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INTRODUCTION

Murdoch et al. (2003) state that "Although the cerebral cortex has traditionally been considered the neural substrate of language, over the past two decades this traditional view has been challenged by the findings of a proliferating number of clinico-neurological correlation studies that have noted the occurrence of language disorders in association with apparently subcortical lesions. In particular the introduction in recent decades of new neuroradiological methods for lesion localization in vivo, including computed tomography (CT) and more recently magnetic resonance imaging (MRI), has led to an increasing number of reports in the literature of aphasia following apparently isolated subcortical lesions involving the striato-capsular region and/or thalamus. Consequently, in recent years, there has been growing acceptance of a role for subcortical structures such as the globus pallidus and thalamus in language processing" (p. 65).

Plenty of theoretical models of how subcortical structures are involved in language processing have been developed over the past five decades.

The aim of this diploma thesis is to provide a review of research that has focused on the role of subcortical structures in language and the entity of subcortical aphasia. By concentrating also on recent studies I want to describe the "state of the art" as best as possible.

I will start out by providing a short definition of the concept of aphasia followed by an historical overview of how this concept developed over the centuries.

After a description of today's standard classification of aphasia syndromes I will concentrate on their clinico-anatomical correlations and the most frequent neurological disorders causing this disturbances. Furthermore I will concentrate on the entity of subcortical aphasia, giving an overview of the development of this theoretical concept and its clinico-anatomical correlations over the past decades and discuss the validity of this topic today. Finally, I want to undertake a comparison of subcortical lesions followed by aphasia after stroke to language disturbances arising in Parkinson's disease (PD), another neurological disorder that especially involves the degeneration of subcortical structures.

1. Classical concepts of aphasia

Aphasias are due to an acquired lesion in subjects who have developed language normally. Language pertains to the ability to handle (decode, encode, and interpret) the symbols used within a cultural group for the communication of information, feelings and thoughts (Brandt et al 2003, Hartje und Poeck 2006).

Aphasia must be distinguished from other disorders which can affect the communication process. They have to be distinguished from developmental disorders of language acquisition, which are usually associated with different forms of congenital neurological dysfunction. In particular, aphasia must be distinguished from impairments in the motor realisation of language, i.e. from disorders of articulation (dysarthria) or phonation (dysphonia). Of course these disorders may be associated with aphasia, but not necessarily so. Aphasia is an entity independent from the motor and sensory channels used for linguistic production and comprehension by individual subjects. For example, aphasia can be observed after left hemispheric brain lesions in deaf people, which use manual signing instead of vocal articulation to produce language (Benson, 1988).

Cerebrovascular lesions are the leading cause of adult aphasia: this fact has not been without consequences for theoretical research in language disturbances, infarctions and haemorrhages do not occur randomly in the brain, but have predilection sites in consequence to the vessel anatomy of blood supply of the brain. These lesion localisations tend to be associated with relatively predictable constellations of linguistic symptoms, which are the traditional aphasic syndromes recognised in clinical neurology from the end of last century (Brandt et al. 2003, Hartje und Poeck, 2006).

1.1 Historical aspects

1.1.1 The beginnings

An historical overview shows that in one of the earliest medical writings, the Edwin Smith Surgical Papyrus, an Egyptian manuscript that dates back to 3500 B.C., references to the brain as the center of language were made. Observations were made that damage to the head/ to the brain results in symptoms in other parts of the body, also speechlessness was defined as a sign or form of disease. However, no distinction was made between aphasic and peripheral disorders of speech in any medical writing before the first century A.D. The conceptual framework on which the notion of aphasia is based seems therefore to be a comparatively recent development. The notion of language skills, as opposed to other uses of the oral and phonatory organs and to other cognitive abilities, is rarely distinguished in writings before the Renaissance. Not until the beginning of the 15th century a variety of reports of patients with selective disorders involving reading, naming, understanding and speech production emerged (Goodglass, 1988).

1.1.2 17th to 19th century

Benton et al. (1998) noted that “relatively detailed descriptions of cases that leave no doubt that the patient was truly aphasic are first encountered in the seventeenth century. Two of these case reports are of particular interest. One, published in 1676 by Johann Schmidt, described a patient who suffered from a paraphasic expressive speech disorder after a stroke” (p. 3). The authors further add “the second case report, entitled `On a Rare Aphonia´, described a patient with a nonfluent expressive speech disorder and an equally severe incapacity for repetition” (Benton et al. 1998, p. 3). This trend to very detailed case reports, emphasizing the selective nature of the deficits, continued into the 18th century and it was not before the 18th century ended as a new aspect in studies about aphasia

came up: the beginning of theoretical considerations concerning the nature of the deficits.

The monograph of Johann Gesner entitled “Die Sprachamnesie”, published in 1770, was the first major study of the disorder, six case reports described an extraordinary amount of clinical features of language disorders. Benton et al. 1998 argued that “Moreover, in contrast to earlier authors, Gesner emphasized that word-finding difficulties and paraphasic speech reflect not a loss of memory in general but a specific type of memory loss, namely, speech amnesia” (p. 4). Gesner hypothesized that is was produced by inertness in the connections between the different parts of the brain, he then implemented the thought of separability of language use from other aspects of memory. In doing so the distinction between language on the one hand and other motor, memory and cognitive functions on the other took place and a framework for understanding a class of disorders was established (Goodglass 1988, Ahlsen 2006, Tesak 2008).

Another important theoretical formulation regarding the nature of aphasia was that by Jean-Baptiste Bouillard (1796-1881), who discerned two basic types of aphasias, one being articulatory and the other amnesic in nature stating the difference between speech and language disorders. He distinguished the motor component of speech from non-speech activities of the same organs: tongue, lips and glottis. He argued that, since the non-speech activities may be unaffected while motor articulation got lost, a concept of dual neural control mechanisms over these organs has to be considered – one for learned behaviour of speech and one for instinctive behaviour like swallowing (Goodglass 1988).

According to Benton et al. (1998), aphasia research made great progress at the turn of the century, as they put it ”During the first decades of the 19th century, further advances were made along all lines: clinical knowledge, theoretical formulation and neuropathology. A number of clinical studies contributed to the knowledge of the phenomenology of aphasia” (p. 5). The aspect of the neuropathological basis of aphasic disorders was first brought up by the anatomist and phrenologist Franz Joseph Gall (1758-1828).

He was the first person to localize mental abilities in the cortex of the brain. The cortex was earlier thought to be an expansion of the brain membranes, the

meninges, with the function of supplying nourishment to the brain. Gall held that "the human brain was an assemblage of organs, each of which formed the material substrate of a specific cognitive ability or character trait. Among the approximately 30 traits localized in his system there were two cerebral "organs" of language, one for speech articulation and the other for word memory, which he placed in the orbital region of the frontal lobes. Gall´s hypothesis that the brain is not a unitary equipotential organ, but instead consists of an aggregate of functionally specialized areas, attracted both loyal supporters and vigorous opponents" (Benton et al. 1998, p. 6). Gall studied various abilities in a number of persons and examined their skulls because he thought that the development of the skull depended on the size of the cortex beneath. He described two clearly aphasic patients of which one had a residual right-sided weakness and anomia following a stab wound from foil fencing which penetrated upwards into his frontal lobe. The other patient with severe speech output problems following a stroke, pointed to his forehead as the source of his difficulties. In Gall´s opinion these two patients supported his theory of a bilateral frontal seat of language (Goodglass 1988, Ahlsen 2006, Tesak 2008). Also representative of the direction of the thinking of the period is the work of Lordat (1843-1904). Having experienced a transient episode of aphasia himself, he reflected his own aphasia in terms of an intuitive analysis of the progress of language processes in certain stages. According to Lordat´s analysis, the first stage of a speech act is the isolation of the general idea of the intended message followed by the arrangement of the preverbal thought units, which are then brought into verbal form with their sound put into order following the rules of a given language, and finally realised motorically. Lordat postulated that several forms of aphasia depict breakdowns at different stages of this process or of the reverse, receptive process. However, having experienced an aphasic episode himself, he was convinced that there is no intellectual impairment in aphasia (Goodglass 1988, Benson 1988, Tesak 2008).

So, in the early 19th century linguistic research regarding speech and language pathologies had reached a state which in principle changed little over the next 85 years. Language was distinguished from other intellectual abilities. Focus was upon the psychological nature of language processes, the disturbances induced by the

various forms of aphasia and on drawing inferences from the lesion-symptom relationship for understanding the anatomy of language (Goodglass 1988).

1.1.3. The classical period

The surgeon and anthropologist Paul Broca (1824-1880) examined the brains of two aphasic patients who had been under his care during the last months of their lives. The autopsy findings showed that the lesion which was ostensibly responsible for the nonfluent aphasic disorder shown by these patients was situated in both cases in the posterior part of the left frontal lobe. At that time (1861), Broca interpreted his findings as supporting Gall's thesis that the seat of language was in the frontal lobes, and he made no particular reference to the fact that the lesions were left-sided. As he studied several other patients with similar symptoms however, his attention was drawn to the unilateral nature of the lesions causing the nonfluent impairment of speech which he named "aphemia". Benton et al. (1998) described that "The validity of Broca´s generalization was readily confirmed, and the doctrine of hemispheric cerebral dominance was born" (p. 7). Further Benton et al. 1998 placed "When Broca made his localization, he emphasized that he did not mean to imply that all forms of aphasia were related to left frontal lobe disease but only the motoric type, which he called aphemia and which was essentially the same as the articulatory and asynergic types of the disorder described by Bouillaud and Lordat" (p. 8). Broca also distinguished between the loss of articulate speech, which he called "aphasia", from "verbal amnesia", which is, from his account, similar to the sensory aphasia of Wernicke. This dichotomy was recognized also by a number of other contemporaries some time before the appearance of Wernicke´s monograph in 1874 (Goodglass 1988, Ahlsen 2006, Tesak 2008).

In his monograph Wernicke established a syndrom which he called "sensory aphasia". He designated the following characteristics "These features were fluent but disordered speech, analogous disturbances in writing, impaired understanding of oral speech, and impairment in both oral and silent reading. The crucial, or at least the most frequently occurring, lesion associated with this syndrome was

situated in the hinder part of the first temporal gyrus of the left hemisphere" (Benton et al. 1998, p. 8-9). Wernicke´s monograph with its mapping of psychological processes onto anatomical data, localizing sensory aphasia in the posterior part of the superior temporal gyrus, though was an extremely influential contribution in the history of aphasia. On the one hand he explicitly attributed sensory aphasia to destruction of a center for auditory word images and accounted for paraphasia as a failure of auditory monitoring, on the other hand he put the principle of anatomic association on a firmer basis as anyone before had. Adopting Meynert´s view on the existence of a fibre pathway from the temporal gyrus to Broca´s motor speech area, Wernicke even went so far as to predict the existence of a special type of aphasia, conduction aphasia, resulting by damage to this pathway (Goodglass 1988, Ahlsen 2006, Tesak 2008).

Benton et al. report "Broca and Wernicke were not only localisationalists but also associationists. Like Gesner and Crichton, they thought of aphasic disorders as disturbances in attaching appropriate verbal labels to ideas, objects, or events, with basic intellectual capacity remaining essentially intact" (p. 9). In addition, their discoveries provided a basis for classifications of aphasic disorders as well as schematic models to explain their nature. For the most part, these models depicted the anatomic structures and neural mechanisms that were presumed to underlie language performances. As Benton et al. (1998) put it "The formulations were in terms of interconnected cortical centers that served as depositories for the auditory and visual memories of words and of the movement patterns of speech and writing. Models of this type were proposed by most of the leading aphasiologists of the late nineteenth century" (p. 9).

In 1881 Kussmaul published his own book, *Die Störungen der Sprache*, presenting a view of aphasia that had some features in common with Wernicke´s model, but also included a conceptual center and a visual center. Kussmaul introduced the terms "word deafness" and "word blindness". Like Wernicke, he designed his model as a series of centers with connections linking them but in his opinion this connections were missing any anatomical substrate. Kussmaul regarded aphasia as an artificial term for various autonomous disorders affecting speech

production, word retrieval, production of sentences as well as word deafness and word blindness (Benson 1988).

Ludwig Lichtheim, a German physician, postulated a third language center with an unspecified localisation, the “concept centre”, which was the storehouse of the meaning attached to the auditory word images of Wernicke´s area and which was also the source of messages to be implemented by the motor speech center. In Lichtheim´s monograph (1884) the connection between the auditory word center and the motor speech center becomes the pathway for repetition. Conduction aphasia, which results from an interruption of that pathway, is principally marked by failure of repetition. Interruption of the pathway to or from the concept center results in transcortical aphasia, in which repetition is spared (Goodglass 1988, Ahlsen 2006, Tesak 2008).

Major and minor modifications of the Wernicke-Lichtheim typology were introduced in the latter part of the 19th and 20th centuries. Déjerine (1901) took a position very similar to that of Wernicke’s, but adding a visual verbal zone in the angular gyrus. He insisted on considering the long and short cortico-cortical connection linking these zones more rigorously than any of his predecessors. He also paid attention to the role of the corpus callosum and to the need to take into account the bilateral innervation of the oral motor apparatus (Benson 1988, Ahlsen 2006).

After Broca, Wernicke and Lichtheim, localism and associationism became the dominant views. Although opposing positions had been claimed in earlier stages, not until the 1920s they became influential, when the holistic, so-called cognitive school started to dominate. The reaction against associationism had its roots in Hughling Jackson’s writings who generally avoided issues of anatomy. On this topic his views may be summed up by the quote “…the nearer the disease is to the corpus striatum, the more likely is the defect of articulation to be the most striking thing, and the farther off, the more likely is it to be mistakes of words” (Jackson 1932, in H. Goodglass, Handbook of Neuropsychology, 1988, Vol.1, Chapter 13, p. 254). Jackson dealt with general psychological principles which applied to aphasia of almost any type, and he attempted to show how certain general principles of neural activity operated broadly across systems – including language

and perception. He made an essential distinction between automatic and volitional behaviours, which he considered to involve different levels of neural organization. To his opinion, considering language, these are represented by interjections and memorized series on the one hand and by propositional speech on the other, aphasia primarily affecting the propositional use of language. Jackson suggested that the automatic level of speech may be mediated by the right hemisphere, since it might survive massive left-hemisphere destruction. He also cautioned against identifying the lesion site that produces a functional deficit with the localization of the impaired function (Goodglass 1988, Tesak 2008).

