Chapter 2
Translational Neuroscience of Aphasia and Adult Language Rehabilitation

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Abbreviations

AF	Arcuate fasciculus
BA	Brodmann area
CIT	Constraint-induced therapy
(f)MRI	(Functional) magnetic resonance imaging
IFG	Inferior frontal gyrus
IFOF	Inferior-fronto-occipital fasciculus
PET	Positron-emission tomography
SLF (I,II,III)	Superior longitudinal fasciculi (segments I, II, III)
tfEmC	Temporo-frontal extreme capsule
UF	Uncinate fascicle

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2.1 Perspectives and Challenges in Contemporary Aphasia Rehabilitation

Stroke is one of the most devastating neurological conditions, leading to deaths and, for stroke survivors, to motor and cognitive deficits, including aphasia. It is without doubt that the study of brain anatomy and pathophysiology, at the macroscopic as well as the neuronal level, has been of great value in the attempt to understand compensatory mechanisms after stroke and recovery processes in aphasia.

Subsequent to brain injury or disease, different molecular, biochemical, and anatomical changes occur that lead to motor, sensory, and/or cognitive deficits (Whishaw & Kolb, 1988). In the last 15 years, neuroscience research has focused on the relationship between molecular/cellular changes and cognition, in order to classify neural circuits amenable to rehabilitation strategies (Pal, Alves, Larsen, & Møller, 2014; Vallon, Chang, Zhang, & Kuo, 2014). However, the specific cortical mechanisms which could result in recovery from and rehabilitation of neurocognitive disorders, such as aphasia, are yet to be elucidated.

Even though lesion studies in acute and chronic post-stroke phases have been quite popular and have made great progress during the two last decades (Eaton et al., 2008; Fridriksson et al., 2018; Price & Crinion, 2005), it still remains difficult to clarify the exact mechanisms of the brain's structural and functional reorganization and how this is related with the observed behavior, in terms of linguistic ability (Saur et al., 2006). This is due to several reasons, including the huge individual variability concerning both brain anatomy (Ojemann, 1979; Steinmetz & Seitz, 1991) and post-stroke language deficits (Alexander, Naeser & Palumbo, 1987; Kasselimis, Simos, Peppas, Evdokimidis, & Potagas, 2017) that affect recovery (Lazar & Antoniello, 2008; Lazar, Speizer, Festa, Krakauer, & Marshall, 2008). On the other hand, despite the long history of neuroanatomical research, there are still many questions to be answered regarding the "localization" of distinct language processes in the healthy brain and the role of specific brain areas and/or networks in language function (Campbell & Tyler, 2018; Fedorenko & Thompson-Schill, 2014; Friederici, 2011; Skeide & Friederici, 2016a, 2016b).

Ever since the first postmortem findings of Broca (1865) and Wernicke (1874), there is a long history of advanced neuroimaging studies in healthy brain structure and function, incorporating data from architectonical investigation of cortex (see for a review Amunts & Zilles, 2012) and comparative studies with primates such as the macaque monkey (e.g., Petrides & Pandya, 2009) but also studies of structural and functional neuroanatomy in relation to specific language functions (see for a review Price, 2012). It is worth mentioning that studies on nonhuman primates using autoradiographic methods provide more accurate results regarding white matter tracts connecting cortical regions, as current neuroimaging methods do not suffice to trace the exact nature of anatomical structure (Vernooij et al., 2007). However, that even if such methods are more accurate compared to noninvasive neuroimaging methods, these studies cannot provide direct evidence for brain-language relationships, given that language is unique to humans.

Beyond the importance of investigating the neural underpinnings of language and the phylogenetic history of the brain regions supporting it, along with the pathophysiological mechanisms underlying its breakdown, the thorny question of the efficacy of intervention strategies implemented in neurological patients remains. While aphasia rehabilitation began to gain major popularity after World War II (Basso, 2003), one of the most intriguing questions in contemporary clinical practice is whether individuals with acquired language disorders can improve their language abilities over the course of time (Mazzoni et al., 1995; Pickersgill & Lincoln, 1983; Sarno & Levita 1979a, 1979b). Recent meta-analytic studies on the efficacy of stroke-induced aphasia rehabilitation demonstrate that aphasia treatment is more effective compared to spontaneous recovery. It is however noteworthy that, despite the fact that a large number of studies have focused on different types of treatment for specific language deficits, such as word retrieval (Hicken, Best, Herbert, Howard, & Osborne, 2002; Martin & Laine, 2000), verbal fluency (Belin et al., 1996), and auditory verbal comprehension (Davidoff & Katz, 1985), very little is known about the neural basis of rehabilitation. In order to understand these effects, a shift of focus is required from the value of aphasia treatment to the optimization of rehabilitation strategies, based on the neurobiological phenomena that occur in the brain in response to neural injury or disease. In the following sections, we will present the contemporary view on the brain networks supporting language and then elaborate on the basic mechanisms of post-stroke recovery. Finally, we will discuss issues related to treatment and reflect on future endeavors for research in this field.

2.2 A Dual Model for Language Processing: Evidence from Humans and Nonhuman Primates

It could be argued that the genesis of aphasiology can be traced back to the nineteenth century. Postmortem studies during that era indicated that lesions affecting either one of the two traditional *language centers* (Broca's and Wernicke's areas), or the underlying fibers interconnecting them, would cause a specific language impairment, the characteristics of which would depend on the topology of the cortical lesion and/or subcortical disconnection (Lichtheim, 1885). For more than a century, the Wernicke-Lichtheim model dominated the field of aphasiology, despite the ongoing debate on the specifics of the structure and function of the perisylvian language network (for a historical review and critical discussion, see: Rijntjes, Weiller, Bormann, & Musso, 2012; Weiller, Bormann, Saur, Musso, & Rijntjes, 2011).

At the dawn of the twenty-first century, a dual stream model was introduced in an attempt to interpret the neuroanatomical processing of auditory language (Hickok & Poeppel, 2004, 2007). The newly proposed language network consisted of two major pathways: a dorsal stream connecting prefrontal areas (with stronger connections in BA 44 and premotor areas, i.e., BA 6) with the inferior parietal and posterior temporal cortices, which supported sound-to-articulation mapping, and a ventral

stream, linking prefrontal areas (mostly BA 45 and BA 47) with ventral temporal regions involved in sound-to-meaning mapping (Saur et al., 2008).

