–behaviour relationships that are both localized and distributed' (p. 588). Although 'local operations' occur in particular areas of the brain (e.g. specific areas of the cerebral cortex or specific components of the basal ganglia system) these areas in themselves do not constitute an observable behaviour such as talking or walking. Rather these local processes form part of the

neural ‘computations’ that when linked together in complex neural circuits (e.g. cortico-striato-thalamo-cortical loops; cerebrocortico-ponto-cerebellocortico-dentato-thalamo-cerebrocortical loops) manifest in behaviours such as talking, auditory comprehension, walking, etc. For example, the corpus striatum (caudate nucleus plus the lenticular nucleus), although best recognized for its role in the regulation of motor activities, is known to receive input from most areas of the cerebral cortex. In turn, output from the striatum is targeted not only at the primary motor cortex, but also specific areas of the premotor and prefrontal cortex, suggesting that the corpus striatum has the ability to influence not only motor control but also several types of cognitive, language and limbic function. Similarly it has been hypothesized that output from the lateral deep cerebellar nucleus (the dentate) influences not only motor areas of the cerebral cortex but also areas of the prefrontal cortex involved in language and cognition (Fabbro, 2000; Marien *et al.*, 2001).

One consequence of specific areas of the brain being connected to multiple other areas to form complex neural circuits for the purpose of regulating complex behaviours is that lesions in specific areas of the brain can be associated with an ensemble of seemingly unrelated behavioural deficits. For example, a lesion in the substantia nigra is known to cause the syndrome of Parkinson’s disease, involving symptoms that are primarily motoric (e.g. bradykinesia, tremor, rigidity) but also involving speech (see Chapter 11), and cognitive and linguistic deficits (see Chapter 8).

The premise that complex neural circuits that link anatomically segregated populations of neurones in both subcortical and cortical structures form the neural substrate of complex behaviours will constitute a unifying and repetitive theme throughout the various chapters of this volume. Specifically, later chapters will elaborate on and provide evidence of the importance of subcortical structures to human behaviours, particularly in the context of speech and language function.

This chapter will outline contemporary theories proposed to explain involvement of various subcortical structures in speech and language function and provide a historical context to their development.

Subcortical mechanisms in speech motor control: historical perspective

Speech production requires smooth coordination of orofacial, laryngeal and respiratory muscles. Clinical data indicate that initiation and precise execution of articulatory movements depend upon the integrity of various neural subsystems involving both cortical and subcortical brain structures, such as the primary motor cortex, supplementary motor area, basal ganglia and cerebellum. Consequently, damage to the basal ganglia and cerebellum produces well-described alterations in motor function, such as tremor, rigidity, akinesia or dysmetria, which may affect the speech-production mechanism.

Basal ganglia

Disorders of the basal ganglia are associated with a number of movement disorders which include Parkinson’s disease, Huntington’s disease, chorea, athetosis, dystonia and ballismus, among others. In general, movement disorders associated with basal ganglia lesions are classified into either hypokinetic disorders (e.g. Parkinson’s disease)

and hyperkinetic disorders (e.g. chorea, athetosis, dystonia). Hypokinetic disorders are characterized by significant impairments in movement initiation (akinesia) and reduction in velocity of voluntary movements (bradykinesia), and are usually accompanied by muscular rigidity and tremor at rest. By contrast, hyperkinetic disorders are characterized by excessive motor activity in the form of involuntary movements (dyskinesias) and varying degrees of hypotonia. In line with this division, motor speech disorders associated with basal ganglia lesions have been labelled hypokinetic or hyperkinetic dysarthria (Darley *et al.*, 1975). Full description of the clinical features of hypo- and hyperkinetic dysarthria are presented in Chapter 11.