Another representative of the noetic approach was Trousseau in the middle of the 19th century who challenged the localist view that thinking as such was not affected by aphasia and emphasized the extent of the intellectual impact of the disorder in most patients. Pierre Marie, in a series of articles published 1906, postulated that there is only one truly aphasic disorder – that of Wernicke – and that it must be regarded as a disorder of intelligence with particular manifestations in language. For Marie the motor component of aphasia described by Broca was only a dysarthria which happened to coexist with a true (Wernicke's) aphasia. Pick, whose early approach to aphasia followed the lines of the localisationist tradition, later became a representative of the psychological and linguistic analysis of the disorder. His work on agrammatism (1913) took the form of psychological dissection of the process of formulating and emitting a sentence. Von Monakow (1914) omitted the significance of functional localization of language skills in the brain because to his opinion most linguistic acts are the result of the interaction of various neuronal networks. His concept of "diaschisis" in fact arose from the widespread neuronal impact of any injury that has a depressing effect on functions far from the lesion site (Goodglass, 1988; Benson, 1988).

Henry Head (1926) wanted to establish a purely psychological taxonomy of aphasia. In his view, the underlying cause of all forms of aphasia is a disorder of symbolic formulation and expression which extends to non-verbal as well as verbal cognitive operations. He held aphasia as an impairment of intellect that might impact on any behaviour in which some symbol plays a part between its initiation and its completion. He presented a 4-way classification of aphasia illustrating

various partial disruptions of the symbolic capacity. His “verbal aphasia” most nearly corresponds to the traditional cortical motor or Broca’s aphasia, his “syntactic aphasia” to the traditional sensory or Wernicke’s aphasia, and a “nominal aphasia” which is close to Pitre’s concept of amnesic aphasia. Head also proposed a “semantic aphasia” which represented a new concept in classification: this disorder should spare the basic language skills of phonology, syntax and word retrieval, but is designated to interfere with the capacity to draw inferences and perceive relationship both on a verbal and non-verbal level (Goodglass 1988, Ahlsen 2006).

Kurt Goldstein (1878-1965), a psychiatrist and neurologist influenced by Gestalt theory and experimental rationalism, laid special emphasis on the extensive changes in the aphasic patient’s intellectual and adaptive capacities, which he considered to interact with and even determine the linguistic expression of their symptoms. The theme which runs through Goldstein’s interpretation of aphasia (1948) is the loss of capacity for “abstract behaviour, which entails among other deficits, the inability to deal with symbols, to make believe, or to shift from one task to another” (Goldstein 1948, in H. Goodglass, Handbook of Neuropsychology, 1988, Vol.1, Chapter 13, p. 255). In Goldstein’s opinion the loss of abstract behaviour explained a number of specific symptoms, such as agrammatism (because of the “abstract” nature of grammatical morphemes) and the inability to name. Goldstein interpreted amnesic aphasia, which seemed to coincide with an inability to sort and categorize colours and objects, as a disorder of naming caused by the patient’s inability to designate an object name as an abstract attitude assigned to the object. He believed that the amnesic aphasic patient might occasionally refer to objects by name, but for the patient, the name was functionally the same as the object. Goldstein by no means reduced all of aphasia to the principle of a loss of abstract behaviour; he used the term “instrumentalities of language” to refer to the various components of language use that could be affected in the various forms of the disorder: articulation, syntax, reading, writing and the subskills associated with them. Goldstein’s taxonomy of language disturbances differed little from the set of syndromes proposed by the Wernicke-Lichtheim-model. However, he did not acknowledge the connectionist interpretation of conduction aphasia nor that of

transcortical aphasia. In his view the latter described non-linguistic impairment affecting the initiation of speech (Goodglass 1988, Ahlsen 2006, Tesak 2008).

Theophile Alajouanine (1890-1980) was the leading French aphasiologist in the years before WW II, he was the first neurologist to enlist the collaboration of a psychologist and a linguist in an interdisciplinary study of a particular aphasic disorder: that of articulatory breakdown in aphasia. This was the beginning of the neurolinguistic approach which has seen its full development in the post-war period. Alajouanine put great effort in the study of the psycholinguistic features of aphasia, along with their anatomical foundations, and gained influence through his training and collaboration with other neurologists (Goodglass 1988).

1.1.4 Post War Period

The Second World War had both direct and indirect effects on major movements in aphasiology. In the United States the flow of patients with brain injuries and language impairment into the Veterans hospitals raised a demand for treatment and rehabilitation that was met on a previously unprecedented scale. Granted by funds for rehabilitation and research, large numbers of psychologists and speech pathologists, schooled in experimental and quantitative research methods joined the research field of aphasiology. Both professions were committed to understanding and treating the effects of brain damage. Perhaps the most important new influence in this period was the participation of experimental psycholinguists and cognitive psychologists in formulating the questions that were asked. In the beginning of the 20th century a retreat from the anatomical connectionism of the late 19th century could be observed. Administering various standard test batteries for language and cognitive abilities, a number of competing views on aphasia emerged differing regarding the rationale and content of the authors' batteries (Goodglass 1988, Ahlsen 2006, Tesak 2008).

Hildred Schuell for example, was an American speech pathologist and director of one of the large veterans' aphasia rehabilitation programs. She promoted the systematic study of speech errors of aphasics and was very influential

as a teacher of speech pathologists and in establishing training programs for aphasics. She invented the `Minnesota Test for the Differential Diagnosis of Aphasia' in 1953. With James J. Jenkins, a psychologist, she published the results of a factor analysis of the Minnesota Test, which made the authors propose that a single general language factor accounts for all of the deficits of aphasic patients. Schuell suggested a 5-category typology of aphasia which was based in part on the combination of language difficulties with sensorimotor problems but neither considered psycholinguistic nor anatomically based variables. It had limited acceptance and did not survive (Goodglass 1988).

Roman Jakobson was a Russian-born linguist, associated with the Prague school of linguistics, who became influential for analysing some basic properties of language and their manifestation across a wide range of language-related human activities. His concept of the phoneme as a bundle of distinctive features became one of the fortifications of modern phonology. Jakobson's idea was to examine how language development and language breakdown depicted the operation of universal principles of language. In his 1941 published monograph "Kindersprache, Aphasie und allgemeine Lautgesetze" he pointed out parallels between linguistic universals, children's language development, and symptoms of aphasia. He suggested the order of acquisition of speech sounds by children is the same as the prevalence of these sounds across the languages of the world, and the inverse of the order in which they break down in aphasia. In his view, the first sounds which one acquires are the last to be lost to brain damage and the most likely to be part of the phonemic repertory of every spoken language. Although this theory had not withstood clinical observation, it marked a qualitatively new level of integration in which biological phenomena and linguistic principles are seen as having a common core. At this point Jakobson was the only linguist to systematically describe aphasia within the structuralist framework. In his monograph, shared with Morris Halle (Jakobson and Halle 1956) he proposed two opposing patterns of aphasia, termed `similarity disorder´ and `contiguity disorder´. These represented impairments in `paradigmatic´ functions (associations of a referent to a symbol) and `syntagmatic´ functions (juxtaposition of terms into a grammatical string). In their view, the prototype of `similarity disorder´ would be the aphasic syndrome of anomia in

which syntax is preserved but retrieval of names is impaired. `Contiguity disorder´ would be represented by agrammatism. Jakobson developed the logical implications of the concept of `contiguity disorder´ to account for and even predict the character of agrammatic speech: utterances which were free of syntactic links or implications (e.g. free standing nouns) should be best preserved, whereas in inflected languages the nominative would replace oblique case endings of nouns, and inflections signalling syntactic relations would be more vulnerable than those marking number or gender (Goodglass 1988, Benson 1988, Tesak 2008).

Joseph Wepman, an American psychologist whose military service in caring for brain-injured patients brought him into the field of aphasiology considered the types of aphasia entirely in terms of psycholinguistic functions, without reference to neuroanatomical correlates. Wepman and Jones (1961) suggested an aphasia examination, in which language operations could be defined in terms of the combination of sensory input and motor output channels that they sampled. Factor analyses of scores from patients tested with this procedure revealed five dimensions of language that could be autonomously damaged. These were: visual-to-oral transmission, aural-to-oral transmission, aural-to-graphic transmission, and matching to oral or visual stimulation (Ahlsen 2006).

Luria's approach to the analysis of aphasias (Higher Cortical Functions in Man 1966, Traumatic Aphasia 1970) put the emphasis on impairment of motor articulatory aspects of language, associated with injury to the anterior language zone, and the emphasis on disorders involving auditory language processing and the association of sound to meaning, arising from lesions of the temporal lobe. Luria however introduced distinctions within the sensory and motor categories that resulted from both his analysis of their symptomatology and from his conception of the functional interaction between the primary cortical analyzers, the associated secondary and tertiary fields surrounding them, and the role of feedback in controlling and correcting performance. In his opinion motor aphasia can be separated into afferent and efferent subtypes related to the immediately postrolandic zone and to the traditional Broca's area, respectively. Luria held that afferent (or kinaesthetic) motor aphasia, was due to a breakdown of sensory feedback controlling articulatory movements, and resulted in difficulties realizing

individual articulatory positions, while efferent motor aphasia manifested in difficulties in moving from one position to the next. Regarding receptive aphasias, Luria distinguished between sensory acoustic aphasia of the posterior superior temporal gyrus and sensory amnestic aphasia of the middle and inferior temporal gyri, particularly at the temporo-parietal junction. He attributed the difficulty underlying the sensory-acoustic form to a breakdown in `phonemic hearing´, i.e. loss of the ability to distinguish the individual sounds of the speaker's language. Luria proposed that the amnestic form was due to an instability or `alienation` of the semantic value of the word, although speech sound discrimination was intact. Luria's typology included two more forms of aphasia of which one, frontal `dynamic aphasia`, is close in symptomatology to the transcortical motor aphasia of the classical school, and the other, `semantic aphasia`, is very close to the disorder described earlier by Head (1926) under the same name. Dynamic aphasia is described by an absence of spontaneous initiation of speech and impairment to formulate ideas, which is assigned by Luria to the impact of injury of the prefrontal cortex on self-initiated behaviour. Semantic aphasia, as Luria conceived it, is due to an impairment to seize and manipulate the relationships between concepts, caused by parieto-occipital injury. It is associated with disorders of calculation and of visuospatial processing and reveals itself in language by the inability to process logico-grammatical relations and by an impoverishment of word semantics due to a decline of the network of meaning relationships of individual words. In contrast to the classical associative scheme Luria avoided the concept of disconnection between centers and its theoretical consequences. Although the preservation or impairment of repetition played no special role in his model, he explicitly rejected the existence of conduction aphasia. In his view, impairment of repetition is to be found in both forms of motor aphasia and in both forms of sensory aphasia and belongs to the basic deficit specific to each syndrome. While laying emphasis on careful analysis of neural physiology in the interpretation of disorders of language and other higher functions, Luria was aware of the psychological and psycholinguistic factors that cannot be accounted for in terms of functional neuroanatomy (Goodglass 1988, Benson 1988).

Norman Geschwind was also well experienced in contemporary contributions of psycholinguistic studies and of aphasic symptomatology that called for characterisation in linguistic terms. Unlike Luria, his major theme focussed on the symptoms that could be accounted for in terms of the transmission of information between the sensory and motor processing centres. It was him who rediscovered associationism and made it known as “connectionism”. Geschwind and Kaplan in `A Human Cerebral Disconnection Syndrome´ (1962), revitalized the syndrome of the corpus callosum, emphasizing Liepmann’s first description of interhemispheric disconnection caused by a natural lesion. For the first time unilateral tactile anomia was described, attributed to the disconnection of tactile information reaching the right hemisphere from the language zone of the left hemisphere. At the same time Gazzaniga, Bogen and Sperry (1962) reported analogous effects in the visual modality after surgical section of the callosum through the splenium. In his influential 1965 paper on disconnection syndromes, `Disconnection syndromes in animals and man`, Geschwind drew on the obvious anatomo-behavioural relationships of the callosal syndrome as a model for intrahemispheric disconnection which in his view also accounted for conduction aphasia and apraxia. With this article and his 1968 paper with Quadfasel and Segarra on isolation of the speech area he highlighted clinico-anatomical evidence in support of the classical typology of aphasia, as schematized in the Wernicke-Lichtheim diagram. Geschwind was also responsible for the introduction of the terms `non-fluent` versus `fluent` to characterize the two major subclasses of aphasic syndromes. While the conceptual roots of this polarity reached back to descriptions of virtually every aphasiologist, the simple directness of these terms and their correspondence to the anterior/posterior location of the lesion in the language zone quickly brought them into wide use, replacing the ambiguous terms `expressive´ versus `receptive´. Furthermore, Geschwind established the concept of the posterior parietal lobe as an intermodal convergence area, which integrates associations between auditory, visual and other channels of experience. Geschwind argued that this capacity to respond to symbols in the absence of immediate limbic reinforcement is unique to man. He emphasized the role of white matter tracts in bringing the various information sources together, a feature which permitted

describing selective impairments in terms of intrahemispheric disconnections. This postulation not only provided clinical support for Lichtheim's view of conduction aphasia as an intrahemispheric disconnection syndrome, it also added anatomical justification to the argument that transcortical aphasia was based on disconnection of the Broca-Wernicke area complex from other parts of the left hemisphere. The Wernicke-Lichtheim diagram had schematized this disconnection as cutting the links between a `concept center` and either the auditory input or motor output centres. For Geschwind, such a disconnection would be a result of an extensive destruction of tissue concentric to the speech area, produced by a border zone infarct or a severe anoxic lesion. Geschwind put great effort in promoting a clinico-anatomical correlation, i.e. the detailed correlation of lesion sites, revealed by modern imaging techniques with specific components of aphasic syndromes (Goodglass 1988, Ahlsen 2006, Tesak 2008).

So, from the middle of the 20th century on the approaches to aphasia changed in many ways: semi-anecdotal accounts of single cases gave way to formal controlled experiments, commonly on groups of patients, but occasionally experiments in depth on single cases of particular interest. Standards of statistical significance were demanded. New methods of neuroimaging, electroencephalography, and the experimental use of event related potentials allowed better insight to brain lesions than ever before. Models of language processes or language impairment were used as the basis for explicit, testable productions and aphasia became a testing ground for theories derived from normal language. These new approaches did not replace earlier taxonomies in the field of aphasia but sharpened the awareness of inconsistencies and inaccuracies in existent taxonomies and the need to modify them. A topic of investigation that has had an extensive overlap with aphasiology is that of cerebral dominance. The introduction of the non- invasive techniques of dichotic listening (Kimura 1961), visual half-field presentation (Mishkin and Forgays 1952) and event-related potentials (Morrell and Salamy 1971) was the first opportunity to group studies of normal subjects, unilaterally brain-damaged patients and patients who had undergone callosal sections. The contribution of the right hemisphere to the language capacity had become a topic of research and led to the decomposition of language use into

prosodic aspect, its pragmatic value, and its affective dimension, in addition to the traditional factors of phonology, lexicon and semantics (Goodglass 1988, Ahlsen 2006, Tesak 2008).