Collectively, neuroimaging studies using diffusion tensor imaging and functional connectivity methods have provided insight to the properties of these two major streams, as well as to the way in which language-related information is integrated. The superior longitudinal fasciculi segments (SLF I, II, III; Makris et al., 2004; Petrides, 2014; Petrides & Pandya, 2009) and the arcuate fasciculus (AF) (Catani, Jones, & Ffytche, 2005; Frey, Campbell, Pike, & Petrides, 2008) are considered to be dorsal pathways, while the temporo-frontal extreme capsule (tfEmC) (Makris & Pandya, 2009; Petrides & Pandya, 2009), the uncinate fascicle (UF) (Duffau, Gatignol, Moritz-Gasser & Mandonnet, 2009), and the inferior-fronto-occipital fasciculus (IFOF) (Sarubbo, De Benedictis, Maldonado, Basso & Duffau, 2013) constitute the ventral system (Saur et al., 2008; Weiller et al., 2011). Diffusion data of probabilistic tractography in humans are comparable with task-based functional imaging results (Saur et al., 2008, 2010), thus allowing to assess the expected language-related function of the two streams and further strengthening the validity of the dual-path model (for a review in human and monkey brains, see Axer, Klingner, & Prescher, 2013; for an extensive discussion, see Rijntjes, Weiller, Bormann, & Musso, 2012; but see also Catani, Jones, & Ffytche, 2005). Structural and functional connectivity studies associate dorsal stream tracts with mapping sound onto articulation processes, as required for word- and nonword-repetition tasks (Saur et al., 2008), but also with hierarchical structure manipulation, as required in syntax (Friederici, 2012b, 2018). Similarly, task-based fMRI (Saur et al., 2008, 2010) and electrical stimulation studies (see Duffau, 2012 for a critical review) provide evidence for the role of the ventral stream and more specifically tfEmC in mapping sound onto meaning in healthy individuals (for a discussion, see Friederici, 2012a).

The aforementioned findings are in accordance with evidence derived from different patient cohorts, including tumors (Duffau, Herbet, & Moritz-Gasser, 2013), post-stroke aphasia (Fridriksson et al., 2018; Kümmerer et al., 2013; Holland, Johns, & Woollams, 2018), primary progressive aphasia (Agosta et al., 2013), and central alexia (Aguilar et al., 2018).

Moreover, there is a close correspondence between neuroimaging findings in humans and autoradiographic tracing studies in nonhuman primates. Macaque monkeys seem to have similar ventral tracts, and especially the tfEmC, connecting ventrolateral frontal and temporal and inferior parietal regions (Petrides & Pandya 2006, 2007, 2009; Schmahmann & Pandya 2006). It is noteworthy that in studies implementing autoradiographic tracing, the tfEmC has been delineated as a separate tract from the UF, which is considered to be a limbic pathway (Duffau, Gatignol, Moritz-Gasser, & Mandonnet, 2009; Schmahmann & Pandya 2006). Regarding the dorsal tract, AF and SLF have been delineated in the macaque monkey brain as distinct association fiber pathways (Schmahmann et al. 2007), while the middle and inferior longitudinal fasciculi contribute to the formation of both the AF/SLF and the tfEmC (Petrides & Pandya, 2007). It can be argued that comparative studies in human and nonhuman primates lend support to this dual stream language network,

yet differences arise concerning tract delineation and cortical representation. There is some evidence that connectivity patterns in the AF (Eichert et al., 2019; Rilling et al., 2008) and IFOF (Eichert et al., 2019) are different between humans and macaque monkeys. More specifically, Eichert et al. (2019) showed that the left frontal cortex is connected via the AF with the ipsilateral middle and inferior temporal gyri in the human brain, but not in the brain of chimpanzees or macaque monkeys, a finding also supported by Rilling et al. (2008).

In sum, most structural and functional brain connectivity studies confirm the existence of and illuminate the properties of an extensive language network that incorporates two major pathways connecting different cortical areas. Future research will benefit from further development in comparative anatomical and neuroimaging techniques to shed light on the mechanisms supporting language processes in the healthy brain and to expand findings in aspects of post-lesion brain reorganization. Along these lines, understanding the underlying mechanisms of stroke and, most importantly, post-stroke recovery is crucial, in order to integrate the available data derived from several fields of neuroscience and eventually formulate a multidisciplinary framework for aphasia recovery and treatment. In the following section, we attempt to describe the mechanisms of recovery after stroke.

2.3 Mechanisms of Post-stroke Recovery

Ischemic episodes are by far the most common types of stroke. Several events occur during an ischemic episode: mitochondria failure, breakdown of potassium and sodium pump, oxitoxicity following the release of glutamate and other neurotransmitters, and oxidative stress after the production of free radicals, ending with cell death (for a review, see Brouns & De Deyn 2009; Deb, Sharma, & Hassan, 2010). Hemorrhagic strokes cause more deaths compared to ischemic ones and often result in comparatively more severe motor and cognitive deficits. The hemorrhage leads to the death of cells and possible damage can also occur from secondary injuries. In general, hemorrhagic strokes have worse prognosis with regard to survival and cognitive outcome (Lezak, 2012).

Although full neural tissue regeneration cannot take place after a stroke (or any other event causing brain damage), mammalian brains have a specific mechanism which allows them to adapt and change based on external stimuli. This unique mechanism is usually referred to as "neuroplasticity." The design of the human brain may facilitate brain reorganization, given that it has a rather high number of neurons/body mass ratio and its cognitive processes are supported by diffuse functional connectivity (Turkstra, Holland, & Bays, 2003).

Over the last decades, advances in basic neuroscience have improved our knowledge in neural plasticity, a core principle in the field of neurorehabilitation. The unique ability of neurons to alter their structure and function in order to change behavior has been demonstrated even in the simplest animals, such as the nematode *C. elegans* (Bozorgmehr et al., 2013). The existing data suggest that neuroplasticity

is a prerequisite for learning new behaviors or relearning the lost ones. This is confirmed by a growing body of neuroimaging studies that demonstrate the plastic potential of the brain in healthy subjects (Raichle et al., 1994; Sowell, Thompson, Tessner, & Toga, 2001; van Turennout, Ellmore, & Martin, 2000) and in brain-damaged individuals as well (Belin et al., 1996; Musso et al., 1999; Small, Flores, & Noll, 1998).

