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Lesion characteristics driving right-hemispheric language reorganization in congenital left-hemispheric brain damage

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ABSTRACT

Pre- or perinatally acquired ("congenital") left-hemispheric brain lesions can be compensated for by reorganizing language into homotopic brain regions in the right hemisphere. Language comprehension may be hemispherically dissociated from language production. We investigated the lesion characteristics driving inter-hemispheric reorganization of language comprehension and language production in 19 patients (7–32 years; eight females) with congenital left-hemispheric brain lesions (periventricular lesions [n = 11] and middle cerebral artery infarctions [n = 8]) by fMRI. 16/17 patients demonstrated reorganized language production, while 7/19 patients had reorganized language comprehension. Lesions to the insular cortex and the temporo-parietal junction (predominantly supramarginal gyrus) were significantly more common in patients in whom both, language production and comprehension were reorganized. These areas belong to the dorsal stream of the language network, participating in the auditory-motor integration of language. Our data suggest that the integrity of this stream might be crucial for a normal left-lateralized language development.

1. Introduction

1.1. Language reorganization in adults and children

In adults, damage to the left cerebral hemisphere commonly results in specific aphasic symptoms associated with the lesion site (Gottesman & Hillis, 2010; Kreisler et al., 2000). Satisfying recovery from aphasia is often associated with left-hemispheric perilesional activation (Lidzba, Staudt, Zieske, Schwilling, & Ackermann, 2012; Saur et al., 2006; Szaflarski, Allendorfer, Banks, Vannest, & Holland, 2013), with right-hemispheric language activation more commonly seen in the more impaired patients, i.e., those with large lesions (Sims et al., 2016) or incomplete recovery (Saur et al., 2006; Szaflarski et al., 2013). In contrast to this pattern, children with left hemispheric brain damage (i.e., acquired pre- or perinatally) do not usually show persisting and substantial language deficits. Language development after congenital brain lesions may be delayed (Chilosi et al., 2005), but by school-age, such patients are perceived as competent speakers of their native language (Bates & Roe, 2001; Ilves et al., 2014). Only when confronted with linguistically complex tasks do children and adolescents with early left-hemispheric brain lesions show deficits in grammar processing (Knecht & Lidzba, 2016; Lidzba, Konietzko, Schwilling, Krägeloh-Mann, & Winkler, 2013; Schwilling, Krägeloh-Mann, Konietzko, Winkler, & Lidzba, 2012) and discourse (Reilly, Bates, & Marchman, 1998; Reilly, Wasserman, & Appelbaum, 2013). The neural mechanisms underlying language recovery in adult aphasics and language acquisition in patients with perinatal stroke seem to differ with respect to the brain tissue involved: Directly comparing children with perinatal left-hemispheric stroke with recovered adult aphasics, Szaflarski and colleagues demonstrated that the pediatric group recruited a bilateral network for language production, while the adult group was indistinguishable from healthy controls regarding lateralization (Szaflarski et al., 2014). That many (but not all) patients with left-hemispheric pre-/perinatal pathology may rely on a right-hemispheric language network has repeatedly been demonstrated for patients with and without epilepsy (Liegeois et al., 2004; Rasmussen & Milner, 1977; Tillema et al., 2008). The reorganized, right-hemispheric activation pattern

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encompasses areas homotopic to those involved in left-hemispheric language organisation, as investigated in patients with congenital white-matter lesions (Staudt et al., 2002), and in patients with left-hemispheric brain damage after epilepsy surgery (Tivarus, Starling, Newport, & Langfitt, 2012). Interhemispheric reorganization seems to affect networks connecting various regions of the brain, including the cerebellum (Lidzba, Wilke, Staudt, Krägeloh-Mann, & Grodd, 2008). This mirrored topography in cortical representation is also reflected in a corresponding reorganization of the subcortical fibre tracts in the right as compared to the left hemisphere (Duffau, Peggy Gatignol, Mandonnet, Capelle, & Taillandier, 2008).