The major components of the basal ganglia include: the putamen and caudate nucleus, collectively known as the neostriatum; the globus pallidus; the substantia nigra pars compacta and pars reticulata; and the subthalamic nucleus (for a full description of the neuroanatomy of the basal ganglia and their connections see Chapter 2). Participation of the basal ganglia in the control of movement is a well-established idea dating back to the early part of the twentieth century when Wilson (1912) described a disease characterized by muscular rigidity, tremor and weakness with pathological changes in the liver and basal ganglia (hepatolenticular degeneration). Wilson (1912) noted that several features usually associated with damage to the pyramidal tracts were not present in this disease and postulated that the motor abnormalities were due to dysfunction of what he called an 'extrapyramidal motor system'. Further, Wilson (1912) proposed that the basal ganglia were the major constituents of this extrapyramidal motor system that he viewed to be parallel to and independent of the pyramidal (corticospinal) motor system. In a subsequent publication Wilson (1928) developed the view of two motor systems, the phylogenetically 'old' extrapyramidal system and the 'new' pyramidal system, the function of the former being automatic, postural, static and minimally modifiable and that of the pyramidal system being voluntary, phasic and readily modifiable.

Links between basal ganglia pathology and the occurrence of movement disorders had previously been suggested by Jackson (1868), who proposed that instability of activities of the striatum led to chorea. Hunt (1917, 1933) postulated further that large cells in the striatum and globus pallidus constituted the pallidal system which was the output of basal ganglia motor functions, and that lesions in the pallidal system caused Parkinsonism. He also postulated that small cells in the striatum inhibited large cells and lesions in the striatum released the pallidal system and resulted in chorea, while lesions involving both the pallidal system and small cells in the striatum produced athetosis.

In the 1960s and 1970s more modern anatomical techniques showed that the bulk of the basal ganglia output passed via the thalamus to motor cortical areas (Nauta and Mehler, 1966). Thus it appeared that the basal ganglia output was prepyramidal rather than extrapyramidal. This finding contributed to the development of hypotheses that the basal ganglia initiate movement via their output to the motor cortex. Currently, the basal ganglia are generally considered to be comprised of a group of 'input' structures (the caudate nucleus, putamen and ventral striatum) that receive direct input essentially from areas of the cerebral cortex and 'output' structures (the internal segment of the globus pallidus, the substantia nigra pars reticulata and the ventral pallidum) that project back to the cerebral cortex via the thalamus. Originally the striatum was considered to serve primarily to integrate diverse inputs from the entire cerebral cortex and to 'funnel' these influences via the ventrolateral thalamus to the primary motor cortex alone. This thinking was consistent with the view held at the time that the basal ganglia functioned primarily in the domain of motor control.

Based on recent research, it is now clear that output from the basal ganglia terminates in thalamic regions that gain access to a wider region of the frontal lobe than just the primary motor cortex, including areas thought to have cognitive functions (Alexander *et al.*, 1986; Middleton and Strick, 1994). Consequently, the original notion has been superseded by the view of the striatum as a 'multi-laned throughway' which forms part of a series of multi-segregated circuits connecting the cerebral cortex, the basal ganglia and the thalamus (Alexander *et al.*, 1986; Graybiel and Kimura, 1995; Middleton and Strick, 2000). Thus basal ganglia anatomy is characterized by their participation in multiple 'loops' with the cerebral cortex, each of which follows the basic route of cortex → striatum → globus pallidus/substantia nigra → thalamus → cortex in a unidirectional fashion.

Alexander *et al.* (1986) identified at least five separate, parallel corticobasal ganglion circuits according to the specific region of the frontal lobe that serves as a target for their thalamocortical projections. One of these circuits projected to the skeletomotor areas of the frontal cortex while another projected to the oculomotor areas. The three remaining circuits projected to non-motor areas of the frontal cortex, including the dorsolateral prefrontal area (Brodmann area 46), the lateral orbitofrontal cortex (Brodmann area 12) and the anterior cingulate/medial orbitofrontal cortices (Brodmann areas 24 and 13). Importantly, these circuits appear to be functionally segregated to a large extent, suggesting that structural convergence and functional integration occur within rather than between each of the identified circuits. Given the segregated nature of the corticobasal ganglia circuits, collectively they may be viewed as having a unified role in modulating the operations of the entire frontal lobe, thereby influencing such diverse frontal lobe processes as motor activities, behavioural, cognitive, language and even limbic processes. This anatomical arrangement, whereby the output from the basal ganglia gains access to multiple areas of the frontal lobe including non-motor areas, has profound consequences for the possible functional roles of the basal ganglia system and provides a basic neuroanatomical mechanism whereby these subcortical structures can influence aspects of behaviour, cognition and language as well as motor function.