In general, there are three ways in which an injured brain could compensate for lost tissue: (1) reorganization of all neuronal networks, (2) formation of new networks, and (3) regeneration of the lost tissue (Kolb, 1995). It is thus essential to understand that the "old" brain is developing into a "new" one, resulting into functional reorganization, even in the absence of rehabilitation (Kleim & Jones, 2008). In animal studies, rehabilitation training after unilateral cortical damage seems to improve motor function and to enhance neural plasticity in the remaining brain regions (Biernaskie & Corbett, 2001; Jones, Chu, Grande, & Gregory, 1999). However, there is evidence that plastic changes are not always beneficial (Mark & Taub, 2004). As a result, one key aspect of neurorehabilitation is to increase or induce neuroplasticity in order to maximize functional gains (Keefe, 1995). In the aphasia literature, there are studies indicating a relationship between neuroplastic changes and aphasia recovery, which indicates functional reorganization of the brain (for a review, see Thompson, 2000). There are sparse studies indicating that rehabilitation can induce neuroplasticity as well, leading to and possibly resulting in functional gains (Marcotte et al., 2012, Marcotte, Perlbarg, Marrelec, Benali, & Ansaldo, 2013; Meinzer et al., 2004). Importantly, the type of treatment appears to play a role in the reorganization of language networks (Musso et al. 1999; Wierenga et al., 2006). However, further evidence for neuroplasticity is needed in order to enhance the translation of this area into aphasia research and rehabilitation.

The main factors affecting neuroplasticity are the diffuse functional connectivity (which allows the brain to remap the neural connections), along with the location and size of brain damage. In cases of smaller lesions, the adjacent, intact regions may undertake the recovery of the lost function. In massive strokes resulting in extensive lesions, this capacity is associated with more distant areas of the lateral and contralateral hemisphere (Murphy & Corbett, 2009). Several events occur during this process, such as changes in synaptic strength, axonal remodeling, and contribution of the healthy areas of the brain (for further review, see Green, 2003). The process may be modulated by the Hebbian rule, according to which repeated activity and stimulation of the presynaptic cell is expected to strengthen the synapses that a particular neuron forms with other neurons (Hebb, 1949). In other words, neurons that fire together wire together. This could result in the alternation of the representation areas on the cortex. In addition, homeostatic mechanisms may be triggered by a cerebrovascular accident, in order to preserve adequate synaptic input, and thus Hebbian plasticity may redistribute synaptic strength (Marsh & Hills, 2006). Following this general pattern, a brain-damaged individual may regain, at least partially, a lost function. Indeed, many studies show how neuroplasticity works in a cortical and subcortical level (for a review, see Green, 2003), facilitating brain remapping, as well as how ipsilateral and/or contralateral unaffected regions may

play a compensatory role, as an alternative neural substrate of the lost function. An example regarding the role of the left hemisphere in aphasia is provided by a study conducted by Fridriksson, Bonilha, Baker, Moser, and Rorden (2010), who showed that improved naming performance was accompanied by increased cortical activation in the left hemisphere in a sample of aphasic patients with naming deficits. Apart from the processes taking place within the hemisphere ipsilateral to the lesion, there is accumulating evidence highlighting the role of contralateral (usually the right in the case of post-stroke aphasia) regions in language recovery. There is substantial evidence suggesting that language recovery relies on increased activation in the homologous right hemisphere areas ("theory of right hemisphere compensation"), in the residual undamaged left hemispheric areas ("map extension"), or in both (Thompson, 2000). For example, Rosen et al. (2000), in their PET/fMRI study, found that patients with aphasia due to lesions centered at the left inferior frontal gyrus (IFG) showed increased activation in the right IFG and left perilesional areas during language tasks; activation of the right IFG did not however correlate with verbal performance. The authors therefore attributed the activation of the contralesional IFG to either a recruitment of a healthy network via compensating behavioral strategies or a possible anomalous response to verbal stimuli in the absence of an intact left-lateralized IFG. A similar fMRI study (Staud et al., 2002) revealed that left-stroke survivors showed right-lateralized activation similar to the activation of the left hemispheric regions in healthy right-handed individuals during a silent word-generation task, thus indicating the recruitment of the homologous areas of the right hemisphere after brain damage. Similarly, in an attempt to explain the involvement of the contralateral hemisphere in recovery, Hamilton, Chrysikou, and Coslett (2011) have suggested that right-lateralized cortices homologous to the left perisylvian region may be activated during processing of linguistic stimuli due to a preexisting language network which was inhibited by the dominant hemisphere before brain damage occurred.

It should be however noted that, although some studies acknowledge the contribution of the right hemisphere in reorganization, the majority of studies suggest that the most crucial lesion-related prognostic factors are dependent on the integrity of the (left) affected hemisphere (Laska, Hellblom, Murray, Kahan, & Von Arbin, 2001; Lazar et al., 2008; for a review, see Kasselimis & Potagas, 2015). Moreover, other studies have highlighted that right hemisphere changes could be maladaptive and that increased activation in those areas is associated with worse performance (Martin et al., 2009; Price & Crinion, 2005). As a means of preventing right hemisphere excitability, recent studies have applied transcranial magnetic stimulation (TMS) to individuals with aphasia and have shown improved language abilities after stimulating right homologues of the language network, such as pars triangularis (Naeser et al., 2005; for a review on TMS and aphasia recovery, see Hamilton et al., 2011). Taking into consideration the evidence highlighting the importance of the integrity of the left-lateralized perisylvian region, as well as the indications of the detrimental effects of right hemisphere functionality during post-stroke aphasia recovery, Hamilton et al. (2011) suggest a hierarchical model for the recovery of language functions in such patients. Hamilton et al. (2011) summarize a hierarchical

model to illustrate the recovery of patients with aphasia: (1) best recovery can be achieved when brain regions originally involved in the language network regain their normal function; (2) good recovery can be achieved when the functionality of perilesional areas is restored to counterbalance the function of the damaged areas originally involved in language; (3) limited recovery can be achieved when language recovery is based primarily on the right hemisphere.

In summary, the contribution of the left and right hemisphere changes in aphasia is not fully understood. Undoubtedly, in order to maximize treatment effects, other stroke factors need to be taken into account, such as the site and size of the lesion (Raymer et al., 2007), as well as individual differences in relation to brain remapping and the contribution of the right hemisphere to language recovery (Gainotti, 1993).