Post-war experimental neuropsychology is represented by various experts in many countries. Italian neuropsychology is best represented by Ennio De Renzi, who also founded the Journal Cortex in 1964. With Vignolo he devised the popular Token Test for auditory word comprehension. The leading German laboratory for aphasiology was under Klaus Poeck in Aachen. In the United States, Harold Goodglass and Norman Geschwind were identified with the `Boston School` of aphasiology, they led the way to the application of experimental psycholinguistics to problems of auditory word and sentence processing, agrammatism and naming disorders. The Boston Diagnostic Aphasia Examination (Goodglass and Kaplan 1983) represented the assumptions of the classical taxonomy of aphasia, along with contemporary psycholinguistic and measurement principles.

This development over centuries resulted in the classification of aphasia syndromes as they are now known and accepted by clinicians and the scientific community.

2. Classification of aphasias today

As Benson (1988) puts it “The clinical/anatomical classification of aphasias depends on clusters of symptoms which are called syndromes”. Syndromes are a theoretical construct and consist of an assembly of clinical findings that “tend to occur together and therefore suggest a common underlying disorder” (p. 269). As it comes to aphasias, up until today no uniform international classification has been made up so far.

There are 4 big different schools that have dealt with the classification of aphasias, the French school, the Russian school, the German school and the Anglo-American school. Their classification systems have become accepted to various degrees. In German-speaking regions aphasias are classified according to the work from Leischner (1979), Poeck (1983, 1975) and Huber (1983). Leischner distinguished global aphasia, mixed aphasia, motor amnesic aphasia, sensory amnesic aphasia, central (conduction) aphasia, semantic aphasia and remains of aphasia which means residual states of aphasias which cannot be clearly assigned to one of the cited syndromes. Today widely accepted in German-speaking regions is the concept of aphasias by Poeck and Huber. They distinguish Broca’s aphasia, Wernicke’s aphasia, global aphasia and amnesic aphasia (in the anglo-american world also known as anomia or anomic aphasia or nominal aphasia). In addition to these standard syndromes Poeck and Huber described two special forms of aphasia, namely conduction aphasia and transcortical aphasia (sensory transcortical, motor transcortical and mixed transcortical aphasia). This classification has been especially accepted also because of the widespread application of the Aachener Aphasie-Test. Nevertheless, the aphasia syndromes have been critizised as weak by many authors because they describe features that can be produced by more than one site of brain damage. They do, however, aid the clinician and have been useful for investigations of brain-language correlations (Benson 1988, Biniek 1993).

However, the classification of aphasia has many inadequacies. A great number of aphasic patients cannot be clearly assigned to a syndrome. Additionally, in the acute phase manyaphasias present with combinations of symptoms

inconsistent with one of the classic syndrome, but these combinations may be transient. A delay of at least 3-4 weeks following the onset of aphasia may be necessary before sufficient stability in the language pattern is reached to allow placement in one of the aphasic syndromes.

An additional problem in classifying individual aphasics is that many patients have acquired more than one cerebral lesion, so the symptoms are based on several anatomical loci. Despite the above mentioned difficulties, aphasia syndromes provide valuable features for language and aphasia studies because the classification is supported by more than a full century of correlation of the clinical syndromes with anatomical localizations. The original studies using post-mortem data have been both confirmed and supported in recent years by modern brain imaging techniques as computed tomography, magnetic resonance imaging, positron emission tomography and radioisotope brain scans. So, as these syndromes provide strong brain-function correlation information they remain an important tool for linguistic and neuropsychological studies of language. Also, the syndrome approach represents a useful tool for the physicians and therapists caring for patients suffering from aphasia. They offer a proven diagnostic approach and a format for communication (Benson 1988, Hartje und Poeck 2006, Huber und Poeck 2006).

2.1. Aphasia Syndromes

2.1.1 Broca's aphasia

This aphasia syndrome has been called motor aphasia, expressive aphasia, efferent motor aphasia, anterior aphasia and frontal aphasia.

Broca's aphasia is a disorder with strikingly nonfluent verbal output: the general appearance of speech is telegraphic, as Benson (1988) puts it due to "limited number of words per minute, considerable effort in word production, disordered articulation, short-phrase length, abnormal prosody, relatively uncommon paraphasic substitutions" (p. 270), agrammatic especially with a relative decrease in number of relational words and the absence of inflected words. In many cases no grammatical structure can be found and words are just arranged according to their content. The prosody of speech is also disturbed; the melodic contour of spoken language is flat. Patients with Broca's aphasia often pause and produce many interjections. Gestures and facial expression often suggest great distress and unhappiness. Comprehension of spoken language seems on the other hand relatively well preserved, although formal testing reveals that it is never entirely intact. In particular, the understanding of syntactical structures and the sequencing of verbal material are deranged. Though it seems that patients with Broca's aphasia are able to compensate for their handicap in conversation, they have good interpretation of gestures and facial expression. Furthermore one can find a clear disturbance in repetition and naming (phonemic and semantic paraphasias), though additional help like contextual aid or phonetic prompting may be supportive. So while a patient with Broca's aphasia usually fails to name on confrontation, production of the name can be frequently prompted by offering the beginning sound or an open-ended sentence in which the name of the object would be used. Reading is nearly in all cases disturbed in a way that the patient reads, both aloud and for comprehension, meaningful content words but omits grammatical words. Also writing is invariably disturbed, paragraphias that match the phonemic paraphasias in spoken language and agrammatic structure of sentences can be

found. Most patients with Broca`s aphasia have a right-sided weakness, varying from mild paresis to total hemiplegia, additionally sensory loss may accompany the syndrome (Benson 1988, Brandt et al. 2003, Hartje und Poeck 2006, Huber und Poeck 2006).

2.1.2 Wernicke's aphasia:

"The second most widely recognized aphasic syndrome is named after the first person to define it, Carl Wernicke (1874). This cluster of findings has also been called sensory aphasia, receptive aphasia, central aphasia, acoustic-amnestic aphasia, and other names" (Benson 1988, p. 271).

Wernicke's aphasia features a fluent verbal output with normal word count and phrase length. The number of words presented ranges from low normal to excessive (logorrhoea). There are no effort, or articulatory problems, neither prosodic difficulties, but difficulties in word finding exist and language is almost always contaminated by paraphasic substitutions (semantic and phonemic), neologisms or additional syllables may be put to the end of words (augmentation). The number of paraphasic substitutions may be so great that the output, then termed jargon aphasia, is unintelligible. The most striking abnormality of Wernicke's aphasia is a disturbance of comprehension, which may range from a total inability to understand spoken language to a partial difficulty in understanding. Even though the pragmatic rules of turn taking in conversations may be preserved, patients suffering from Wernicke's aphasia may be talking at cross-purposes at all in a conversation. The ability to repeat reflects the limitations of comprehension. Syntactic structure appears less disturbed than in Broca's aphasia, but it is reasonable to say that both Wernicke's and Broca's aphasics exhibit some form of paragrammatism. agrammatism. Confrontation naming is almost always abnormal (semantic and phonemic paraphasias or neologisms), prompting is, in opposition to patients with Broca's aphasia, of little help. In many cases patients tend to describe attributes or the handling of the shown object. Many perseverations can be found, sometimes the target word can be reached by approaching semantically or

phonematically similar words (conduit d´approche). In general, both reading and writing are disturbed. The syndrome may be accompanied by right-sided hemiparesis, although infrequent or transient, and right visual field defects (Benson 1988, Hartje und Poeck 2006, Huber und Poeck 2006, Brandt et al. 2003).

2.1.3 Global aphasia

A severe language impairment in which all modalities – verbal output, comprehension, repetition, naming, reading and writing – are seriously impaired is known as global or total aphasia. Propositional speech may be reduced to a few words, the remainder of verbal communication consisting of emotional exclamations and serial utterances. Verbal stereotypes are frequent, e.g. a single word or a syllable used consistently (recurring utterances), and may be used for limited communication. In addition, non-verbal language, e.g. gestures or melody of the utterances may be relatively functional. Besides recurring words or syllables there may be words altered in phonetic structure which are not part of the native language itself anymore, these are called phonemic neologisms. Often, some automatic speech activities like counting are surprisingly preserved in patients with otherwise global aphasia. Auditory comprehension is often reduced to a variable number of nouns and verbs, while the comprehension of functor words or of syntactically organized sentences is virtually negligible. Most patients respond to some aspects of verbalization, but are far more influenced by gesture or prosodic aspects of language. Repetition is also severely disturbed and contaminated with phonemic paraphasias and perserverations. In most cases, these patients suffer from severe hemiparesis or hemiplegia (Benson 1988, Brandt et al. 2003, Hartje und Poeck 2006, Huber und Poeck 2006).

2.1.4 Anomic Aphasia

The term amnesic aphasia is widely used in the German-speaking region while in the Anglo-American world anomic aphasia or nominal aphasia is more common.

Patients suffering from amnesic aphasia do not have problems with identifying objects, persons, actions or attributes but they have trouble retrieving the appropriate word from their lexicon. The difficulty in word finding causes multiple pauses, a tendency to circumlocution, and a somewhat stumbling verbal output. In principle the output is fluent, has normal phrase length and articulation is not affected, with repetition and comprehension relatively intact, but naming to confrontation is significantly disturbed. Semantic or phonetic cueing may be helpful, though. Patients suffering from amnesic aphasia present mainly semantic, to lesser degree also phonemic paraphasias whereas the semantic parpahasias in most cases are within a narrow semantic field to the target word. Most patients monitor themselves appropriately and realize their mistakes; the patient, aware of his paraphasic errors, may produce repeated approximations of the intended word, as if he is trying to untangle it. This may end up in a somewhat halting flow of words or aborted sentences. Many patients develop compensatory strategies and tend to circumscribe the target word, add gestures or invent replacemental words. Auditive comprehension is not disturbed, reading and writing may be altered to some degree. Some authors interpret this syndrome also as a common residual following improvement from other types of aphasia (Benson 1988, Brandt et al. 2003, Hartje und Poeck 2006, Huber und Poeck 2006).

2.1.5 Conduction Aphasia

Conduction aphasia features in principle a fluent verbal output in combination with an interrupted quality due to plenty of word finding pauses. Patients show good ability to comprehend, but severe disturbance in repetition which dominates words and sentences. Usually the patients repeat words with phonemic paraphasias, but often they omit or substitute words, and they may fail to repeat anything at all if function words rather than nouns are requested. Error awareness is frequent with attempts of the patients to correct themselves. This combined with commonly found phonemic paraphasias create the image of dysprosody. Comprehension of spoken language seems relatively preserved. Patients with conduction aphasia though have difficulties with understanding long and complex sentences because

they can comprehend the nouns and verbs in a sentence, but would not be able to understand grammatical morphemes such as prepositions and conjunctions. Also, naming tends to be limited by paraphasic intrusions, substitution or omission of syllables and words. Also patients may distort words by adding syllables or sounds to a word which are called intrusive additions. The patient may insist that the correct name is known but he or she cannot produce it correctly. Reading aloud is severely disturbed, but reading comprehension may be fully normal. Writing is often abnormal, based on substitution, omission or altered sequence of letters or words. Conduction aphasics often have some accompanying motor signs as paresis of the right side of the face and of the right upper extremity. Visual field defects are variable, cortical sensory loss is frequently present (Benson 1988, Brandt et al. 2003, Hartje und Poeck 2006, Huber und Poeck 2006).

2.1.6 Transcortical aphasias

As the exploration of aphasia syndromes increased in complexity during the last two centuries, cases with true aphasia but intact repetition were noticed. Originally called transcortical aphasia (Wernicke,1881), these aphasia syndromes were later defined by Goldstein (1917). Three major entities have been classified – transcortical motor aphasia, transcortical sensory aphasia and mixed transcortical aphasia (isolation of the speech area). The major factor underlying the transcortical aphasias is preservation of the ability to repeat spoken language in the face of distinct language impairment (Benson 1988, Brandt et al. 2003, Hartje und Poeck 2006, Huber und Poeck 2006).

2.1.6.1 Transcortical sensory aphasia

According to Goodglass and Kaplan (1983) transcortical sensory aphasia features significant comprehension disorder, a fluent but often paraphasic verbal output and good ability to repeat while a severe impairment of auditive comprehension can be observed. Patients can repeat very long, complicated utterances. Also, automatic speech is very good and they can produce lengthy chunks of memorized material like prayers and song lyrics if they can be made to understand the task. In addition, patients may echo their conversation partners in such a way that they sound as if they do understand language and are participating in the conversation. Within the repeated phrases, phonology and prosody are intact. Also reading comprehension is seriously disturbed and reading aloud is often defective, also the patients cannot write intelligibly (Benson 1988, Brandt et al. 2003, Hartje und Poeck 2006, Huber und Poeck 2006).

2.1.6.2 Transcortical motor aphasia

Transcortical motor aphasia resembles Broca`s aphasia, patients suffer from non-fluent output, troubled by phonemic and global paraphasias, perseveration and loss of connective words which changes dramatically concerning repetition. They are able to repeat fluently even though their spontaneous verbal output is sparse, takes considerable effort and is of shortened phrase length and dysprosodic. The patient will have great difficulty initiating and organizing responses in conversation and will be unable to answer highly structured questions. Comprehension of spoken language is relatively intact, but the handling of more complex sentences and sequences may be disturbed. Repetition is accurate up to a certain span level which may be somewhat short. Naming is relatively preserved but patients often need articulatory prompts, contextual or phonemic cues. Reading comprehension is relatively intact and the patients often read aloud with only minimal difficulty. In opposition writing is almost invariably disturbed (Benson 1988, Brandt et al. 2003, Hartje und Poeck 2006, Huber und Poeck 2006).

2.1.6.3 Mixed transcortical aphasia

Mixed transcortical aphasia features a combination of the motor and sensory forms: the patient presents with severe impairment except for preservation of the ability to repeat. The ability to handle speech signals but inability to interpret the language therein resulted in the use of the term `isolation of the speech area´ (Goldstein 1948, Geschwind et al. 1968) for the disorder. Intact repetition stands in sharp contrast to total failure of all other language functions including naming, reading and writing. The patients present with little spontaneous output, but when spoken to, may respond with a short fluent verbalization. The response is an almost direct repetition of the examiner's words, true echolalia. Spoken language is not understood, even though the patient can repeat accurately, up to a certain span level, the word said by the examiner (Benson 1988, Brandt et al. 2003, Hartje und Poeck, 2006, Huber und Poeck 2006).

2.2. Neuroanatomical foundations of the Aphasias

Over the past centuries many researchers have sought to determine the neuroanatomical correlates of language and aphasia. Damasio (1998) argued that "the history of cerebral localization of the aphasias begins with Broca's discovery of a relation between a disturbance of language and damage to the lower posterolateral aspect of the left frontal lobe by Paul Broca" (p. 43). With this postulation Broca on the one hand created awareness for the asymmetry of the brain regarding language, in other words he laid the ground for the concept of cerebral dominance, on the other hand he "prepared the groundwork for further correlations between acquired aphasia and cerebral lesions. The next historical step came with Wernicke's report (1874) of the association between the symptom complex of Wernicke's aphasia and damage to the posterior aspect of the first left temporal gyrus. This finding strengthened the notion of left cerebral dominance for language, and helped establish the concept that varied pathological behaviours could be related to different brain lesions (Damasio 1998, p. 43-44). Wernicke even

went so far to predict the anatomical lesion responsible for a third aphasia type, conduction aphasia. In his opinion, the affected anatomical structure would lie between the lesions responsible for Broca's and Wernicke's aphasia and assigned the localization to the insular region.