Each corticobasal ganglia circuit has been proposed to contain a direct and indirect pathway from the striatum to the internal globus pallidus and substantia nigra pars reticulata, the output nuclei of the basal ganglia (Delong and Georgopoulos, 1981). This direct and indirect pathway theory makes it easy to explain various clinical signs of basal ganglia diseases, including hypo- and hyperkinetic movement disorders. Imbalance between the activity in the direct and indirect pathways and the resulting alterations in the activity of the internal segment of the globus pallidus and substantia nigra pars reticulata are thought to account for hypo- and hyperkinetic features of basal ganglia disorders, including hypo- and hyperkinetic dysarthria. The possible roles of the direct and indirect pathways in the development of the various hypo- and hyperkinetic movement disorders, including hypo- and hyperkinetic dysarthria, are discussed in detail in Chapter 10 of the present volume. Neuroanatomical details of each of these pathways are provided in Chapter 2.

Cerebellum

The most obvious signs of damage to the cerebellum are disturbances in motor function, characterized by incoordination of the limbs (dysmetria), wide-based gait, dysarthria and disturbed ocular movements (nystagmus). Consequently, the cerebellum

has traditionally been viewed as a structure that contributes primarily to motor coordination and control. Although there are suggestions in the writings of Aristotle that the anatomical functions of the 'little brain' were known in ancient Greece, one of the first researchers to document the functions of the cerebellum was Gall (1809) who, in his cartographic scheme of psychological characteristics of the skull, designated the cerebellum as the organ of 'amativeness'. At the same time Luigi Rolando was the first researcher to report the outcome of removal of the cerebellum in animals. He noted that cerebellar lesions impaired posture and movement, leaving sensory and cognitive functions intact. Flourens (1824) continued experiments of cerebellar ablation in animals and demonstrated that 'all movements persist after ablation of the cerebellum; all that is missing is that they are not regular and coordinated' (p. 181). The physiological experiments conducted by Ludwig Edinger further confirmed that the cerebellum was involved in coordination of movements and maintenance of muscle-tonus and equilibrium.

The first systematic descriptions of the neurological symptoms specific to what was named 'the cerebellar syndrome' were provided by Babinski (1913) and Holmes (1917, 1922). Currently, cerebellar syndrome is considered to basically involve ataxia, hypotonia, dysmetria and essential tremor (Trouillas *et al.*, 1997). They described in detail the role of the cerebellum in the coordination of extremity movement, gait, posture, equilibrium and speech. In relation to speech, Holmes (1917, 1922) noted that acute and chronic cerebellar lesions may provoke alterations in both phonation and articulation. Darley *et al.* (1975) later classified this speech disorder as ataxic dysarthria, the predominant features of which include a breakdown in the articulatory and prosodic aspects of speech. Unlike some forms of dysarthria (e.g. flaccid dysarthria), where the speech disorder can be linked to deficits in individual muscles, ataxic dysarthria is associated with decomposition of complex movements arising from a breakdown in the coordinated action of the muscles of the speech-production apparatus to produce speech (for a complete description of the clinical features and neuropathophysiological basis of ataxic dysarthria see Chapter 11).

To be able to perform its primary function of synergistic coordination of muscular activity, the cerebellum requires extensive connections with other parts of the nervous system. Briefly, the cerebellum functions in part by comparing input from the motor cortex with information concerning the momentary status of muscle contraction, degree of tension of the muscle tendons, positions of parts of the body, and forces acting on the surfaces of the body originating from muscle spindles, Golgi tendon organs, etc., and then sending appropriate messages back to the motor cortex to ensure smooth, coordinated muscle function. Consequently, the cerebellum requires input from the motor cortex, muscle and joint receptors, receptors in the internal ear detecting changes in the position and rotation in the head, and skin receptors, among others. Conversely, pathways carrying signals from the cerebellum back to the cortex are also required to complete the cerebrocerebellar loop. Traditionally the output of cerebellar processing was thought to be directed at only a single cortical area, namely the primary motor cortex, consistent with the belief the corticocerebellar circuits function primarily in the domain of motor control. It is now known that the cerebellum is a relay for many segregated neural circuits involved in the control process of several physiological functions; for example, vestibulo-cerebellar-vestibular loops are involved in the regulation of equilibrium and ocular motility, while reticulo-cerebello-reticular loops are involved in muscle tone, the control process of posture and the regulation of many vegetative functions. Spino-cerebello-rubro-spinal loops subservise regulation of the motor apparatus at the spinal level.