Post-stroke reorganization/recovery follows a specific process, comprising three phases (Marsh & Hills, 2006): (1) the acute phase, which involves tissue restoration and lasts for a few hours to days, in which some patients might see rapid improvement, due to restoration of the blood flow in the areas surrounding ischemia (i.e., the penumbra), where the damage is reversible, because the energy-dependent metabolic processes are still active (Hossmann, 1994); (2) the subacute phase, which involves recovery from diaschisis and reorganization, during which new synapses may form; and (3) the chronic phase, which is reflected in the development of new strategies with regard to cognitive skills in general, among which are language functions. This process could last for months, or even years in some cases (Marsh & Hills, 2006). Duration and degree of recovery depends on several factors, such as lesion type and extent, severity of cognitive and language deficits, as well as age and health status (Kasselimis & Potagas, 2015; Pedersen, Stig-Jørgensen, Nakayama, Raaschou, & Olsen, 1995). With regard to aphasia recovery in particular, Saur et al. (2006) have suggested that there are three phases of post-stroke language recovery, involving different brain areas: (1) in the acute phase, activation of the remaining left perisylvian areas is reduced; (2) in the subacute phase, activation of homologous right hemisphere regions is increased; (3) in the chronic phase, activation patterns tend to approach normalization.

2.4 Timing and Intensity of Treatment

Studies investigating the optimal conditions under which neural repair and consequent remediation of sensorimotor and/or cognitive deficits can be achieved have shown that timing of intervention is a key element in neurorehabilitation. Recent findings suggest that training is more effective when applied shorty after injury (Kleim, Jones, & Schallert 2003; Woodlee & Schallert, 2004). Biernaskie, Chernenko, and Corbett (2004) observed that a 5-week rehabilitation program in rats initiated 30 days after brain injury was far less efficacious in improving motor function compared to the same treatment program starting 5 days post-infarct. A meta-analysis carried out by Robey (1998) concluded that treatment which initiates

early in the acute/subacute phase (less than 3 months post-onset) is more effective compared with rehabilitation sessions starting at 3 or 12 months post-onset. It should be also noted that delays in treatment delivery may even induce the development of compensatory behavioral strategies that may conflict with future rehabilitation efforts (Kleim & Jones, 2008). In sum, timing of treatment seems to be a crucial factor severely affecting the outcome. However, further research is needed in order to clarify the specifics of rehabilitation gains in relation to the onset of treatment and the different improvement patterns that may emerge in the acute, subacute, and chronic stages after brain injury in humans and other animals (Raymer et al., 2007).

Another critical aspect which is shown to have a significant effect on rehabilitation course and outcome is the intensity of treatment. Kleim (2003) found that intense training on a skilled reaching task changes the synapse formation within the motor cortex in rats, eventually resulting in reorganization of motor mapping in the brain. Taub, Uswatte, and Elbert (2002) suggest that motor rehabilitation programs implemented in the chronic stage in humans may be most effective if they are delivered with high intensity over a relatively short period. However, one potential drawback of training intensity after brain damage is that the possible overuse of an impaired function may inhibit overall plasticity and worsen overall function (Molteni, Zheng, Ying, Gomez-Pinilla, & Twiss, 2004). Despite such possible shortcomings, the general consensus is that intense treatment programs are beneficial in aphasia. A recent review of ten studies showed that the optimal duration for significant rehabilitation effects is 8.8 h of treatment per week for an overall period of 11.2 weeks (Bhogal, Teasell, & Speechley, 2003). Results showed that intensity in general is beneficial in aphasia rehabilitation (Basso, 2005; Baumgaertner et al., 2013).

2.5 "Use It or Lose It"

In addition to a number of physiological changes after brain injury, individuals develop behavioral compensatory strategies in order to perform daily activities, such as the constant use of the unaffected limb by stroke survivors with hemiparesis (Kwakkel, Kollen, & Lindeman, 2004). Research from basic neuroscience indicates that these strategies lead to a significant restructuring and neuronal growth in the contralesional hemisphere (Adkins, Voorhies, & Jones, 2004; Jones & Schallert, 1994). However, avoidance of using the injured limb ("learned nonuse") may lead to further degradation of structure or function and may inhibit improvement, even after treatment (Taub et al., 2002). Based on this notion, constraint-induced therapy (CIT) has shown promising results with regard to recovery of motor abilities in patients with post-stroke chronic hemiplegia (Kunkel et al., 1999). In motor rehabilitation, the key principles of CIT are massed practice, constraint of the unaffected limb with forced use of the affected limb, and behavioral shaping of the response. Pulvermüller et al. (2001) implemented CIT in an attempt to treat individuals with chronic aphasia. In their study, nonverbal communication was constrained, and 17

patients were forced to interact exclusively by talking, practicing their language skills for 3 hours on each weekday over a 2-week period. In comparison with patients that received the standard treatment of the institution, CIT-treated patients improved in tests both of language ability and in ecological verbal competence, under everyday living conditions. It should be however noted that the amount of training patients were given in conventional therapy was significantly smaller than that in CIT.

2.6 Future Endeavors for Aphasia Rehabilitation

Language is a rather complex behavior that can be broken down to several subfunctions and is supported by a widely distributed network, while its associations with other aspects of cognition are not yet fully understood. In addition, the phenomenology and underlying pathological mechanisms of acquired language disturbances remain, at large, elusive. Despite the different approaches adopted with regard to testing, intervention strategies, as well as measuring alterations in activation patterns through brain imaging and post-injury cortical remapping, in both humans and animal models, the exact mechanisms behind the restoration of language functions after brain damage have yet to be identified. Findings from basic neuroscience have revealed principles that are crucial to human studies and remain a major influence on the development of rehabilitation research in patients with aphasia. Undoubtedly, there are limitations in the translation of findings from animal studies to aphasia rehabilitation. In order to bridge that gap, computational models of cognition and language could translate basic neuroscience to human models of treatment (Nadeau, 2000). It should be emphasized that further evidence is needed about how intensity and timing can interact efficiently in individuals with aphasia, thus avoiding the negative effects of plasticity (Raymer et al., 2007). Finally, using human in vivo imaging, identification of changes in brain organization in individuals with aphasia under treatment could aid in the attempt to customize intervention programs for specific aspects of language, taking into consideration possible individual differences (Turkstra et al., 2003).