During the following 100 years many studies were conducted which basically confirmed the innovative findings noted above, but more detailed correlations between lesion localization and aphasia were not possible until the introduction of modern cerebral imaging to the field of aphasiology. Damasio (1998) argued that "the advent of computerized tomography (CT) in 1973 changed the way of anatomical studies of higher cognitive functions in man dramatically and was particularly beneficial for the field of aphasia. CT provided the possibility of studying with considerable anatomical detail not only a large variety of cerebral lesions but also the surrounding intact cerebral tissue" (p. 46). In the 1980s an even more powerful technique, magnetic resonance imaging (MRI) was used to detect morphological abnormalities in the living tissue and achieved an unexampled insight to anatomical structures in living individuals. . So called functional neuroimaging has emerged over the last decades as powerful new tool to provide data regarding the localization of language processing in healthy subjects. For example functional magnetic resonance imaging (fMRI), positron emission tomography (PET) with radiolabeled deoxyglucose and single proton emission computed tomography (SPECT) have been used to identify regions of cerebral hypometabolism in patients, for correlation with language deficits. The regions of hypometabolism so identified are typically much larger than those in which necrosis is visible on CT or MRI

Clinical studies indicate that the association cortex in the region of the sylvian fissure is responsible for language processing in the auditory-oral modality. This region includes the posterior half of the pars triangularis and the pars opercularis of the third frontal convolution (Broca's area), the association cortex in the opercular area of the precentral and postcentral gyri, the supramarginal and angular gyri of the parietal lobe, the first temporal gyrus from the supramarginal gyrus to a point lateral to Heschl's gyrus (Wernicke's area), and possibly a portion of the adjacent second temporal gyrus. Language in the visual-gestural modality in deaf people is also based in the perisylvian cortex, although it may recruit more superior regions

of cortex in frontal and parietal lobes as well. Written language is a secondary development that depends on instruction and appears to involve areas of the brain that are more closely associated with visual processing. The supplementary motor area is the only other cortical structure that has been suggested to play a role in language processing. Several subcortical nuclei have also been suggested to play a role in language. These include the thalamus, the caudate, and possibly parts of striatum. White matter tracts are thought to play important roles on transmitting the products of processing in one cortical area to another and to lower motor centers (Benson 1988, Brandt et al. 2003, Hartje und Poeck 2006).

2.2.1. Broca's aphasia

When a patient presents with the syndrome of Broca's aphasia brain lesion "involving the posterior inferior frontal lobe of the dominant (almost always left) hemisphere can be anticipated" (Benson 1988, p. 279). The lesion affects the third frontal convolution (both the gyrus and the sulcus) of the left frontal lobe. This location is called Broca's area and corresponds to Brodmann's areas 44 and 45, making up the lower part of the pre-motor cortex. The size of the lesion varies greatly, however. The pathology involves either only the cortical layers and/or subcortical structures immediately underlying Broca's area, or a larger lesion not only involving the posterior inferior frontal cortex but in addition, extending into underlying white matter and basal ganglia as well as the insula and internal capsule can be observed. According to Goodglass and Kaplan (2001) the damage often extends down into the white matter and, in some cases, extends posteriorly to the most inferior part of the motor strip. It has been suggested by Alexander et al. (1986) that "Broca's aphasia is not a true clinical entity [], rather, it represents a combination of distinct and separable frontal cortex and basal ganglia speech and language disturbances. Variations in Broca's aphasia symptomatology would be based on the combination of separable disorders included" (Benson 1988, p. 271).

2.2.2 Wernicke's aphasia

Damasio (1998) explains that "the core of the lesions in Wernicke's aphasia maps to the posterior region of the left superior temporal gyrus" (p. 49). Classically, Wernicke's aphasia is associated with brain damage involving the posterior superior portion of the temporal lobe of the dominant, almost always the left, hemisphere, also called Wernicke's area, corresponding to Brodmann's areas 21, 22 and 42. The lesion often extends into the parietal lobe, affecting the angular gyrus (Brodmann's area 39). It has been argued by various authors that "extension more medially in the temporal lobe is associated with a greater degree of word deafness, more posteriorly (toward the inferior parietal region) with a greater degree of word blindness" (Benson 1988, p. 272). So, based on the size of the lesion and the direction of extension of brain damage, considerable variation can be anticipated in the clinical findings of Wernicke's aphasia (Benson 1988, Szentagothai 1993, Williams 1999, Brandt et al. 2003, Hartje und Poeck 2006).

2.2.3 Global aphasia

Global aphasia almost always indicates a large lesion involving much of the perisylvian area of the language-dominant hemisphere, often as the result of an infarction in the territory of the left middle cerebral artery. Damasio 1998 specifies:"All of the perisylvian language areas are involved. The damage extends from Brodmann's areas 44 and 45 anteriorly to prefrontal cortices, as well as posteriorly to the insula, to auditory areas 41, 42, and 22, to area 40, and in part to areas 39 and 37. The motor and somatosensory areas 4, 3, 1, and 2 are also involved. The damage however, is not limited to the cortex: the underlying white matter is involved as well as part of the lenticular and the caudate nuclei "(p. 58) . This syndrome can also be due to ischemic infarction in the vascular border zones of the frontal lobe including Broca's area and the temporo-parietal junction region affecting Wernicke's area. In patients with persistent global aphasia but few associated neurological findings (e.g. hemiparesis or hemiplegia, sensory loss or

visual field defects) it was initially hypothesized that the pathological tissue defect could be found only in the perisylvian cortical structures including both Broca's area and Wernicke's area but Damasio (1998) holds that "one other anatomical pattern in global aphasia is that of a patient with a lesion in the left frontal operculum, underlying white matter, basal ganglia, insula, and even part of the parietal operculum, but it spares the temporal lobe"(p. 60-61). (Benson 1988, Szentagothai 1993, Williams 1999, Brandt et al. 2003, Hartje und Poeck 2006).

2.2.4 Anomic aphasia

According to Goodglass and Kaplan (1983) amnesic aphasia can be localized with the least reliability of any of the aphasic syndromes. It seems that damage to the left anterior temporal cortices is essential. Whether anomic aphasia can arise out of a middle and anterior temporal lesion alone, without involvement in structures anterior to it, remains unclear at this point. The angular gyrus may also be affected which results in alexia and agraphia (Benson 1988, Szentagothai 1993, Williams 1999, Brandt et al. 2003, Hartje und Poeck 2006).

2.2.5 Conduction aphasia

The clinical syndrome of conduction aphasia is associated with brain lesions that affect the arcuate fasciculus, a bundle of white matter fibre tracts lying below the supramarginal gyrus in the temporal lobe connecting cortical areas (Broca's and Wernicke's) within one hemisphere, in this case located in the dominant, almost always left, hemisphere. Any lesion causing disconnection of the above mentioned cortical regions responsible for Broca's or Wernicke's aphasia is capable to produce the clinical features of conduction aphasia. In terms of Brodmann's areas, "conduction aphasia is associated with left perisylvian lesions involving the primary auditory cortex (areas 41 and 42), a portion of the surrounding auditory association cortex (areas 21 and 22), and to a variable degree the insula and its subcortical white matter as well as the supramarginal gyrus (area 40). Not all of these regions

need to be damaged in order to produce this type of aphasia. In some cases without involvement of auditory and insular regions, the compromise of area 40 is extensive. In others the supramarginal gyrus may be completely spared and the damage limited to insula and auditory cortices or even to insula alone" (Damasio 1998, p. 46). For many years the existence of this syndrome was controversial, but with upcoming improvements of imaging techniques, conduction aphasia has been recognized as relatively common, although the underlying pathology is less specific as originally thought, it stands in line with the hypothesis proposed by Wernicke (Benson 1988, Szentagothai 1993, Williams 1999, Hartje und Poeck 2006, Brandt et al. 2003).

2.2.6 Transcortical aphasia

2.2.6.1 Transcortical sensory aphasia

Transcortical sensory aphasia is associated with involvement of the posterior cortical border zone particularly that between the middle cerebral artery and posterior cerebral artery on the left side, the watersheds of the cerebral blood supply in this region. Both damage to the cortical tissue layers as also damage to deeper subcortical structures may be present. In most cases the brain areas affected focus at the parieto-temporal junction, posterior to Wernicke's area with extension to more inferior and/or posterior areas, such as the posterior sector of the middle temporal gyrus (Brodmann's area 37) and the angular gyrus (Brodmann'sarea 39) as well as lesions in Brodmann's area 22 in the superior temporal gyrus which is never entirely affected in this type of aphasia. The same applies to the primary auditory cortices (Brodmann's areas 41 and 42) (Benson 1988, Szentagothai 1993, Williams 1999, Brandt et al. 2003, Hartje und Poeck 2006).

2.2.6.2 Transcortical motor aphasia:

Original descriptions of transcortical motor aphasia emphasized involvement of the language-dominant frontal cortex, anterior and/or superior to Broca's area but leaving Broca's area intact. Lesions are typically smaller than those that cause Broca's aphasia and are either anterior or superior to Broca's area, either deep in the left frontal substance or in the cortex. The lesions are usually small and barely touch area 44 (Broca`s area). With development of better neuroimaging techniques and improved clinical testing it was demonstrated that transcortical motor aphasia also is due to infarction in the territory of the left anterior cerebral artery. Communication between Broca's area and the pre-motor or supplementary motor area (Brodmann's Area 6) is cut off, but sparing of Wernicke's area and the arcuate fasciculus repetition is good. This type of lesion may also be due to damaged links between Broca's area and the basal ganglia and/or the thalamus because of motor areas in the thalamus and the basal ganglia that may also have some kind of pre-motor function (Benson 1988, Szentagothai 1993, Williams 1999, Brandt et al. 2003, Hartje und Poeck 2006).

2.2.6.3 Mixed transcortical aphasia

Brain lesion in mixed transcortical aphasia affects the border zone between the middle cerebral artery territory and the anterior and posterior cerebral artery territories. The damage involves not only cortical but also subcortical tissue. It is thought that sparing of the immediate perisylvian structures allows the speech signals to be accepted by the primary auditory area (Heschl's gyrus and Wernicke's area) and transmitted via the arcuate fasciculus to the motor speech area (Broca's area) for production of speech signals. Thus the patient accurately reproduces speech signals without comprehending them (as in repetition of a foreign language) (Benson 1988, Szentagothai 1993, Williams 1999, Brandt et al. 2003, Hartje und Poeck 2006).

2.3 Language, aphasias and neuroanatomical correlates: Opposing theoretical frameworks

Two opposite general positions regarding theories on the relationship between anatomical requirements and the language processing system can be taken, one based on a holistic view of neural function and one based on localizationist principles.

The basic theme of holistic or distributed theories of the functional neuroanatomy for language is that linguistic representations are distributed widely and that specific stages of linguistic processing recruit widely scattered areas of perisylvian association cortex. That means that the brain works as a whole to accomplish higher cognitive functions. The evidence supporting holist theories consists of the ubiquity of general factors in accounting for the performance of aphasic patients. From an anatomical-based position the finding that multiple individual language deficits observed in patients with small perisylvian lesions, often in complementary functional spheres stands against the holist model.

Localism holds that various higher cognitive functions are localised in different centers of the brain, mainly cortical areas. These centers can be seen either as equipotential, or one center may be seen as superordinate to others. Additionally, associationism or connectionism adds the importance of, also anatomically existing, connections between different centers. The connectionist model of language representation and processing in the brain revived by Geschwind and colleagues in the 1960s and 1970s probably remains the best known localizationist model of the functional neuroanatomy of language. The basic connectionist model of auditory-oral language processing postulates three basic centers for language processing, all in cerebral cortex and could be described simply as follows: the first center, located in Wernicke's area, stores the permanent representations for the sounds of words. The second, located in Broca's area, contains the mechanisms responsible for planning and programming speech. These localizations were thought to evolve from the relationship of these areas of the brain to primary sensory and motor regions. The third center, diffusely localized in cortex in the nineteenth century models, stores the representations of concepts.

Geschwind proposed that parts of the inferior parietal lobe, namely the supramarginal and angular gyri, are the site at which the fibres projecting from sensory, visual, and auditory association cortices converge, and that as a consequence, associations between word sounds and the sensory properties of objects can be established in this area.

Language processing in this model involves the activation of linguistic representations in these cortical areas and the transfer of these representations from one center to another, largely by means of white-matter tracts. Functional neuroimaging has recently been used to study the regions of cortex that are activated during the performance of a number of language tasks by normal subjects. On the basis of these studies (e.g. Papanicolaou and Billingsley 2003, van Lancker Sidtis 2006), a number of localizations have been suggested and the study results are generally compatible with the result of deficit – lesion correlation. Overall, the picture that is beginning to emerge is that different components of the language processing system are localized in different parts of the perisylvian neocortex. The correlations between lesion sites and aphasic syndromes are far from perfect, however, even in vascular cases, and it can be observed that they become less reliable in other neurologic conditions (Cappa 1997, Benson 1988, Ahlsen 2006, Tesak 2008).

3. Subcortical structures

3.1 What are "subcortical structures"?

Subcortical structures consist of the thalamus and the basal ganglia which comprise the caudate nucleus and the lentiform nucleus. These anatomical structures are intersparsed with numerous white matter fibers which are involved in any grey matter subcortical lesion because of proximity.

3.2 Thalamus

The thalamus which measures about 3 cm in length consists of paired oval masses of grey matter organized into nuclei with interspersed tracts of white matter, lying "deep within the central and medial portions of each cerebral hemisphere. For the most part, the left and the right thalamus are separated by the third ventricle, a thin cavity containing cerebrospinal fluid. Within each hemisphere the putamen and globus pallidus, structures of the basal ganglia, are lateral and somewhat inferior to the thalamus. They are separated from the thalamus by a band of white matter, the posterior limb of the internal capsule. The head of the caudate nucleus, the other major structure of the basal gaglia, lies anterior to the thalamus, and the tail of the caudate nucleus is posterior and somewhat lateral to the thalamus" (Crosson 1984, p. 492).