The main loops involved in the regulation of voluntary movement and possibly cognitive and language functions are the cerebrocortico-ponto-cerebellocortico-dentato-thalamo-cerebrocortical loops (Middleton and Strick, 1997; Schmahmann, 1997) and the cerebrocortico-rubro-olivo-neodentato-cerebrocortical loops (Leiner *et al.*, 1993). Importantly, it is now recognized that the thalamo-cerebrocortical projections of these latter two loops project not only to the motor cortex but also to non-motor regions of the cerebral cortex, including the major speech/language centres, thereby providing a neuroanatomical basis for the cerebellum to influence functions such as cognition and language in addition to motor activities. The role of the cerebellum in language is further discussed briefly below and in detail in Chapter 7.

Motor speech disorders associated with subcortical pathology

It is well established that neurological disorders considered to be attributable primarily to lesions involving subcortical structures such as the basal ganglia and cerebellum are frequently associated with the occurrence of motor speech disorders, implying that these structures have a role in the normal regulation of the motor functioning of the speech musculature (Darley *et al.*, 1975; Murdoch, 1998). For instance, hypokinetic dysarthria, a motor speech disorder characterized by features such as monotony of pitch and loudness, decreased use of all vocal parameters for effecting stress and emphasis, breathy and harsh vocal quality, reduced vocal intensity, variable speech rate, including short rushes of speech or accelerated speech, consonant imprecision, impaired breath support for speech, reduction in phonation time, difficulty in the initiation of speech activities and inappropriate silences has been reported to occur in association with Parkinson's disease, a condition caused by nerve cell loss in the pigmented brain stem nuclei, most markedly the pars compacta of the substantia nigra (Darley *et al.*, 1975; Theodoros and Murdoch, 1998). Likewise, a variety of motor speech disorders collectively referred to as 'hyperkinetic dysarthria' may occur in association with the abnormal involuntary movements encountered in a range of other neurological conditions caused by neuropathological changes in the basal ganglia system, including chorea, dystonia, etc. (Darley *et al.*, 1975). Further, lesions to, or diseases of, the cerebellum or its afferent or efferent connections may disrupt the motor components of speech production at the segmental or suprasegmental level, giving rise to ataxic dysarthria, a motor speech disorder characterized by articulatory inaccuracy (imprecision of consonant production, irregular articulatory breakdowns and distorted vowels), prosodic excess (excess and equal stress, prolonged phonemes, prolonged intervals and slow rate), and phonatory-prosodic insufficiency (harshness, monopitch and monoloudness) (Murdoch and Theodoros, 1998).

In recent years, several models have been proposed in an attempt to further elucidate the contribution of subcortical structures to motor control, and to explain the occurrence of movement disorders subsequent to basal ganglia and cerebellar lesions. These models are discussed in Chapter 10.

Subcortical mechanisms in language: historical perspective

The basal ganglia and cerebellum are two groups of subcortical nuclei that have classically been regarded as motor structures. In addition to their role in motor functions,

anatomical studies and clinical research conducted over the past two decades have increasingly implicated the basal ganglia and cerebellum in a range of behavioural functions, including several different types of cognitive, linguistic and limbic function. Consequently, the traditional view that the basal ganglia and cerebellum are only involved in motor functions has been challenged. A major reason for this reappraisal has been new information regarding basal ganglia and cerebellar connections with the cerebral cortex.