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References

Adkins, D. L., Voorhies, A. C., & Jones, T. A. (2004). Behavioral and neuroplastic effects of focal endothelin-1 induced sensorimotor cortex lesions. *Neuroscience, 128*, 473–486.

Agosta, F., Galantucci, S., Canu, E., Cappa, S. F., Magnani, G., Franceschi, M., … Filippi, M. (2013). Disruption of structural connectivity along the dorsal and ventral language pathways in patients with nonfluent and semantic variant primary progressive aphasia: A DT MRI study and a literature review. *Brain and language, 127*(2), 157–166.

Aguilar, O. M., Kerry, S. J., Crinion, J. T., Callaghan, M. F., Woodhead, Z. V., & Leff, A. P. (2018). Dorsal and ventral visual stream contributions to preserved reading ability in patients with central alexia. *Cortex, 106*, 2000–2212.

Alexander, M. P., Naeser, M. A., & Palumbo, C. L. (1987). Correlations of subcortical lesion sites and aphasia profiles. *Brain, 110*(4), 961–988.

Amunts, K., & Zilles, K. (2012). Architecture and organizational principles of Broca's region. *Trends in cognitive sciences, 16*(8), 418–426.

Axer, H., Klingner, C. M., & Prescher, A. (2013). Fiber anatomy of dorsal and ventral language streams. *Brain and language, 127*(2), 192–204.

Basso, A. (2003). *Aphasia and Its Therapy*. New York: Oxford University Press.

Basso, A. (2005). How intensive/prolonged should an intensive/prolonged treatment be? *Aphasiology, 19*(10–11), 975–984.

Baumgaertner, A., Grewe, T., Ziegler, W., Floel, A., Springer, L., Martus, P., & Breitenstein, C. (2013). FCET2EC (From controlled experimental trial to= 2 everyday communication): How effective is intensive integrative therapy for stroke-induced chronic aphasia under routine clinical conditions? A study protocol for a randomized controlled trial. *Trials, 14*(1), 308.

Belin, P., Zilbovicius, M., Remy, P., Francois, C., Guillaume, S., Chain, F., … Samson, Y. (1996). Recovery from nonfluent aphasia after melodic intonation therapy: A PET study. *Neurology, 47*(6), 1504–1511.

Bhogal, S. K., Teasell, M. D., & Speechley, M. (2003). Intensity of aphasia therapy, impact on recovery. *Stroke, 34*, 987–993.

Biernaskie, J., Chernenko, G., & Corbett, D. (2004). Efficacy of rehabilitative experience declines with time after focal ischemic brain injury. *Journal of Neuroscience, 24*, 1245–1254.

Biernaskie, J., & Corbett, D. (2001). Enriched rehabilitative training promotes improved forelimb motor function and enhanced dendritic growth after focal ischemic injury. *Journal of Neuroscience, 21*, 5272–5280.

Broca, P. (1865). Sur le siege de la faculte du langage articule. *Bulletin de la Société d'anthropologie, 6*, 337–393.

Brouns, R., & De Deyn, P. P. (2009). The complexity of neurobiological processes in acute ischemic stroke. *Clinical Neurology and Neurosurgery, 111*(6), 483–495.

Bozorgmehr, T., Ardiel, E. L., McEwan, A. H., & Rankin, C. H. (2013). Mechanisms of plasticity in a caenorhabditis elegans mechanosensory circuit. *Frontiers in Physiology*, https://doi.org/10.3389/fphys.2013.00088

Campbell, K. L., & Tyler, L. K. (2018). Language-related domain-specific and domain-general systems in the human brain. *Current Opinion in Behavioral Sciences, 21*, 132–137.

Catani, M., Jones, D. K., & Ffytche, D. H. (2005). Perisylvian language networks of the human brain. *Annals of Neurology, 57*(1), 8–16.

Davidoff, M., & Katz, R. (1985). Automated telephone therapy for improving auditory comprehension in aphasic adults. *Cognitive Rehabilitation, 3*, 26–28.

Deb, P., Sharma, S., & Hassan, K. M. (2010). Pathophysiologic mechanisms of acute ischemic stroke: An overview with emphasis on therapeutic significance beyond thrombolysis. *Pathophysiology, 17*(3), 197–218.

Duffau, H. (2012). The "frontal syndrome" revisited: Lessons from electrostimulation mapping studies. *Cortex, 48*(1), 120–131.

Duffau, H., Gatignol, P., Moritz-Gasser, S., & Mandonnet, E. (2009). Is the left uncinate fasciculus essential for language? *Journal of Neurology, 256*(3), 382.

Duffau, H., Herbet, G., & Moritz-Gasser, S. (2013). Toward a pluri-component, multimodal, and dynamic organization of the ventral semantic stream in humans: Lessons from stimulation mapping in awake patients. *Frontiers in Systems Neuroscience, 7*, 44.

Eaton, K. P., Szaflarski, J. P., Altaye, M., Ball, A. L., Kissela, B. M., Banks, C., & Holland, S. K. (2008). Reliability of fMRI for studies of language in post-stroke aphasia subjects. *Neuroimage, 41*(2), 311–322.

Eichert, N., Verhagen, L., Folloni, D., Jbabdi, S., Khrapitchev, A. A., Sibson, N. R., … Mars, R. B. (2019). What is special about the human arcuate fasciculus? Lateralization, projections, and expansion. *Cortex, 118*, 107–115.

Fedorenko, E., & Thompson-Schill, S. L. (2014). Reworking the language network. *Trends in cognitive sciences, 18*(3), 120–126.

Frey, S., Campbell, J. S., Pike, G. B., & Petrides, M. (2008). Dissociating the human language pathways with high angular resolution diffusion fiber tractography. *Journal of Neuroscience, 28*(45), 11435–11444.

Fridriksson, J., Bonilha, L., Baker, J. M., Moser, D., & Rorden, C. (2010). Activity in preserved left hemisphere regions predicts anomia severity in aphasia. *Cerebral Cortex, 20*(5), 1013–1019.

Fridriksson, J., den Ouden, D. B., Hillis, A. E., Hickok, G., Rorden, C., Basilakos, A., … Bonilha, L. (2018). Anatomy of aphasia revisited. *Brain, 141*(3), 848–862.