The thalamus itself is not a homogenous structure, but consists of more than 30 anatomically and functionally separable nuclei. These can be divided into the following main nuclear groups: anterior (rostral) nuclei, medial nuclei, lateral nuclei, ventral nuclei, medial geniculate body, intralaminar nuclei, midline nuclei, and reticular nuclei. The thalamus is the principal relay station for somatosensory impulses that reach the cerebral cortex from the spinal cord, brain stem, cerebellum and other parts of the cerebrum. The nuclei within each half of the thalamus have various roles. Some relay impulses to sensory areas of the cerebrum: the medial geniculate body relays auditory impulses; the lateral geniculate nucleus

relays visual impulses; and the ventral posterior nucleus relays visual impulses; the ventral posterior nucleus relays impulses for taste and somatic sensations such as touch, pressure, vibration, heat, cold and pain. Other nuclei relay impulses to somatic motor areas of the cerebrum: the ventral lateral nucleus receives impulses from the cerebellum, and the ventral anterior nucleus receives impulses from the basal ganglia. The anterior nucleus in the floor of the lateral ventricle is concerned with certain emotions and memory. The thalamus, especially the median nucleus also plays an essential role in awareness and in the acquisition of knowledge, namely storage of learning in long-term memory (Szentagothai 1993, Williams 1999, Brandt et al. 2003).

Regarding the role of the thalamus in language, mainly lesions of the ventral group of nuclei and the pulvinar have been related to language dysfunction. Also, Crosson postulated that certain nuclei within the lateral nuclear complex would be especially apt to play a role in language than other nuclei because these structures, the ventral lateral nucleus, the pulvinar and ventral anterior nuclei, project to and receive input from the motor cortex, the premotor cortex and the temporoparietal cortex. The anterior and lateral nuclei of the thalamus are the main thalamic target structures of pallidal and cerebellar neurons and they themselves project upon motor and premotor cortical areas. Also the dorsomedial nucleus plays an important role as it is the thalamic relay nucleus for most of the prefrontal cortex. The pulvinar is bi-directionally connected with the retrorolandic cortex including the posterior language area (Crosson 1984, Wallesch 1997).

3.3 Basal Ganglia

The basal ganglia consist of several paired nuclei; the two members of each pair are situated in opposite cerebral hemispheres. The largest nucleus in the basal ganglia is the corpus striatum, which consists of the caudate nucleus and the lentiform nucleus. Each lentiform nucleus, in turn, is subdivided into a lateral part called the putamen and a medial part called the globus pallidus which again is divided into a

globus pallidus externa and interna. Furthermore the subthalamic nucleus, and substantia nigra pars compacta and reticularis belong to the basal ganglia. The basal ganglia receive input from and provide output to the cerebral cortex, thalamus and hypothalamus. In addition, many nerve fibres interconnect the nuclei of the basal ganglia. All these anatomical structures play a major role in controlling voluntary movements. The basal ganglia show no direct connection with the descending tracts to the spinal cord, mainly the pyramidal tract which is responsible for information flow from the motor cortex (first motor neuron) via spinal cord (second motor neuron) to the skeletal muscles. “Instead they form neural loops extending from the motor cortex to the motor thalamus and back to the cortex. The loops have been anatomically divided into four groups: motor, oculomotor, premotor and limbic loops which run in parallel without much collateral branching. The limbic (allocortical) projections tend to synapse in cellular islands in the caudate known as striosomes, whereas the motor loops (neocortex) synapse in the homogenous matrix of the putamen. Within the motor loop, the somatotropic arrangement of the cortex is preserved throughout the circuit. These different loops seem to control movements at varying levels of complexity, as well as in different anatomical areas. The primary neurotransmitters within these loops are glutamate and gamma-aminobutyric acid (GABA). These loops contain direct (excitatory) and indirect (inhibitory) pathways; the excitatory pathway passes via the subthalamic nucleus” (Burch et al. 2005, p.622-623). The dopaminergic input from the substantia nigra pars compacta seems to modulate the balance between the inhibitory and excitatory motor loops. According to Burch et al. (2005) “the basal ganglia are thought to play a role in the initiation of voluntary movement, facilitation of some motion suppressing others, and comparison of motor commands with feedback from evolving motion. In addition to their role in motor control, they are involved in various emotional and cognitive functions regarding adaptive motor learning, working memory and flexibility of thought” (p. 917). (Szentagothai 1993, Brown et al 1997, Williams 1999, Brandt et al. 2003, Burch et al. 2005).

3.3 The impact of subcortical structures on aphasia

The advent of the modern neuroimaging techniques led to the identification of the left basal ganglia as the lesion correlate for a group of aphasias known as “atypical” for lack of a better term. These aphasias are generally of the fluent type, in some way resembling Wernicke’s aphasia. Yet, unlike typical fluent aphasias, these are also characterized by disturbances of articulation and, even more deviantly, a right-sided hemiparesis is present. The lesions are located deep in the left hemisphere and invariably include portions of the caudate nucleus and putamen and the anterior limb of the internal capsule.Another atypical aphasic syndrome, with strong resemblance to transcortical sensory aphasia, can occur with infarcts in the left thalamus when the anterior nuclei are involved. (Szentagothai 1993, Williams 1999).

It seems worthy to be interested in exploring the role of subcortical structures in language. Evaluation of subcortical effects on language may explain facets of language that theories of cortical functions cannot explain. Discovery of principles relating subcortical functions to language may have application also to other areas such as memory or nonverbal functions (Crosson 1984).

3.4 White matter tracts

There are conflicting reports regarding the language disorders that follow white matter lesions. According to some reports, the aphasic syndromes that follow white matter lesions do not differ from those that occur with perisylvian cortical lesions, and the classic aphasic syndromes correlate with subcortical lesion site. The language disorders seen with subcortical lesions in neuroimaging techniques are not easily classified as any of the standard aphasic syndromes, it can even be observed that language disturbances of all sorts occur with lesions in all subcortical areas and that total sparing of language functions can follow lesions in identical subcortical areas. A relative sparing of language functions has been noted in multiple sclerosis;

however this may be because multiple sclerosis lesions do not affect white matter tracts in a manner needed to interrupt language processes (Szentagothai 1993, Williams 1999, Brandt et al. 2003).

3.5 Grey matter nuclei

Aphasic disturbances can follow strokes in the thalamus, caudate and parts of the striatum. It is likely that at least some aphasic symptoms seen after deep gray-matter lesions reflect the effects of disturbances in other cognitive functions on language. Intraoperative stimulation studies of the interference with language functions after dominant thalamic stimulation also suggest that the language impairments seen in at least some thalamic cases are due to disturbances of attentional mechanisms. Perhaps the most important consideration regarding language disorders after subcortical lesions is the question of whether they result from altered physiologic activity in the overlying cortex, not from the subcortical structures themselves. The availability of patients with focal strokes that are visible only subcortically, in whom metabolic scanning is used to assess lesion site and size in both cortical and subcortical structures, provides an opportunity to investigate the role that both cortical and subcortical structures play in language. Some cases show perfect correspondence between the presence or absence of cortical hypometabolism or hypoperfusion and the presence or absence of aphasic impairments in patients with focal strokes visible only subcortical (Szentagothai 1993, Williams 1999, Brandt et al. 2003).

4. Neurological diseases causing subcortical lesions

4.1 Stroke

Stroke is the leading cause for aphasia, followed by traumatic brain injury, cerebral tumor and infectious diseases of the cerebral nervous system (Schöler 2004). This also applies to language disturbances involving lesions of subcortical structures.

"In industrialized countries, stroke is the third most common cause of death (behind heart disease and cancer) and the most important cause of permanent disability (Sacco 1999). In epidemiological studies the incidence of stroke in Europe is 150-280 / 100 000 per annum (Barnett et al. 1998). In Austria roughly 15 000 persons per year suffer a stroke. 15-20% of hospitalised patients die within the first 30 days and 5-year survival-rate is about 50%. In Austria approximately 50 000 persons suffer from sequels caused by stroke, 2/3 show markedly reduction of their activities in daily life (Willeit 2001). Ischemic stroke is the most common form constituting about 80% of all strokes. Intracerebral hemorrhage constitutes 10-15%, subarachnoid hemorrhage 5-10% and cerebral venous thrombosis 2-4% of all strokes (Warlow et al. 1996, Kolominsky-Rabas et al. 2001)" (Tentschert 2002, p. 2).

4.1.1 Etiology of Ischemic Stroke

"Compared to coronary artery disease the different causes of stroke are more heterogenous. The most important etiologies of ischemic stroke include large-artery atherosclerosis (macroangiopathy), cardioembolism and cerebral small vessel disease (microangiopathy). Less common causes of ischemic stroke are cervical artery dissection, cerebral vasculitis, coagulopathies, hematologic disorders and others (Warlow 1996)" (Tentschert 2002, p.2) .

The strongest claims on localization in aphasia have been made for the major sydromes: Broca's aphasia is associated with a lesion in the supply area in the left prerolandic artery; Wernicke's aphasia is associated with a lesion in the supply area of the left superior temporal artery; stable global aphasia is associated with a large lesion in the supply area of the left middle cerebral artery; amnesic aphasia is

not associated with a particular vascular territory but is assumed to be due to a small retrorolandic infero-sylvian lesion (Willmes and Poeck 1993).

Regarding stroke in subcortical structures, the blood supply for the most deep-seated areas comes from the middle cerebral artery, namely its small deep perforating branches. Only the thalamus is mostly supplied via the posterior cerebral artery. The special regions of interest for language pathology, the anterior and lateral group of thalamic nuclei receive blood from a small branch of the posterior cerebral artery, the tuberothalamic artery. It has to be noted though that the thalamus is known for abnormalities in vascular architecture (Brandt et al. 2006).

From an etiological point of view, isolated ischemic infarcts as well as hemorrhagic lesions of subcortical structures (thalamus, basal ganglia and deep white matter) belong to the group of cerebral small vessel disease or microangiopathy.

4.1.2 Epidemiology of ischemic stroke subtype

“Petty et al. (1999) identified all residents of Rochester, Minnesota, with a first ischemic stroke from 1985 through 1989 using the resources of the Rochester Epidemiology Project medical records linkage system. After reviewing medical records and imaging studies, they assigned patients to 4 major ischemic stroke categories based on National Institute of Neurological Diseases and Stroke Data Bank criteria. Among 454 residents of Rochester with first ischemic stroke during the time period of the study subtype assignment was as follows: 16% large-vessel cervical or intracranial atherosclerosis with stenosis, 29% lacunar, 16% cardioembolic, 36% undetermined and 3% other or unusual causes. Age-adjusted incidence rates of ischemic stroke due to large-vessel cervical or intracranial atherosclerosis with stenosis were nearly 4 times higher for men than for women. No significant sex-related differences in incidence rate were detected for the other subtypes (Petty et al. 1999)” (Tentschert 2002, p. 2-3).

4.1.3 Risk factors

“Since the pathogenetic processes underlying the various stroke types differ, it is reasonable to expect that risk factors are also differently distributed among stroke subtypes (Barnett 1998). Stroke risk varies widely from one person to another, from very low to very high, depending on the number of risk factors possessed by the individual and the relative risk for stroke associated with each. Stroke risk factors can be characterized into modifiable and non-modifiable risk factors. To the first group belong factors such as hypertension, diabetes mellitus, cardiac morbidity, blood cholesterol levels, blood homocysteine levels and various lifestyle factors as smoking habits, alcohol consumption, physical inactivity and diet. To the second group belong age, sex, ethnicity and other genetic predisposition” (Tentschert 2002, p. 3).

5. The concept of Subcortical Aphasia

Although, since the work of Paul Broca and Carl Wernicke it is accepted that language functions are assigned to the cortical structures of the dominant, usually left, hemisphere, some studies that ascribed a role in language to subcortical structures can be found. In the year 1959, Fisher described a case of aphasia following hemorrhage in the dominant thalamus. Also 1959 Penfield and Roberts suggested the thalamus as an important factor for integrating language functions. Hildred Schuell and her colleagues (Schuell, Jenkins, and Jimenz-Pabon 1965) had also seen the thalamus responsible for complex feedback processes between language and non-language systems. Since then, many studies have dealt with the question if and what role subcortical structures play in language (Crosson 1984).

5.1 Clinical characteristics of Subcortical Aphasia

Patients with subcortical lesions show a moderate to severe impairment of language output, contaminated with semantic and phonemic paraphasias and word finding difficulties which sometimes gives the impression of non-fluent speech. Sometimes paraphasias can deteriorate spoken language into incomprehensible jargon. Additionally, perseverations and anomia can be observed. Impairment of language comprehension is nearly always described as mild, repetition is the least impaired function. It is reported that aphasia symptoms following thalamic lesions show inconsistent duration, some studies report vanishing of language symptoms within weeks and months, whereas nearly half of the cases persist for years (Naeser et al. 1982, Damasio et al. 1982, Crosson 1984).

Wallesch in his 1997 paper “Symptomatology of subcortical aphasia” sought to analyse clinical profiles of aphasia following subcortical lesions and wanted to identify specific symptoms and symptom constellations. He divided subcortical structures involved in language deficits into three groups: the thalamus, the basal ganglia and the deep white matter. He found that aphasia due to thalamic lesion

varies regarding fluency, it is characterized by semantic and phonematic paraphasias, neologisms, intact repetition and less disturbed grammar. Comprehension seems well preserved. In addition, patients with thalamic lesion frequently show rapid fluctuations in performance that have been accounted for by attentional dysfunction (Wallesch 1997, p. 271).

Regarding language disturbances, lesions of the basal ganglia show no clear picture, the majority of patients presents affected propositional language, sometimes also semantic paraphasias. Anatomically, lesions mostly affect nuclear and white matter structures and are rather small (Wallesch 1997). Crosson, in his 1985 review article held that lesions in the anterior limb of the internal capsule tend to be responsible for non-fluent language output, especially if they extend ventrally and anteriorly. Electric stimulation of white matter tracts located frontocaudal produce interruptions of ongoing speech whereas stimulation of the head of the caudate produced fluent language, but distorted by paraphasias. For putaminal lesions, both fluent and non-fluent language has been reported (Crosson 1985).

Concerning white matter lesions, destruction of the anterior limb of the internal capsule usually also involve the lateral part of the head of the caudate. Clinically, they often correspond to “fluent or non-fluent paraphasic aphasia with comprehension deficit and largely preserved repetition. Finally, lesions of the knee of the internal capsule and the internal pallidum (regardless of which vessel supplies the region) have been related to the presence of transient transcortical motor aphasia, although without regularity” (Wallesch 1997, p. 271).

In the 1960s thalamectomy (surgical destruction of small parts of the thalamus) was established as treatment for Parkinson’s disease and other movement disorders, which comprised tremor or certain types of pain. To control the motor symptoms of Parkinson’s disease, the surgical target was usually a single thalamic nucleus, the ventral lateral which was destroyed to better tremor and rigidity in the patient. In contrast, thalamectomy on therapeutic purpose for pain-syndromes has usually focused on the pulvinar, but has been far less common than surgical extraction of the ventral lateral nucleus. As Crosson (1984) puts it “The frequency of aphasia symptoms following such surgical procedures varied considerably between studies, aphasia after left ventral lateral lesion ranged

between 16 and 70%" (p. 501), in some studies aphasia symptoms were even reported after rightsided lesions. The symptom characteristics were the same as those reported in cases after stroke. In general, language disturbance after ventral lateral thalamectomy was reported to remit rapidly, usually within a few days to weeks, the persistence seems definitely shorter than with aphasias following subcortical stroke (Crosson 1984).