Recently reported anatomical studies have noted that these connections are organized into discrete, segregated neural circuits, or loops. Rather than simply enabling widespread cortical areas to gain access to the motor system, these loops reciprocally interconnect a large and diverse set of cerebral cortical areas with the basal ganglia and cerebellum, enabling the latter structures to influence a range of cognitive functions in addition to their more traditional motor roles. For example, Alexander *et al.* (1986) proposed that the output of the basal ganglia targeted not only the primary motor cortex, but also specific areas of the premotor and prefrontal cortex, thereby suggesting that the basal ganglia have the ability to influence not only motor control but also several different types of cognitive and limbic (e.g. memory) function. Similarly, it has been hypothesized that output from the lateral deep cerebellar nucleus (the dentate) influences not only motor areas of the cerebral cortex but also areas of the prefrontal cortex involved in language and cognition. Evidence to support this functional diversity of the basal ganglia and cerebellum comes from several sources, including neuroanatomical studies documenting the presence of extensive connections between the basal ganglia and cerebral cortex, animal studies reporting a range of behavioural correlates documented by single-cell recordings from basal ganglia neurones, observations of the behavioural effects of disease-induced lesions in the basal ganglia, clinico-neuroradiological studies documenting the presence of speech disorders and other behavioural deficits in association with subcortical lesions, the findings of studies based on functional neuroimaging, including positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) and, more recently, observations of the behavioural effects of deep-brain stimulation and surgically induced lesions in the globus pallidus (pallidotomy), thalamus (thalamotomy) and subthalamic nucleus, carried out as part of the treatment for Parkinson's disease and other basal ganglia syndromes.

Role of the basal ganglia and thalamus in language: historical perspective

As outlined above, ever since the era of phrenological science the cerebral cortex has been considered the neural substrate of higher psychological function, including language. In keeping with this view, the standard 'associationist' anatomo-functional model of language organization was deeply rooted in cortical areas and their fibre connections (Lichtheim, 1885; Wernicke, 1874). According to this still influential model, linguistic representations are stored in discrete cortical areas and consequently subcortical brain lesions were thought to only produce language deficits if they disrupted the white matter fibres that connect the various cortical language centres.

Despite the emphasis on the cerebral cortex, evidence to suggest the occurrence of language disorders associated with subcortical brain lesions has been available since the late nineteenth century. More than a century ago, Broadbent (1872) proposed that

words were 'generated' as motor acts in the basal ganglia. Marie (1906) challenged the traditional view of aphasia and described a clinical syndrome that he called 'anartria' secondary to dysfunction of a specific subcortical region involving the caudate nucleus, putamen, internal capsule and thalamus (Marie's quadrilateral space). Monakow (1914) also championed the participation of the lentiform nucleus in the pathogenesis of aphasia. Perusal of the monumental anatomico-clinical summaries published in the early twentieth century, such those by Moutier (1908), Henschen (1922) and Nielsen (1946), also reveals a number of cases of language disturbance associated with lesions apparently limited to subcortical structures. Unfortunately, these empirical data were subjected to radically different interpretations by the various authors. Moutier supported the '*quadrilatère*' proposed by his teacher Pierre Marie. In contrast Nielsen explicitly denied any role of subcortical structures in mental activities, interpreting his observations in strict adherence to the traditional Wernicke-Lichtheim model. Later Fisher (1959) described aphasia as a clinical feature in a patient with left-thalamic haemorrhage. Penfield and Roberts (1959) suggested that the thalamus had an integrative function in language processing.