Friederici, A. D. (2011). The brain basis of language processing: From structure to function. *Physiological reviews, 91*(4), 1357–1392.

Friederici, A. D. (2012a). The cortical language circuit: From auditory perception to sentence comprehension. *Trends in cognitive sciences, 16*(5), 262–268.

Friederici, A. D. (2012b). Language development and the ontogeny of the dorsal pathway. *Frontiers in evolutionary neuroscience, 4*, 3.

Friederici, A. D. (2018). The neural basis for human syntax: Broca's area and beyond. *Current Opinion in Behavioral Sciences, 21*, 88–92.

Gainotti, G. (1993). The riddle of the right hemisphere's contribution to the recovery of language. *International Journal of Language & Communication Disorders, 28*(3), 227–246.

Green, J. B. (2003). Brain Reorganization After Stroke. *Topics in Stroke Rehabilitation, 10*(3), 1–20.

Hamilton, R. H., Chrysikou, E. G., & Coslett, B. (2011). Mechanisms of aphasia recovery after stroke and the role of noninvasive brain stimulation. *Brain and language, 118*(1-2), 40–50.

Hicken, J., Best, W., Herbert, R., Howard, D., & Osborne, F. (2002). Phonological therapy for word-finding difficulties: A re-evaluation. *Aphasiology, 16*, 981–999.

Hickok, G., & Poeppel, D. (2004). Dorsal and ventral streams: A framework for understanding aspects of the functional anatomy of language. *Cognition, 92*(1-2), 67–99.

Hickok, G., & Poeppel, D. (2007). The cortical organization of speech processing. *Nature Reviews Neuroscience, 8*(5), 393.

Holland, R., Johns, S. L., & Woollams, A. M. (2018). The impact of phonological versus semantic repetition training on generalisation in chronic stroke aphasia reflects differences in dorsal pathway connectivity. *Neuropsychological rehabilitation, 28*(4), 548–567.

Hossmann, K. A. (1994). Viability thresholds and the penumbra of focal ischemia. *Annals of Neurology, 36*(4), 557–565.

Hebb, D. O. (1949). *The organization of behavior* (Vol. 65). New York: Wiley.

Jones, T. A., Chu, C. J., Grande, L. A., & Gregory, A. D. (1999). Motor skills enhances lesion-induced structural plasticity in the motor cortex of adult rats. *Journal of Neuroscience, 19*, 10153–10163.

Jones, T. A., & Schallert, T. (1994). Use-dependent growth of pyramidal neurons after neocortical damage. *Journal of Neuroscience, 14*, 2140–2152.

Kasselimis, D. S., & Potagas, C. (2015). Language Disorders, Treatment and Remediation of. In D. James (Ed.), *Wright (editor-in-chief), International Encyclopedia of the Social & Behavioral Sciences* (Vol. 13, 2nd ed., pp. 329–336). Oxford: Elsevier.

Kasselimis, D. S., Simos, P. G., Peppas, C., Evdokimidis, I., & Potagas, C. (2017). The unbridged gap between clinical diagnosis and contemporary research on aphasia: A short discussion on the validity and clinical utility of taxonomic categories. *Brain and language, 164*, 63–67.

Keefe, K. A. (1995). Applying basic neuroscience to aphasia therapy: What the animals are telling us. *American Journal of Speech-Language Pathology, 4*, 88–93.

Kleim, J. A., & Jones, T. A. (2008). Principles of experience-dependent neural plasticity: Implications for rehabilitation after brain damage. *Journal of Speech, Language, and Hearing Research, 51*, S225–S239.

Kleim, J. A., Jones, T. A., & Schallert, T. (2003). Motor enrichment and the induction of plasticity before or after brain injury. *Neurochemistry Research, 28*, 1757–1769.

Kolb, B. (1995). *Brain plasticity and behavior*. Mahwah: Lawrence Erlbaum Associates.

Kümmerer, D., Hartwigsen, G., Kellmeyer, P., Glauche, V., Mader, I., Klöppel, S., … Saur, D. (2013). Damage to ventral and dorsal language pathways in acute aphasia. *Brain, 136*(2), 619–629.

Kunkel, A., Kopp, B., Muller, G., Villringer, K., Villringer, A., Taub, E., & Flor, H. (1999). Constraint-induced movement therapy for motor recovery in chronic stroke patients. *Archives of Physical Medicine and Rehabilitation, 80*, 624–628.

Kwakkel, G., Kollen, B., & Lindeman, E. (2004). Understanding the pattern of functional recovery after stroke: Facts and theories. *Restorative Neurology and Neuroscience, 22*, 281–299.

Laska, A. C., Hellblom, A., Murray, V., Kahan, T., & Von Arbin, M. (2001). Aphasia in acute stroke and relation to outcome. *Journal of Internal Medicine, 249*(5), 413–422.

Lazar, R. M., & Antoniello, D. (2008). Variability in recovery from aphasia. *Current Neurology and Neuroscience Reports, 8*(6), 497–502.

Lazar, R. M., Speizer, A. E., Festa, J. R., Krakauer, J. W., & Marshall, R. S. (2008). Variability in language recovery after first-time stroke. *Journal of Neurology, Neurosurgery & Psychiatry, 79*(5), 530–534.

Lezak, M. (2012). *Neuropsychological assessment* (5th ed.). New York: Oxford University Press.

Lichtheim, L. (1885). On aphasia. *Brain, 7*, 433–484.

Makris, N., Kennedy, D. N., McInerney, S., Sorensen, A. G., Wang, R., Caviness, V. S., Jr., & Pandya, D. N. (2004). Segmentation of subcomponents within the superior longitudinal fascicle in humans: A quantitative, in vivo, DT-MRI study. *Cerebral Cortex, 15*(6), 854–869.

Makris, N., & Pandya, D. N. (2009). The extreme capsule in humans and rethinking of the language circuitry. *Brain Structure and Function, 213*(3), 343.

Marcotte, K., Adrover-Roig, D., Damien, B., de Préaumont, M., Genereux, S., Hubert, M., & Ansaldo, A. I. (2012). Therapy-induced neuroplasticity in chronic aphasia. *Neuropsychologia, 50*(8), 1776–1786.