Another hint for language disturbances following dysfunction of subcortical structures comes from the technique of electrical stimulation of the brain, an instrument widely used during the 1950s to the 1970s. This technique has been widely used for mapping the human cortex during brain surgery especially for epilepsy therapy (e.g. by Penfield and Roberts, Ojemann) but also for the limbic system and the basal ganglia. Studies of the latter have been conducted primarily during surgical procedures which control the motor symptoms of Parkinson's disease. In general the effects of such electric stimulation of brain regions have been tested according to Crosson (1984) in two ways: on the one hand to observe which "activities or sensations stimulation evokes in a passive subject", and on the other hand to observe "how stimulation affects some activity which the patient is requested to perform during the stimulation" (p. 506). The latter, however, has been more frequently used to assess speech and language. Regarding stimulation of the subcortical structures and speech and language showed that disruption of object naming and naming from recall occurred almost exclusively with stimulation of the dominant thalamus (Crosson 1984).

The explanation of how the mechanism of electrical stimulation of subcortical structures impairs language function is best summoned by Ojemann, 1976 (as reported in Crosson 1984) "the researchers then thought that electric stimulation introduced a signal into the neural system that this system could not interpret and therefore was processed as noise" (p. 509). Such noise, the author thought would act like a temporary lesion, preventing the participation of stimulated tissue in language tasks. According to Crosson (1984) electrical stimulation could also have initiated some neural process opposite to a language task. Other possible reasons for interference with language tasks are the excitation of mechanisms inhibiting certain language functions or the overloading of neural

mechanisms with stimulation, making these processes refractory to further neural responses involved in language processing (Crosson 1984).

Another important caveat for this kind of research is the fact that these stimulation studies almost always have been performed with patients suffering from Parkinson's disease. It should be expected that at the time point of electric stimulation the disease has already altered brain functions and the results might not reflect what happens to unaffected brain tissue (Crosson 1984).

5.2 Theories of subcortical function in language

From the 1960s to the 1980s a number of researchers have speculated, on the basis of lesion studies or electric stimulation studies, about the role of subcortical structures, especially the thalamus played in language. It must be kept in mind that neuroimaging at this time if available was basically computed tomography scans, even their quality is far from comparable to today's techniques. The theories about the influence of subcortical structures on language can be grouped according to the mechanism with which they account for the effects of lesion or electric stimulation.

5.2.1 Descriptive theories

Within the *descriptive theories* Jonas (1982) held that thalamic aphasias resemble transcortical aphasias, in which repetition remains intact in the presence of other severe language disturbances. "Most often, the paraphasic speech in thalamic aphasia, sometimes degenerating into jargon, has been similar to language output in transcortical sensory aphasia. However, Alexander and LoVerme (1980) noted that comprehension usually has been less impaired in thalamic aphasia than in transcortical sensory aphasia" (Crosson 1984, p. 509). The functional conclusion that can be drawn from this comparison is that "transcortical aphasias were thought to be caused by a severing of language cortex from other cortical areas while still maintaining connections between the anterior areas for language formulation and the posterior areas for language decoding (Crosson 1984, p. 509).

So, as a consequence the disruption resulting in transcortical aphasias may involve also connections between cortical areas and subcortical nuclei. (Alexander and LoVerme 1980, Jonas 1982)

5.2.2 Nonspecific theories

Also, various theories, best summoned under the term *nonspecific theories* have been developed. Crosson (1984) noted that the common feature of these theories is the emphasis on the "numerous connections between cortical and subcortical structures, especially the thalamus" (p. 511). The role assigned to the thalamus for language is not specific, rather it is postulated that "subcortical lesions affect information processing at a predominantly diffuse and unlateralized stage" (Crosson 1984, p. 509). Lesions therefore disrupt language processing as well as other cognitive functions in an unspecific manner. These theories have soon been contradicted by evidence pointing out lateralisation of language processing functions of the dominant hemisphere and dominant subcortical structures (Riklan and Levita 1965, Brown 1975, Crosson 1984).

5.2.3 Activation theories

Other theories can best be described as *activation theories* indicating that various authors have thought "thalamic aphasia to be a reflection of the role the thalamus plays in cortical arousal or activation" (Crosson 1984, p. 519).). One representative was Luria (1977) who suggested that language disorder after thalamic lesion was not a function of disruption in the language system per se. He thought that these language disturbances were due to a disturbance of vigilance mechanisms in the dominant thalamus directly connected to the language system, as the thalamus is connected via white matter fiber tracts with the reticular formation in the brainstem. If this were the case, however, more uniformly depressed language functions would be expected. Crosson (1984) criticized that various characteristics after thalamic lesions could not be explained, especially because anatomically the

formatio reticularis, related to cortical arousal, is connected especially with the ventral anterior nucleus of the thalamus, and the most prominent lesion localisations of language disturbances have been shown to lie elsewhere, namely in the ventral lateral nucleus and the pulvinar (Riklan and Cooper 1975, Luria 1977, Horenstein et al. 1978, McFarling et al 1982).

5.2.4 Multiple function theories

Others, like Cooper et al. (1968) and Samra et al. (1969) combined the thalamic function of activation and integration in language, their theories could be best described as *multiple function theories*. The authors postulated that the dominant thalamus is "involved in the direction of activation important for the modulation and integration of speech and language. In other words,the dominant thalamus would function to achieve a level of activation high enough for the other important language structures to accomplish the integration" (Crosson 1984, p. 511). Crosson (1984) pointed out that the power of these theories "depends upon the degree of specificity regarding language functions. If one merely implies generalized arousal of the language system, then this explanation suffers from the same flaws as arousal theory" (p. 511). That means the weakness of these theories consists of an inability to explain the documented pattern of deficits which are quite specific. Crosson (1984) held that "specific samples of language disturbances would be better explainable if the explanation was valid for the arousal of specific patterns as semantic encoding or feedback mechanisms that comprise parts of language integration" (p. 509).

5.2.5 Integration theories

Others, namely *integration theories* assigned the dominant thalamus and other subcortical structures a role in integrating language. Representatives of this theoretical concept were Penfield and Roberts (1959), Ojemann et al. (1968) or Botez and Barbeau (1971). They postulated the existence of "cortico-thalamo-

cortical circuits under the control of brain stem and basal attention mechanisms. These circuits were seen as responsible for the final matching or understanding of verbal messages and as playing a part in the formation of new motor patterns for spoken language. The common denominator in these activities was the use of memory traces related to language" (Crosson 1984, p. 510). These authors further postulated hypothesised "an attention mechanism gating storage and retrieval for verbal memory" (Crosson 1984, p. 510). They also held that "the dominant thalamus was responsible for release or inhibition of preformed speech patterns and the temporal ordering of speech" (Crosson 1984, p. 510). Crosson (1981) differentiated between phonemic and semantic features of language and postulated that the dominant thalamus plays a part in semantic functions. He held that "the dominant thalamus is involved in a preverbal semantic feedback mechanism that monitors potential language output via the word-selection process. This is accomplished through a feedback loop between the anterior cortical areas for language formulation and the posterior centers for semantic decoding. In other words the dominant thalamus provides the mechanism by which the posterior centers for language decoding monitor verbal output" (Crosson 1984, p. 511). (Penfield and Roberts 1959, Botez and Barbeaux 1971, Schaltenbrand 1975 Cappa and Vignolo 1979).

Within this theoretical framework, two theories, one postulated by Bruce Crosson/ Stephen Nadeau (1997) and one by Claus Wallesch and Costanza Pappagno (1988) gain special attention because of their extraordinary elaboratedness (Wallesch and Pappagno 1988, Crosson and Nadeau 1997).

5.2.5.1 Crosson's Response Release / Semantic Feedback Model (Crosson, 1985)

Crosson (1985) proposed an integrated model of subcortical-cortical language production which included a role for the basal ganglia in regulating the release of preformulated language segments. Regarding language function, he made three premises establishing his model: firstly, he postulated that "motor and sensory

systems, in the broadest sense of the words, are to some degree separable in the human brain. Here, motor refers not only to motor execution but also to the plan and intent to act, and sensory refers not only to the reception of sensory information but also to the initial decoding of such information" (Crosson 1985, p. 271). Secondly, he held that "language is monitored by its speaker, not only externally through hearing oneself speak, but also internally before it is actually executed in speech" (Crosson 1985, p. 271). Thirdly, he made a rather general proposition that the "motor and sensory systems involved in language interact in a complex way to produce spoken language" (Crosson 1985, p. 271).

According to his model "language formulation is presumed to be a function of the more anterior language zones, which most likely include the posterior inferior frontal gyrus, the frontal operculum, the parietal operculum, the temporal operculum and the insula. The term `language formulation´ encompasses the conceptual, word finding, and syntactic processes necessary for the encoding of language" (Crosson 1985, p. 272). The decoding of language takes place in the temporoparietal cortex, but in collaboration with the anterior language areas. These areas are connected by the arcuate fasciculus. "Bidirectional cortico-thalamo-cortical pathways are involved in semantic monitoring mechanisms. Internal semantic monitoring of language formulated by the anterior language zones is performed by the temporoparietal cortex prior to the execution of the language segments in speech" (Crosson 1985, p. 276). The author further held that "pathways through the thalamus (particularly the anterior superior lateral and pulvinar) act as conduit for semantic information and messages to refine semantic content during this monitoring process. Excitatory impulses are also conveyed from the ventral anterior nucleus to the anterior language zones which provide the proper level of activation for language formulation" (Crosson 1985, p. 276). In his opinion the basal ganglia are responsible for integrating inputs from the cortex and subsequently influencing thalamic mechanisms. On the one hand "the basal ganglia influence tone in the anterior cortical language areas by regulating the flow of excitatory impulses from the ventral anterior thalamus" (Crosson 1985, p. 277). On the other hand they are responsible for a motor release mechanism "which allows language

segments to be released at the proper time, after semantic monitoring has taken place" (Crosson 1985, p. 277).

Murdoch (2001) in his review article stated that "according to this model, the conceptual, word-finding and syntactic processes which fall under the rubric of language formulation occur in the anterior cortex. The monitoring of anteriorly formulated language segments as well as the semantic and phonological decoding of incoming language occurs in the posterior temporoparietal cortex. Language segments are conveyed from the anterior or language formulation center to the posterior language centre via the thalamus (specified as the pulvinar in later revisions) prior to release for motor programming. This operation allows the posterior semantic decoding centres to monitor the language segment for semantic accuracy. If an inaccuracy is detected, then the information required for correction is conveyed via the pulvinar back to the anterior cortex. If the language segment is found to be accurate during monitoring, then it is released from a buffer in the anterior cortex for subsequent motor programming"(p. 243).

Further Crosson proposed that the "release of the formulated language segment for motor programming occurs through the cortico-striato-thalamo-cortical loop as follows. once language segments have been verified for semantic accuracy, the temporoparietal cortex releases the caudate nucleus from inhibition. The caudate nucleus then serves to weaken inhibitory pallidal regulation of thalamic excitatory outputs in the anterior language centre, which in turn arouses the cortex to enable the generation of motor programmes for semantically verified language segments. Once motor programming is complete, the circuit resumes its resting state where the temporal cortex inhibits the head of the caudate nucleus" (Murdoch 2001, p. 243).

Murdoch et al. (2003) stated that "Crosson (1985) hypothesised that lesions of the globus pallidus would result in disinhibition of the thalamus and hence, hyperarousal of the anterior language centre, leading to the production of extraneous verbal output, including semantic paraphasias. On the other hand, lesions in the thalamus would lead to disruption of the arousal of the cortex and thereby disturb the process of preverbal semantic monitoring. It was suggested that the loss of spontaneous speech noted after thalamic lesions may be due to the

interruption of excitatory input from the thalamus to the cortex. Further, thalamic lesions would, according to this model, interrupt the transfer of information between the anterior and posterior language centres, disrupting preverbal semantic monitoring and leading to poor monitoring of the semantic content of language, characterised by the production of semantic paraphasias"(p. 66).

5.2.5.2 The Lexical Selection Model of Wallesch and Papagno (Wallesch and Papagno, 1988).

Murdoch et al. (2003) describe that "Wallesch and Papagno´s (1988) model also proposed that subcortical structures participate in language processes via a cortico-striato-pallido-thalamo-cortical loop. They postulated that the subcortical components of the aforementioned loop constituted a "frontal lobe system" comprised of parallel modules with integrative and decision-making capability rather than the regulatory function proposed in Crosson's (1985) model. Specifically, the basal ganglia system and thalamus were hypothesised to process situational as well as goal-directed constraints and lexical information from the frontal cortex and posterior language area, and to subsequently participate in the process of determining the appropriate lexical item, from a range of alternatives, for verbal production. The most appropriate lexical alternative is then released by the thalamus for processing by the frontal cortex and programming as speech. Cortical processing of selected lexical alternatives is made possible by inhibitory influences of the globus pallidus upon a thalamic gating mechanism. The most appropriate lexical alternative has an inhibitory effect on the thalamus, promoting closure of the thalamic gate, resulting in activation of the cerebral cortex and the production of the desired response. Cortical processing of subordinate alternatives is suppressed as a consequence of pallidal disinhibition of the thalamus and the inhibition of cortical activity" (p. 67). It is important to note that the role of subcortical structures in mediating parallel processing would only be invoked or required in certain situations where Wallesch and Papagno suggested that there were increased "degrees of freedom" or potential responses. The degrees of

freedom allowed in selecting the lexical content of a sentence are greater than in morphosyntactical operations or in reactive speech tasks such as repetition, where all parallel cortical response modules would be the same, negating the need for competitive selection.

According to Murdoch et al. (2003) “Wallesch and Papagno hypothesised that lesions of the globus pallidus would result in characteristics of non-fluent language pathology (e.g. difficulty in initiating speech). They suggested that, in the case of such lesions, the thalamus is disinhibited so that the thalamic gate is opened, the cortex is inhibited, and no language (or more difficulty initiating language) is produced” (p.67). Further “they suggested that lesions in the thalamus may lead to the release of inappropriate, poorly monitored responses by the frontal cortex (due to disinhibition of the cortex). In such a lesion, the thalamus would receive inhibitory input from the globus pallidus in order to produce a response, but due to the thalamic lesion, all gates in the thalamus are permanently closed. The cortex is disinhibited and all parallel circuits may arrive at the cortex for a response. Unfortunately the first response completing the circuit and reaching the cortex will be produced (possible semantic paraphasia) rather than the correct response”(Murdoch 2003, p. 68).