Since the late 1970s the traditional view of language processing in the brain has been challenged by the findings of an increasing number of cliniconeuroradiological correlation studies that have documented the occurrence of adult language disorders in association with apparently subcortical vascular lesions. The introduction in recent decades of new neuroradiological methods for lesion localization *in vivo*, including computed tomography in the 1970s and more recently MRI, has led to an increasing number of reports in the literature of aphasia following subcortical lesions (for reviews of correlation studies *in vivo* see Alexander, 1989; Cappa and Vallar, 1992; Murdoch, 1996). In particular, these new neuroimaging techniques have allowed more precise identification and localization of subcortical lesion parameters (Alexander, *et al.*, 1987; Cappa and Wallesch, 1994) and hence the ability to evaluate the influence of specific lesions in producing motor and cognitive anomalies. Therefore, although the concept of subcortical aphasia remains somewhat controversial, recent years have seen a growing acceptance of a role for subcortical structures in language and the development of a range of theories that attempt to explain the nature of that role. These theories, largely developed on the basis of speech and language data collected from subjects who have had cerebrovascular accidents involving the thalamus or striato-capsular region, have been expressed as neuroanatomically based models. The most influential models of subcortical participation in language proposed to date include the Subcortical White Matter Pathways (Alexander *et al.*, 1987), Response-Release Semantic Feedback (Crosson, 1985), Lexical Decision Making (Wallesch and Papagno, 1988) and Selective Engagement (Nadeau and Crosson, 1997) models. The Subcortical White Matter Pathways model dismisses a role for the subcortical nuclei in language and advocates cortico-cortical, corticostriatal, thalamocortical and corticobulbar white matter pathways as critical to the facilitation of auditory comprehension and verbal expression. In contrast, the Response-Release Semantic Feedback model proposes a role for subcortical structures in regulating the release of preformulated language segments from the cerebral cortex via a complex neural circuit called the cortico-striato-pallido-thalamo-cortical loop. Likewise, the Lexical Decision Making model also proposes a cortico-striato-pallido-thalamo-cortical loop as the neural platform for linguistic operations. Specifically, Wallesch and Papagno (1988) postulated that the subcortical components of the loop constitute a frontal lobe system comprised of parallel modules with integrative and decision-making capabilities rather than the

simple neuroregulatory role proposed in Crosson's (1985) model. The Selective Engagement model represents the most contemporary schema of subcortical participation in language and principally proposes a frontal-inferior thalamic peduncle-nucleus reticularis-centrum medianum system to subserve the 'engagement' of cortical components which mediate attentional and behavioural processes, including language. In particular, the Selective Engagement model disputes a role for the basal ganglia in language and redefines non-specific thalamic nuclei (i.e. nucleus reticularis, centrum medianum and parafascicular nucleus) as critical to the mediation of language (a full discussion of the above models of subcortical participation in language is presented in Chapter 3). Although the basal ganglia, thalamus and subcortical white matter pathways represent the subcortical structures which have been afforded the most consideration within contemporary models of subcortical participation in language, more recently studies based on deep-brain stimulation have also indicated a possible role for the subthalamic nucleus in language processes (Whelan *et al.*, 2003, 2004).

Role of the cerebellum in language: historical perspective

Investigation of a possible role for the cerebellum in the mediation of cognitive processes, including language, has historically been overshadowed by research interest in cerebellar coordination of motor control. Over the past two decades, however, the question of a possible participation of the cerebellum in language processing itself has come to the forefront. In particular, recent advances in our understanding of the neuroanatomy of the cerebellum combined with evidence from functional neuroimaging, neurophysiological and neuropsychological research, has, however, extended our view of the cerebellum from that of a simple coordinator of autonomic and somatic motor function. Rather it is now more widely accepted that the cerebellum, and in particular the right cerebellar hemisphere, participates in modulation of cognitive functioning, especially to those parts of the brain to which it is reciprocally connected (Marien *et al.*, 2001). Indeed, the discovery of major reciprocal neural pathways between the cerebellum and the frontal areas of the language-dominant hemisphere, including Broca's area and the supplementary motor area, was a major impetus in the development of the concept of cerebellar involvement in non-motor linguistic processes.

Much of the credit for this development goes to Leiner, Leiner and Dow, who wrote a series of articles reviewing the potential role of the cerebellum in cognition. In their first publication (Leiner *et al.*, 1986) they reviewed long-neglected evidence that portions of the lateral cerebellar hemispheres and dentate nuclei were greatly expanded in humans. They hypothesized that these cerebellar regions project to prefrontal and other association cortices in humans and higher primates, forming cortical-cerebellar loops used for certain types of cognitive skill. In support of this hypothesis non-motor behavioural deficits associated with cerebellar damage or abnormalities were reported by several investigators and functional neuroanatomical studies using PET during the late 1980s demonstrated the selective activation of some cerebellar structures during language tasks (Petersen *et al.*, 1989). In the early 1990s, Fiez *et al.* (1992) described a patient with an extensive right-cerebellar lesion who presented with language disturbances. Since that time numerous studies have identified the presence of disturbed language processing in association with primary lesions of various aetiologies involving both the right (Marien *et al.*, 2001) and left (Murdoch and Whelan, 2007)

cerebellar hemispheres. A comprehensive review of the evidence supporting a role for the cerebellum in language is presented in Chapter 7.