Marcotte, K., Perlbarg, V., Marrelec, G., Benali, H., & Ansaldo, A. I. (2013). Default-mode network functional connectivity in aphasia: Therapy-induced neuroplasticity. *Brain and Language, 124*(1), 45–55.

Mark, V. W., & Taub, E. (2004). Constraint-induced movement therapy for chronic stroke hemiparesis and other disabilities. *Restorative Neurology and Neuroscience, 22*, 317–336.

Marsh, E. B., & Hillis, A. E. (2006). Recovery from aphasia following brain injury: The role of reorganization. *Progress in Brain Research, 157*, 143–156.

Martin, N., & Laine, M. (2000). Effects of contextual priming on impaired word retrieval. *Aphasiology, 14*, 53–70.

Martin, P. I., Naeser, M. A., Ho, M., Treglia, E., Kaplan, E., Baker, E. H., & Pascual-Leone, A. (2009). Research with transcranial magnetic stimulation in the treatment of aphasia. *Current Neurology and Neuroscience Reports, 9*(6), 451.

Mazzoni, M., Vista, M., Geri, E., Avila, L., Bianchi, F., & Moretti, P. (1995). Comparison of language recovery in rehabilitated and matched, non-rehabilitated aphasic patients. *Aphasiology, 9*(6), 553–563.

Meinzer, M., Elbert, T., Wienbruch, C., Djundja, D., Barthel, G., & Rockstroh, B. (2004). Intensive language training enhances brain plasticity in chronic aphasia. *BioMed Central Biology, 2*(1), 20.

Molteni, R., Zheng, J. Q., Ying, Z., Gomez-Pinilla, F., & Twiss, J. L. (2004). Voluntary exercise increases axonal regeneration from sensory neurons. *Proceedings of the National Academy of Sciences, 101*(22), 8473–8478.

Murphy, T. H., & Corbett, D. (2009). Plasticity during stroke recovery: From synapse to behaviour. *Nature Reviews Neuroscience, 10*(12), 861–872.

Musso, M., Weiller, C., Kiebel, S., Muller, S. P., Bulau, P., & Rijntjes, M. (1999). Training-induced brain plasticity in aphasia. *Brain, 122*, 1781–1790.

Nadeau, S. E. (2000). Connectionist models and language. In S. E. Nadeau, L. J. G. Rothi, & B. Crosson (Eds.), *Aphasia and language: Theory to practice* (pp. 299–347). New York: Guilford Press.

Naeser, M. A., Martin, P. I., Nicholas, M., Baker, E. H., Seekins, H., Helm-Estabrooks, N., … Pascual-Leone, A. (2005). Improved naming after TMS treatments in a chronic, global aphasia patient—Case report. *Neurocase, 11*, 182–193.

Ojemann, G. A. (1979). Individual variability in cortical localization of language. *Journal of Neurosurgery, 50*(2), 164–169.

Pal, R., Alves, G., Larsen, J. P., & Møller, S. G. (2014). New insight into neurodegeneration: The role of proteomics. *Molecular neurobiology, 49*(3), 1181–1199.

Pedersen, P., Stig-Jørgensen, H., Nakayama, H., Raaschou, H., & Olsen, T. (1995). Aphasia in acute stroke: Incidence, determinants, and recovery. *Annals Of Neurology, 38*(4), 659–666.

Petrides, M. (2014). *Neuroanatomy of language regions of the human brain* (1st ed.). New York, NY: Academic Press.

Petrides, M., & Pandya, D. N. (2006). Efferent association pathways originating in the caudal prefrontal cortex in the macaque monkey. *Journal of Comparative Neurology, 498*(2), 227–251.

Petrides, M., & Pandya, D. N. (2007). Efferent association pathways from the rostral prefrontal cortex in the macaque monkey. *Journal of Neuroscience, 27*(43), 11573–11586.

Petrides, M., & Pandya, D. N. (2009). Distinct parietal and temporal pathways to the homologues of Broca's area in the monkey. *PLoS biology, 7*(8), e1000170.

Pickersgill, M. J., & Lincoln, N. B. (1983). Prognostic indicators and the pattern of recovery of communication in aphasic stroke patients. *Journal of Neurology, Neurosurgery & Psychiatry, 46*(2), 130–139.

Price, C. J. (2012). A review and synthesis of the first 20 years of PET and fMRI studies of heard speech, spoken language and reading. *Neuroimage, 62*(2), 816–847.

Price, C. J., & Crinion, J. (2005). The latest on functional imaging studies of aphasic stroke. *Current Opinion in Neurology, 18*, 429–434.

Pulvermüller, F., Neininger, B., Elbert, T., Mohr, B., Rockstroh, B., Koebbel, P., & Taub, E. (2001). Constraint-induced therapy of chronic aphasia after stroke. *Stroke, 32*(7), 1621–1626.

Raichle, M. E., Fiez, J. A., Videen, T. O., MacLeod, A.-M. K., Pardo, J. V., Fox, P. T., & Petersen, S. E. (1994). Practice related changes in human brain functional anatomy during learning. *Cerebral Cortex, 4*, 8–26.

Raymer, A. M., Holland, A., Kendall, D., Maher, L. M., Martin, N., Murray, L., … Gonzalez Rothi, L. J. (2007). Translational research in aphasia: From neuroscience to neurorehabilitation. *Journal of Speech, Language, and Hearing Research, 50*, S259–S275.

Rijntjes, M., Weiller, C., Bormann, T., & Musso, M. (2012). The dual loop model: Its relation to language and other modalities. *Frontiers in Evolutionary Neuroscience, 4*, 9.

Rilling, J. K., Glasser, M. F., Preuss, T. M., Ma, X., Zhao, T., Hu, X., & Behrens, T. E. (2008). The evolution of the arcuate fasciculus revealed with comparative DTI. *Nature Neuroscience, 11*(4), 426.

Robey, R. R. (1998). A meta-analysis of clinical outcomes in the treatment of aphasia. *Journal of Speech, Language, and Hearing Research, 41*, 172–187.

Rosen, H. J., Petersen, S. E., Linenweber, M. R., Snyder, A. Z., White, D. A., Chapman, L., … Corbetta, M. (2000). Neural correlates of recovery from aphasia after damage to left inferior frontal cortex. *Neurology, 55*(12), 1883–1894.