In the 1990s more elaborated studies of language disorders following subcortical lesions have been possible following the upcoming of new and constantly better neuroimaging techniques. These studies seemed very promising in elucidating the role of deep-seated anatomical structures in language, especially within the framework of neural networks involving subcortical structures, cortical areas and their reciprocal connections.

These new imaging techniques demonstrated reductions in blood flow or local metabolism in cortical areas remote from the lesions site located in subcortical structures. This phenomenon was thought to represent the hemodynamic or metabolic epiphenomenon of diminished neuronal activity called “diaschisis” originally described by von Monakow in 1914. Within the medical scientific community “controversial interpretations regarding this phenomenon have been proposed, but the most generally accepted hypothesis ascribes the cortical

dysfunction to a disconnection within a neural network thus leading to a deprivation from afferent input to the cortex (Demeurisse 1997, p. 302).

Demeurisse held that for left-sided subcortical lesions, the presence of language distorders is linked to a diminished neuronal activity involving the left frontal cortex and classical cortical language areas. However, he found that the cortical dysfunction observed differs according to left-sided thalamic and left-sided non-thalamic lesions. Lesions restricted to thalamic nuclei match a mild and diffuse reduction of neuronal activity involving almost the whole cortex whereas lesions of other subcortical structures especially evoke a decrease in activity in frontal and perisylvian regions (Demeurisse 1997).

Hillis et al. reported 37 stroke patients with exclusively left subcortical lesions of which 68% suffered from aphasia. The investigators conducted an MRI including perfusion and diffusion weighted images which showed that all of these patients in the acute phase suffered from cortical hypoperfusion in the territory of the left middle cerebral artery. Some patients who matched this clinical and neuroimaging template had successfully undergone medical treatment to restore perfusion. Clinically, with reversal of the cortical hypoperfusion, the subjects presented with resolution of their aphasic deficit (Hillis et al. 2002).

Olsen and colleagues also studied subjects with subcortical infarcts. The patients in whom no aphasic deficits were noted showed no regional cortical hypoperfusion in SPECT scans whereas patients with aphasia showed lowered cortical perfusion (Olsen et al. 1986). Similar findings in acute and subacute stroke have also been reported by many others (Perani et al 1987, Vallar et al. 1988, Weiller et al. 1993, Okuda et al. 1994).

6. Parkinson’s Disease

Another neurological disorder which gained attention regarding the involvement of subcortical structures in language is Parkinson’s disease (PD) which also is associated with distinct language disturbances. As PD is a neurodegenerative disorder which affects especially the degeneration of subcortical structures and functions via diminished levels of a certain neurotransmitter and also morphological changes. It seems evident to undertake a comparison here.

Parkinson`s disease belongs to the group of movement disorders and has a prevalence of 1-2/1000, affecting 1-2% of the elderly people because of an increased incidence above 50 years. In industrialized countries PD is the second most common neurodegenerative disease following Alzheimer`s disease. It is progressive in nature and procedes over many decades, characterized by motor and non-motor symptoms.

It was first described by the neurologist James Parkinson in 1817 who called the disease “shaking palsy” and assigned the following features ”involuntary tremulous motion, with lessened muscular power, in parts not in action and even when supported; with a propensity to bend the trunk forward, and to pass from walking to a running pace, the senses and intellect being uninjured” (Parkinson, 1817, as cited in Brandt, Dichgans, Diener 2003, p.1023). Parkinson’s description led to the clinical entity of Parkinson`s Disease and since then the knowledge about the neurophysiological background and therapeutic options has grown tremendously.

Histologically, PD is characterized by the loss of dopaminergic neurons in the substantia nigra. Also, intracytoplasmatic eosinophilic inclusions in neurons named Lewy bodies after Friedrich Heinrich Lewy who first described this feature in 1912 can be observed in PD. Carlsson’s observation in 1959 that almost 80% of the brain’s dopamine is localized in the basal ganglia helped elucidating the clinico-anatomical correlation of the disease, so the connection between loss of dopamine and the clinical symptoms was established His observation led to post-mortem biochemical studies of PD patients which confirmed the dopamine dpeletion theory revealing decreased levels of dopamine and its metabolites in the basal ganglia,

especially in the substantia nigra, nucleus caudatus, nucleus accumbens, putamen , and globus pallidus.

When the clinical motor signs of PD become obvious, the dopa uptake of the putamen is diminished by at least 35%. (Leenders et al., 1990 as reported in Bartels et al. 2009). The clinical symptoms of PD are described by Bartels et al. (2009) "Parkinsonism has three cardinal motor symptoms: bradykinesia, rigidity and tremor. Classical for PD is an asymmetrical onset of motor symptoms. The presence of at two of the three primary signs and a consistent response to an adequate dose of levodopa are considered by most experts to be essential for the clinical diagnosis of PD"(p. 919). The authors further specify the motor symptom characteristics describing "in some PD patients tremor is the predominant symptom, while in others tremor is absent or mild, which also led to the distinction of "tremor-dominant PD". Because the clinical presentation of PD can be quite variable, a number of subtypes have been described, including tremor-predominant versus postural instability/gait disorder (PIGD)-predominant type, or benign versus malignant PD according to the progressive course of the disease, and the distinction of young onset PD; however those classifications are arbitray.Tremor results from oscillatory movements of agonist and antagonist muscles. PD tremor is characteristically present at rest, but an action tremor may also be observed. Tremor is most pronounced in the distal parts of the limbs; In later stages of the disease, it can spread to involve the lips, jaw, and tongue. In a later stage of the disease, tremor often subsides and bradykinesia and rigidity are more progressive."(Bartels et al. 2009, p. 919). The second most prominent symptom of PD is bradykinesia, this means a slowness of movements and comprises also hypokinesia (decrease of amplitude of movements when often repeated) and akinesia (the inability to initiate movements). Due to bradykinesia and hypokinesia multiple secondary symptoms of PD can be observed, such as hypophonia, sialorrhea, masked facies and micrographia. Bartels et al (2009) furthermore describe that "gait problems represent another spectrum of PD symptoms, and together with loss of balance reflexes they can cause dramatic immobility and risk of falling in later stages of the disease. PD gait is characterized by shuffling, small steps, decreased armswing and a forward bended posture. Furthermore freezing of

gait (FOG) occurs in 30-60% of the PD patients. FOG is a sudden disturbance of gait where patients feel stuck with their feet being `glued to the floor´. FOG frequently happens in challenging situations with increased mental stress, and can often be overcome by applying external tricks, for example visual cues." (Bartels et al. 2009, p. 919) Additional non-motor symptoms can be observed in the course of PD. Dementia develops in 20-40% of the patients in later stages of the disease whereas in earlier stages the disease is accompanied by many other cognitive deficits such as visuospatial dysfunction, episodic memory impairment, impaired verbal fluency, and executive impairment. Besides motor and cognitive deficits also impairments of psychiatric nature like depression, anxiety, behavioral symptoms (for example excessive gambling, compulsive hoarding) and sleep disturbances may appear. Additionally the patients have to deal with autonomic dysfunctions like orthostatic hypotension, decelerated gastro-intestinal motility, bladder dysfunction, abnormal thermoregulation and increased sweating. Mild vegetative symptoms or cognitive signs are often found to procede the motor symptoms in PD. Bartels et al. (2009) acknowledge: "These clinical observations of early non-motor symptoms led to a novel neuropathological concept of neurodegeneration in PD, which starts in non-dopaminergic areas, notably the enteric nervous system and then rises via spinal cord and brainstem to nigral and subsequently cortical neurons" (p.920).

Most PD patients suffer from sporadic PD, also called idiopathic PD, although their first degree relatives have a two- to threefold increased relative risk of suffering from the disease themselves. Already, some genes have been identified that cause familial PD, usually diagnosed in younger age (<50), although "disease concordance rates between monozygotic and dizygotic twin pairs revealed similar concordance rates when PD was diagnosed after the age of 50, suggesting that heredity is not a major etiologic component in most cases of PD" (Bartels et al. 2009, p.916). They conclude that "Together, epidemiological studies support the importance of both genetic and environmental factors as possible causes of PD, leading to the notion of final common mechanisms in PD pathogenesis. Several possible mechanisms have been proposed, such as exogenous toxins, inflammation, genetic mutations, and combination of these factors. A generally accepted hypothesis is that PD is the result of an interaction between genetic and environmental factors. According to

this theory, an interaction of genetic predisposition and environmental factors induces mitochondrial respiratory failure and oxidative stress within nigral neurons, leading to cell death" (Bartels et al.2009, p.916). So, damage to multiple neuronal systems causing complex biochemical changes may explain the variable clinical picture in PD patients, including various motor symptoms, cognitive dysfunction, depression, vegetative symptoms, etc. The pathophysiological basis of dysfunctional basal ganglia-cortical loops has changed the concept of the PD syndrome, primarily described by James Parkinson as a motor disorder, `the senses and intellects being uninjured´, to a syndrome involving changes in the organization of mental as well as motor function (Brandt et al. 2003, Burch 2005).

6.1. Selected studies of distinctive language features in Parkinson's Disease

6.1.1 Pragmatics

May studies showed that PD patients experience problems when interpreting the intended or "pragmatically appropriate" meanings of language as defined by its social context. These pragmatic features include the processing of metaphorical expressions, paralinguistic behaviour and nonliteral meanings of discourse. Based on previous studies it can be argued that many PD patients exhibit difficulties when it comes to the processing of nonliteral or pragmatically appropriate meanings of language, including the ability to draw appropriate inferences from discourse.

One very elaborated study by Monetta et al. (2009) investigated whether pragmatic language deficits are associated with idiopathic PD especially in the context of interpreting verbal irony from narrative discourse. They tested 11 native English speakers with idiopathic PD with mild to moderate severity vs. 11 healthy controls matched for age, sex and education. For assessment of pragmatic language functions the authors tested the pragmatic interpretation of short stories created by Winner at al. 1998. Monetta et al describe that "Each story (approximately 20

words in length) described a situation where one person (the witness) observes another person (the protagonist of the story) doing something sneaky (e.g. eating a muffin while the person is on a strict diet)" (p. 974). The study participants listened to the story and, at the same time, were shown a written version of the story. To rule out that the prosodic information of the final statement in the spoken version revealed the ironic attribute of the story, "the final statement of each story was read in a neutral tone on the tape" (Monetta et al. 2009, p.975). The study participants then had to decide if the protagonist of the story lied, that meant that he/she did not realize that she/he had been caught and uttered a lie to avoid getting caught, or if the protagonist realized that she/he had been caught and made an ironic statement to hide the embarrassment of being caught. Half of the presented stories were lie stories and half irony stories. Participants then had to answer questions which probed their comprehension of first order and second order beliefs that means if they were able to attribute mental states to others (the protagonists of the stories) and to use these representations to understand, predict and judge their utterances and behaviour.

Monetta and al. found that "PD particpants often fail to interpret the intended, pragmatic meaning of ironic remarks as defined by narrative discourse, although these patients tend to perform at or near ceiling when queried on basic factual content of the same stories" (p.979). For the PD group it seemed that additionally low results in "two of the measures of frontal lobe functioning, namely verbal working memory span and verbal fluency (simple and alternating) were correlated with key measures on the story interpretation task (i.e. second order belief questions and exspectation and pragmatic interpretation questions, respectively)" (Monetta et al. 2009, p. 979). The authors further argue that "the observation that our PD patients displayed poor cognitive flexibility, as reflected by their low verbal fluency task scores" stands in line with many previous studies (Henry and Crawford 2004, as reported in Monetta et al. 2009, p. 979) and further "Given that reduced cognitive flexibility has been associated with rigidity for interpreting language (Walsh, 1985), the relationship we observed within our PD group between their verbal fluency skills and pragmatic interpretation abilities may reflect underlying limitations in cognitive flexibility associated with progressive frontal lobe

compromise in PD" (p.979). Additionally the PD patient´s working memory scores were extraordinarily low which supports the postulation that frontal lobe dysfunction added to the difficulties in irony comprehension. Monetta et al. further argue that "when nonliteral (e.g., ironic) meanings are communicated, inhibition processes are necessary to suppress the literal interpretation in favor of the intended, nonliteral meaning. These processes for inhibiting contextually irrelevant meanings are likely to require greater mental flexibility to activate the nonliteral interpretation in context, which again exemplifies the intimate relationship between frontal lobe functions and many pragmatic aspects of language" (p. 980). Also Theory of Mind deficits, resulting in diminished scores in attributing second order beliefs during the irony task were observed in PD patients. These second order beliefs "are thought to be critical for understanding the intended meaning of speech acts when a counterfactual or ironic statement is made" (Monetta et al. 2009, p. 980). According to the authors the data of the present study suggest that Theory of Mind capacity and irony comprehension are coupled.

Recent neuroimaging studies investigated the relationship between prefrontal regions, pragmatic processes and the ability to attribute mental states to others. Monetta et al (2009) argue that "In general, functional magnetic resonance imaging (fMRI) studies have linked the ability to attribute mental states to others with the left medial prefrontal cortex, the right temporal pole and the medial orbitofrontal cortex" (p. 980). These areas proven to be involved in irony processing by other studies. So, in PD patients it is highly possible that degeneration of the fronto-striatal pathways is linked to these deficits.

6.1.2 Lexicon/Semantic Priming

Semantic processing in PD patients has been found diminished in many studies. To investigate the deficits in semantic processing in PD patients, semantic priming tasks are widely used. Angwin et al. (2005) state "During a semantic priming

task, lexical decisions to `target words´ are typically faster if they are preceded by a semantically related `prime´ word (e.g., tiger – stripes). A generally accepted theory postulates that during a semantic priming task, the presentation of the prime causes an automatic spreading of activation, which partially activates other related concepts, thereby speeding lexical decisions to semantically related target words" (p. 78-79). An important factor to estimate the time course, over which automatic semantic activation occurs, is the manipulation of the stimulus onset asynchrony (SOA) (i.e. the time lapse between presentation of the prime and target). Also, "attentional or controlled processes can induce semantic priming effects, but these processes typically emerge when longer SOAs are used and when the proportion of related word pairs is high" (Angwin et al. 2005, p. 79). Further the authors argue that " disruptions to fast acting/automatic as opposed to controlled semantic processing may be most expected in PD, as it is proposed that dopamine and the striatum have substantial influence on the integrity and speed of information processing" (p. 79).

Angwin et al. (2005) for example used a multi-priming paradigm which "differs from standard semantic priming tasks, by implementing multiple prime words"(p. 79). These are either related to the target word or not (the resulting combinations are related-related (RR), related-unrelated (RU), unrelated-related (UR) or unrelated-unrelated (UU)). The authors explain "Specifically, two prime words can be presented, with either the first, second, or both prime words semantically related to the target word. Consequently, while standard priming effects can be measured from one related prime that directly precedes the target (e.g., soup-stripe-TIGER), semantic priming effects can also be measured when only the first prime or both prime words are related to the target. Therefore the measurement of semantic activation across conditions that are not available in traditional single prime lexical decision tasks may provide further information about the integrity of semantic activation in both PD and healthy adults" (p. 79). Additionally an auditory comprehension task with sentence stimuli was administered, the result divided the patient group into good vs. poor comprehenders.