Functional neuroimaging

Further clarification of the role of subcortical structures in language is likely to come through the use of functional neuroimaging techniques and neurophysiological methods such as electrical and magnetic evoked responses. Functional neuroimaging techniques such as fMRI and PET enable brain images to be collected while the patient is performing various language-production tasks (e.g. picture naming, generating nouns) or during language comprehension (e.g. listening to stories). These techniques therefore enable visualization of the brain regions involved in a language task, with a spatial resolution as low as a few millimetres. Although functional neuroimaging does therefore offer promise of a tool to unravel the role of subcortical structures in language, results from functional neuroimaging studies to date have proven less than definitive (Cabeza and Nyberg, 2000). These studies have, however, revealed a number of cortical and subcortical structures beyond the perisylvian cortex to be active during linguistic processing (Petersen *et al.*, 1989; Warburton *et al.*, 1996; Crosson *et al.*, 1999), providing support for a distributed network model of language organization (Mesulam, 2000). In particular, word-generation studies have shown consistent activation of the medial frontal cortex, usually near the boundary of the pre-supplementary motor area and the rostral cingulate zone. Although the supplementary motor area is known to have extensive subcortical connections, including projections to the striatal grey matter spanning the internal capsule and to the caudate nucleus and putamen as well as receiving connections from the ventral anterior and dorsal medial thalamus, in the majority of functional neuroimaging studies these subcortical components have not shown consistent activity in studies of word generation. This reported inconsistency in activation of the basal ganglia and thalamus may be the product of limitations in numbers of subjects studied, number of trials during functional neuroimaging and experimental design. Recently, Crosson *et al.* (2003) using fMRI observed significant activity in the subcortical structures during lexical generation tasks but not during nonsense syllable generation. They inferred the existence of a left pre-supplementary motor area-dorsal caudate-ventral anterior thalamic loop involved in lexical retrieval. Further, Crosson *et al.* (2003) hypothesized 'that activity in this loop was related to maintaining a bias toward the retrieval of one lexical item versus competing alternatives for each response during word generation blocks' (p. 1075). Several PET studies have also demonstrated activation of the thalamus and basal ganglia during completion of language tasks such as picture naming (Price *et al.*, 1996a) and word repetition (Price *et al.*, 1996b).

In relation to the role of the cerebellum in language, functional neuroimaging studies have provided a possible explanation for the occurrence of language problems subsequent to cerebellar pathology. Specifically, studies based on functional neuroimaging techniques such as single-photon emission computed tomography (SPECT), PET and fMRI have consistently revealed regions of contralateral cortical hypoperfusion in relation to the orientation of the cerebellar lesion (Silveri *et al.*, 1994; Beldarrain *et al.*, 1997), a phenomenon called crossed cerebello-cerebral diaschisis. Several authors have proposed that this phenomenon, reflecting a functional depression of supratentorial language areas due to reduced input via cerebello-cortical pathways, may represent the neuropathological mechanism responsible for

language problems associated with cerebellar pathology (Broich *et al.*, 1987; Marien *et al.*, 2001).

Summary

Although it has been recognized that lesions involving subcortical structures such as the basal ganglia and cerebellum are associated with motor impairments, including motor speech disorders, for more than a century, it is only relatively recently that attention has been directed at the potential role of these subcortical structures in language processing. Although controversy still exists as to whether the structures of the striatocapsular region and the cerebellum participate directly in language processing or play a role as supporting structures for language, contemporary theories suggest that, as in the case of motor functions, the role of subcortical structures in language is essentially neuroregulatory. Evidence based on neuroanatomical, clinical and functional neuroimaging studies indicate that speech and language functions are mediated by complex, segregated neural circuits that comprise networks linking activity in many parts of the brain at both the cortical and subcortical level, with subcortical structures such as the basal ganglia and cerebellum representing important relays in these complex pathways. Subsequent chapters of this volume will explore this concept further as part of discussion of specific aspects of subcortical mechanisms in speech and language function.

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