Sarno, M. T., & Levita, E. (1979a). Recovery in treated aphasia in the first year post-stroke. *Stroke, 10*(6), 663–670.

Sarno, M. T., & Levita, E. (1979b). Recovery in treated aphasia in the first year post-stroke. *Stroke, 10*(6), 663–670.

Sarubbo, S., De Benedictis, A., Maldonado, I. L., Basso, G., & Duffau, H. (2013). Frontal terminations for the inferior fronto-occipital fascicle: Anatomical dissection, DTI study and functional considerations on a multi-component bundle. *Brain Structure and Function, 218*(1), 21–37.

Saur, D., Kreher, B. W., Schnell, S., Kümmerer, D., Kellmeyer, P., Vry, M. S., … Huber, W. (2008). Ventral and dorsal pathways for language. *Proceedings of the national academy of Sciences, 105*(46), 18035–18040.

Saur, D., Lange, R., Baumgaertner, A., Schraknepper, V., Willmes, K., Rijntjes, M., & Weiller, C. (2006). Dynamics of language reorganization after stroke. *Brain, 129*(6), 1371–1384.

Saur, D., Schelter, B., Schnell, S., Kratochvil, D., Küpper, H., Kellmeyer, P., … Mader, W. (2010). Combining functional and anatomical connectivity reveals brain networks for auditory language comprehension. *Neuroimage, 49*(4), 3187–3197.

Schmahmann, J. D., & Pandya, D. N. (2006). *Fiber pathways of the brain*. New York: Oxford University Press.

Schmahmann, J. D., Pandya, D. N., Wang, R., Dai, G., D'arceuil, H. E., de Crespigny, A. J., & Wedeen, V. J. (2007). Association fiber pathways of the brain: Parallel observations from diffusion spectrum imaging and autoradiography. *Brain, 130*(3), 630–653.

Skeide, M. A., & Friederici, A. D. (2016a). The ontogeny of the cortical language network. *Nature Reviews Neuroscience, 17*(5), 323.

Skeide, M. A., & Friederici, A. D. (2016b). The ontogeny of the cortical language network. *Nature Reviews Neuroscience, 17*(5), 323.

Small, S. L., Flores, D. K., & Noll, D. C. (1998). Different neural circuits subserve reading before and after therapy for acquired dyslexia. *Brain and Language, 62*, 298–308.

Sowell, E. R., Thompson, P. M., Tessner, K. D., & Toga, A. W. (2001). Mapping continued brain growth and gray matter density reduction in dorsal frontal cortex: Inverse relationships during post-adolescent brain maturation. *Journal of Neuroscience, 21*, 8819–8829.

Staudt, M., Lidzba, K., Grodd, W., Wildgruber, D., Erb, M., & Krägeloh-Mann, I. (2002). Right-hemispheric organization of language following early left-sided brain lesions: Functional MRI topography. *NeuroImage, 16*(4), 954–967.

Steinmetz, H., & Seitz, R. J. (1991). Functional anatomy of language processing: Neuroimaging and the problem of individual variability. *Neuropsychologia, 29*(12), 1149–1161.

Taub, E., Uswatte, G., & Elbert, T. (2002). New treatments in neurorehabilitation founded on basic research. *Nature Reviews Neuroscience, 3*(3), 228.

Turkstra, L. S., Holland, A. L., & Bays, G. A. (2003). The neuroscience of recovery and rehabilitation: What have we learned from animal research? *Archives of Physical Medicine and Rehabilitation, 84*(4), 604–612.

Thompson, C. K. (2000). Neuroplasticity: Evidence from aphasia. *Journal of Communication Disorders, 33*(4), 357–366. https://doi.org/10.1016/S0021-9924(00)00031-9

Vallon, M., Chang, J., Zhang, H., & Kuo, C. J. (2014). Developmental and pathological angiogenesis in the central nervous system. *Cellular and Molecular Life Sciences, 71*(18), 3489–3506.

van Turennout, M., Ellmore, T., & Martin, A. (2000). Long-lasting cortical plasticity in the object naming system. *Nature Neuroscience, 3*, 1329–1334.

Vernooij, M. W., Smits, M., Wielopolski, P. A., Houston, G. C., Krestin, G. P., & van der Lugt, A. (2007). Fiber density asymmetry of the arcuate fasciculus in relation to functional hemispheric language lateralization in both right-and left-handed healthy subjects: A combined fMRI and DTI study. *Neuroimage, 35*(3), 1064–1076.

Weiller, C., Bormann, T., Saur, D., Musso, M., & Rijntjes, M. (2011). How the ventral pathway got lost–And what its recovery might mean. *Brain and language, 118*(1-2), 29–39.

Wernicke, C. (1874). *Der aphasische Symptomencomplex: Eine psychologische Studie auf anatomischer Basis*. Breslau: M. Cohn und Weigert.

Whishaw, I. Q., & Kolb, B. (1988). Sparing of skilled forelimb reaching and corticospinal projections after neonatal motor cortex removal or hemidecortication in the rat: Support for the Kennard doctrine. *Brain Research, 451*, 97–114.

Wierenga, C. E., Maher, L. M., Moore, A. B., Swearengin, J., Soltysik, D. A., Peck, K., … Crosson, B. (2006). Neural substrates of syntactic mapping treatment: An fMRI study of two cases. *Journal of the International Neuropsychological Society, 12*, 132–146.

Woodlee, M. T., & Schallert, T. (2004). The interplay between behavior and neurodegeneration in rat models of Parkinson's disease and stroke. *Restorative Neurology and Neuroscience, 22*, 153–161.

Further Reading

Hamilton, R. H., Chrysikou, E. G., & Coslett, B. (2011). Mechanisms of aphasia recovery after stroke and the role of noninvasive brain stimulation. *Brain and language, 118*(1-2), 40–50.

Kasselimis, D. S., & Potagas, C. (2015). Language disorders, treatment and remediation of. In J. D. Wright (Ed.), *International encyclopedia of the social & behavioral sciences* (Vol. 13, 2nd ed., pp. 329–336). Oxford: Elsevier.

Raymer, A. M., Holland, A., Kendall, D., Maher, L. M., Martin, N., Murray, L., … Gonzalez Rothi, L. J. (2007). Translational research in aphasia: From neuroscience to neurorehabilitation. *Journal of Speech, Language, and Hearing Research, 50*, S259–S275.