They propose that the presence of an intervening unrelated word interferes with automatic semantic activation in PD, due to a reduction in the signal-to-noise ratio of information processing and/or decreased semantic inhibition. Angwin et al.(2005) state that "the absence of semantic priming effects at 250 ms SOA was evident for the subgroup of PD patients with poor comprehension"(p. 86). This suggests that slowed information processing speed may be linked to the sentence comprehension deficits. Recently, a study conducted by Grossman et al. (Grossman et al. 2002, as reported in Angwin et al. 2005) suggested that the "dopamine dependent frontal-striatal system might be responsible for maintaining an adequate speed of lexical activation during sentence processing, which is consistent with observations of reduced striatal recruitment in PD patients during the processing of complex noncanonical sentences"(p. 88). In the study of Angwin et al. PD patients showed no priming in the RU condition at 250 ms SOA, this may be due to a reduced signal to noise ratio of information processing resulting from diminished dopamine levels. This may "decrease the salience of a related prime word (the signal) and increase the salience of an unrelated prime word (the noise)" (Angwin et al., p. 86).

Both Groups showed an absence of priming at 600 ms SOA, the authors argue that this may be due to interference of automatically and controlled semantic processing. They further argued that "within the PD patient group, good comprehenders presented primarily with a deficit in controlled semantic processes, whereas the poor comprehenders presented with a deficit in both controlled and automatic semantic activation"(p. 88).

Research has shown that in patients with PD unusually large semantic priming effects with long SOAs can be observed. Mari-Beffa et al. (2004) studied the impact of semantic priming of target words in lexical decision tasks which investigated both semantic priming and repetition priming. They studied 10 PD patients optimally medicated during testing and 17 healthy controls. Instead of measuring semantic priming from target words, semantic priming was measured from a distractor word which was always unrelated to the prime and appeared on a screen at the same time. So, they explained "any difference in the size of priming should be due to differences in the activation (or inhibition) of words as opposed to

switch costs" (Mari-Beffa et al. 2005, 639). Consequently the authors conducted a second experiment to test whether PD patients still showed positive priming from distractor words in a situation where controls showed negative priming. The authors found that PD patients showed positive priming in conditions where the expected result was either negative priming or no priming at all. Furthermore they argued that this favors the theory of an enhanced or prolonged semantic activation from words due to the lack of inhibition of previously presented information in PD patients. They acknowledge that it is not clear "whether this lack of inhibition is specific to semantic information, or whether it reflects a more general deficit that would also affect other types of representations" (Mari-Beffa et al. 2005, p. 645) . Former studies, using other types of stimuli (e.g.letters) suggest that PD patients suffer from a general inhibition deficitwhich shows no specificity regarding the type of information that is being abolished. Mari-Beffa et al. conclude that their study demonstrates that PD patients show impaired inhibitory processing in a lexical decision task. They argue that the results "support the argument that semantic hyperpriming is the result of less effective inhibition of words when they are not relevant, rather than reflecting a switching cost between semantically unrelated words.These conclusions highlight a filtering deficit as a fundamental impairment in Parkinson´s disease, which may interact with or underlie other cognitive deficits experienced by PD patients" (Mari-Beffa et al. 2005, p. 646).

6.1.3 Syntax/Sentence comprehension/Grammatical Processing

A growing body of research has indicated that sentence comprehension may be impaired in patients with PD. However, the underlying cause of the impairment is unclear. Limited attentional resources and an impaired understanding of grammatical rules have been suggested as possible origins of the impairment. The present study by Whiting et al. (2004) investigated grammatical processing, specifically verb and context processing using a self- paced online thematic role assignment task. They used a modified version of a thematic role assignment task by Altmann (1999). The authors found a diminished accuracy regarding the

detection of verb selection anomalies, and a weakened sensitivity to context information in the patient group. Regarding response times, PD patients in former studies showed slower response times when processing sentences (Grossman et al., 2000; Lieberman et al., 1992 as reported in Whiting et al., 2004) than healthy controls. In the actual study, response latencies displayed variable differences between PD patients and controls depending on word positions. The authors explained that this variability in latency times was due to the cause that PD patients were less sensitive to sentence anomalies than the control participants. So, at certain word positions under selecting conditions, the control participants may have responded slower than the PD participants due to the extra processing time required by the control participants to process the anomalies. The PD patients "may have been unaware of the anomaly at this point and therefore, may not have required the extra processing time" (Whiting et al. 2004, p. 272). Also it seemed that PD patients were "less able to distinguish between information that had been encountered previously and new information" (Whiting et al. 2004, p. 273). The authors argue that "as the present study required participants to make metalinguistic judgements about sentence plausibility during a self paced reading task, the PD participants may not have had the memory resources available to link sentence elements in the target sentence to antecedents encountered in an earlier sentence in the same test item. Thus, the reduced awareness of context antecedents displayed by PD patients during the present study may have reflected a fusion of global discourse comprehension difficulties and impaired working memory" (Whiting et al. 2004, p. 273).

The findings of several studies regarding neuropsychological performance in PD patients have been inconsistent, this could be observed in study designs when patients were on different amounts of dopaminergic therapy (between patient design) as well as when patients were on and off their levodopa (within patient design). Grossman et al. (2000) investigated sentence comprehension in PD patients depending on the level of levodopa supplementation in 20 non-demented, right-handed, native English speakers with idiopathic PD (Hoehn and Yahr Stage I-II, a clinical assessment scale to estimate the severity of the disease established by Hoehn and Yahr 1967) using a within patient design: testing took place when

patients were either on optimal drug dosage vs. without levodopa for at least 12h. "PD patients performed a 24-item sentence-picture matching test using orally presented sentences. Sentence stimuli were being equally divided into simpler items containing terminal subordinate clauses (e.g. `The hawk chased the eagle that was fast´) and more complex items containing center-embedded subordinate clauses (e.g. `The eagle that the hawk chased was fast´)" (Grossman et al. 2000, p. 124). The study showed that "comprehension of center-embedded subordinate sentences was significantly worse than terminal subordinate sentences only during the „off" phase" (Grossman et al. 2000, p. 126). On the other hand "comprehension of center-embedded subordinate sentences did not differ from comprehension of terminal subordinate sentences during the „on" phase of testing" (Grossman et al. 2000, p. 126) . The authors conclude that "sentence comprehension is influenced by levodopa levels in PD. In particular, we found that differences in understanding grammatically simple and complex sentences when „off" levodopa are diminished by DA supplementation in PD patients. An error analysis revealed that this effect is specifically associated with more accurate grasp of the thematic relations in a sentence, i.e. who is doing what to whom. This aspect of sentence comprehension dependent on executive resources" (p. 127).

Phillips et al. (2012) examined the influence of subthalamic nucleus (STN) deep brain stimulation (DBS) on language in PD patients, in particular on the mental lexicon and the mental grammar. The authors assume "that mental grammar depends in part on frontal/basal-ganglia circuits responsible for procedural memory, which subserves motor and cognitive skills; the mental lexicon depends on a largely different network"(Philips et al. 2012, p. 1), previous studies on STN-DBS regarding mental lexicon and grammar have elicited inconsistent results. "Three groups of subjects were tested: PD patients being treated with STN DBS and optimal drug therapy,[..], patients being treated only with optimal drug therapy and healthy control subjects" (Philips et al. 2012, p.2). First, a past tense production task was administered followed by an object naming task to test higher motor knowledge and processing. This task consisted of „manipulated"objects, "meaning man-made objects that are commonly manipulated or otherwise physically interacted with" (Philips et al. 2012, p.4) (e.g. hammer, umbrella) and „non-manipulated" objects,

represented by animals that are not commonly manipulated or interacted with (e.g. lion, scorpion).The test critera for both tasks were accuracy and response time. The authors concluded that the results, as expected, "further strengthen the evidence that naming manipulated objects depends on motor circuits" (Philips et al. 2012, p.4).

To sum up, PD patients show multiple deficits in multiple fields of language, as pragmatics, lexicon and grammar, of course not in terms of aphasia. In the above cited studies PD patients show low performance in a great variety of tasks: sentence comprehension, irony comprehension, semantic priming, object naming, past tense production and grammatical processing. Often the authors note that until then former research has elicited conflicting results. Also the results of the above mentioned studies show great variety and interpretation of the obtained findings seems often complicated. This may be due to multiple confounding factors: firstly, the studies often have a very complex study design and especially task design, of course due to the complex nature of language and the involvement of other cognitive resources as working memory or executive functioning. Secondly, the patient numbers are very small, often they are even again separated into subgroups. Thirdly, the patient material seems to be very incongruent, all participating patients are in mild to moderate stages of the disease – of course to rule out dementia which accompanies many PD patients in later stages of the disease- however, in these stages of the disease, range of quality and quantity of the symptoms, motor and non-motor, differ greatly between individuals. This becomes evident especially when looking at the medication of the participating patients: some do take levodopa, but in very different dosages, others take dopamine-agonists and are apparently not yet in need of levodopa, and others take no medication at all. One study recruited patients participating in a clinical trial of deep brain stimulation in very early stages of the disease when this surgical therapy is no standard at all. In my opinion, all these factors add up to a bad comparability across research about language in PD. Further research should concentrate on larger patient numbers and tasks designed as simple as possible. The matter seems worth the effort, because Parkinson's disease really allows to get a clinic-anatomical glimpse of the role subcortical structures play in language.

The conclusion that is suggested by this pattern is that subcortical structures play no essential role in language processes themselves but are essential parts of complex neural systems, whose cortical regions are responsible for psycholinguistic computations.

Conclusion

The role of subcortical structures in speech and language is still controversial. Obviously the basal ganglia do play a role in motor processing, articulatory functioning and they play a role in language processing, but the very specific nature of participation in these processes remains undisclosed. Some authors vouch for a “subcortical aphasia” as a distinct clinical entity including a clinico-anatomical correlation whereas others believe that no real language disturbances exist in the absence of a cortical lesion or at least a cortical dysfunction.

Several theoretic models have been developed to explain the existence of aphasia after lesions of subcortical structures, some authors proposed direct involvement of subcortical areas in language (Cappa et al. 1983, Mega and Alexander 1994), others held subcortical structures responsible for monitoring of the regulation and release of cortical formulated language segments (Crosson 1985, 1988) or involvement in monitoring multiple, cortically generated, lexical alternatives to match semantic and motivational demands (Wallesch and Papagno 1988). Other researchers focused on the anatomical destruction of white matter fiber tracts accompanying subcortical grey matter lesions and consequently disconnecting these structures from cortical areas responsible for language functions (Alexander et al. 1987).

More recent studies emphasizing functional neuroimaging techniques favor the concept of diaschisis explaining the language impairment by cortical hypoperfusion and dysfunction related to subcortical lesions. Especially these results greatly contradict the theory of an independent role or function of subcortical structures in language, rather, similar to the conclusion concerning their impact in language disturbances in Parkinson’s disease, they are an essential part of a neural network serving cortical processing.

Subcortical aphasia as a clinical entity may be a useful term describing language disturbances in patients with no obvious cortical lesions in routine neuroimaging conducted within clinical neurological state of the art. It must be kept in mind however, that these patients are prone to cortial hypoperfusion if they underwent functional neuroimaging studies.

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Addendum

Zusammenfassung

In den klassischen Konzepten von Aphasie wird üblicherweise der zerebrale Kortex als morphologisches Substrat für die Störung angesehen. Diese traditionelle Sichtweise wurde im letzten Drittel des vergangenen Jahrhunderts hinterfragt da einige kliniko-anatomische Korrelationsstudien Hinweise erbrachten dass auch Sprachstörungen im Sinne von Aphasien in Assoziation mit rein subkortikalen Läsionen entstanden. Vor allem die Entwicklung der modernen bildgebenden Techniken in der Medizin wie Computertomographie und Magnetresonanztomographie führten zu einem Anstieg von Studien die über Aphasien nach isoliert subkortikalen Läsionen, v.a. der striatokapsulären Region und des Thalamus berichteten.

Die klinische Charakteristik der subkortikalen Aphasien wurde oftmals sehr inkonsistent beschrieben und konnte keinem schon bekannten aphasischen Symptomenkomplex eindeutig zugeordnet werden. Allen Patienten gemeinsam war ein unterschiedlich ausgeprägtes Defizit in der Sprachproduktion oftmals mit semantischen und phonematischen Paraphasien, Perseverationen und Wortfindungsstörungen die die Sprachproduktion unflüssig erscheinen ließen. Die Ausprägung der Störung wurde fast immer als mild bis moderat beschrieben, auch die Dauer der Aphasie über die Zeit wechselte stark, von einigen Wochen bis Monaten hin zu persistierenden Aphasien.

Daraufhin wurden einige theoretische Modelle zu diesen so genannten „subkortikalen“ Aphasien entwickelt die die Rolle dieser anatomischen Strukturen in der Sprache erklären sollten. Die Funktionen die den Basalganglien, insbesondere dem Thalamus zugeschrieben wurden reichten von Aufgaben einer Relaisstation für die Verarbeitung unspezifischer Informationen die die Verarbeitung von Sprache genauso behinderten wie die anderer kognitiver Funktionen bis hin zu spezialisierten Aufgaben die hemisphärendominant und sprachspezifisch waren und auch mit einer gewissen Autonomie gegenüber anderen kortikalen sprachrelevanten Arealen durchgeführt wurden.

Insbesondere die Ergebnisse neuerer Studien mit funktioneller Bildgebung widersprechen einer autonomen Rolle der Basalganglien in Zusammenhang mit Sprache da bei diesen Patenten fast immer auch eine kortikale Hypoperfusion und damit auch Funktionsstörung nachweisbar ist.

Im Rahmen dieser Arbeit wurde auch der Einfluss einer anderen neurodegenerativen Erkrankung auf Sprache untersucht: Morbus Parkinson ist eine Erkrankung deren wesentliches Merkmal eine Degeneration und Funktionsstörung der subkortikalen Strukturen darstellt und sich hier als Vergleich gut eignet.

Zusammenfassend kann gesagt werden dass die Rolle subkortikaler Strukturen bei Sprachproduktion und –rezeption noch immer unklar ist. Die subkortikale Aphasie als eigene klinische Entität konnte sich nicht durchsetzen. Subkortikale Strukturen sind sicher an motorischen Prozessen mitbeteiligt, dies beinhaltet auch Prozesse der Sprachproduktion, das Ausmaß und die Exklusivität dieser Beteiligung werden jedoch kontrovers diskutiert.

Lebenslauf

1982-1986	Volksschule , Purkersdorf, NÖ
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