1.2. Factors related to language reorganization

The driving force of typical or atypical language lateralization both in healthy subjects and patients with early left-hemispheric brain lesions has been a relevant research topic since Rasmussen's and Milner's (1977) seminal report on a large series of Wada tests. Not all patients with early left-hemispheric lesions have right-sided language dominance (Liegeois et al., 2004; Rasmussen & Milner, 1977), and thus, more specific factors must be expected to play a role. Perinatal infarctions of the left middle cerebral artery (predominantly affecting perisylvian cortex including the temporal lobe) seem to be more often associated with reorganization of language comprehension (Jacola et al., 2006) than pre- or perinatally acquired periventricular lesions affecting fronto-parietal white matter only (Brizzolara et al., 2002; Staudt et al., 2001). Small developmental lesions (like vascular malformations) or slowly evolving pathologies (like tumours) are not commonly associated with atypical language (Gaillard et al., 2007; Pataraia et al., 2004). In children with intractable epilepsy due to early lesions, lesion location at or near the typical language areas were not commonly associated with language reorganization in one study (Liegeois et al., 2004), but the likelyhood for atypical language organisation was increased with left frontal malformations of cortical development in another sample (Wilke et al., 2011). Epileptic seizures and even interictal epileptic activity have the potential to interfere with the representation of language function, presumably even independently of a structural lesion (Janszky, Mertens, Janszky, Ebner, & Woermann, 2006). In the absence of epileptic activity, strategically-located lesions affecting the articulatory motor tract may be sufficient for the reorganization of language production in patients with periventricular brain damage and intact cortex (Staudt, Ticini, Grodd, Krageloh-Mann, & Karnath, 2008; Staudt et al., 2001). Thus, the specific topography, extent and timing of a lesion, but also accompanying factors such as epilepsy seem to be important factors driving language (re-) organisation.

1.3. Language networks

When studying language reorganization, it is important to consider that numerous functional imaging studies have shown that language comprehension and language production recruit overlapping, but dissociable neural networks in the brain (for a review see (Price, 2012)). Language production and language comprehension can be hemispherically dissociated not only in children with epilepsy (Kurthen et al., 1992; Wilke et al., 2010) and patients with prenatally acquired periventricular lesions (Staudt et al., 2001), but also in healthy children and adolescents (Lidzba, Schwilling, Grodd, Krageloh-Mann, & Wilke, 2011). Current neuroanatomical models propose that language processing is organized in a dorsal and a ventral language stream ('dual-route model'), where both streams participate both in language comprehension and production (Dick & Tremblay, 2012; Friederici, 2015; Hickok & Poeppel, 2015, chap. 8). In the domain of language comprehension, however, the bilaterally represented ventral stream seems more important. This pathway of temporal and frontal language regions, connected by the extreme capsule fibre system and the uncinate fascicle, is involved in bottom-up language processing, such as phonological word form detection, morphosyntactic and lexical-semantic categorization, and lexical access (Friederici, 2015; Hickok & Poeppel, 2015, chap. 8; Skeide & Friederici, 2016). Consequently, in adult aphasics, comprehension deficits are associated with damage to the ventral extreme capsule fibre system (Kummerer et al., 2013). In the course of typical language acquisition in healthy children, the first two or three years are dominated by bottom-up language processing, relying mainly on the ventral stream (Skeide & Friederici, 2016). In contrast, the strongly left-lateralized dorsal stream is engaged in functions seemingly more crucial for language production. It encompasses the posterior frontal lobe, anterior insula, and the temporo-parietal junction, and it is relevant for the integration of sensory-motor information and the processing of complex syntax (Friederici, 2015; Hickok & Poeppel, 2015, chap. 8). Analogously, impairments in speech repetition are associated with lesions to the dorsal superior longitudinal and arcuate fascicle pathway in aphasic patients (Kummerer et al., 2013).

The usually small and often heterogeneous samples in which language reorganization after congenital brain lesions can be studied pose a methodological challenge. Nevertheless, it is of both clinical and neuroscientific interest to investigate in more detail (1) the gross lesion characteristics forcing the right hemisphere into language processing, and (2) specific brain regions that are crucial for typical language representation. In order to address these issues, we studied a homogeneous sample of patients with pre- and perinatally acquired left-hemispheric brain lesions. As done previously (Staudt et al., 2001, 2002), we included only patients with clearly defined lesions involving only the left hemisphere, i.e., strictly unilateral periventricular white matter lesions or middle cerebral artery infarctions. We here employed functional MRI tasks for language production and comprehension in combination with the voxel-lesion symptom mapping (VLSM) approach to identify brain regions that induce reorganization of language comprehension or language production when damaged. Since infarctions of the middle cerebral artery typically affect the frontal and/or temporal grey and white matter, we expected a higher probability of reorganization of language comprehension in patients with middle cerebral artery infarctions than in those with periventricular lesions (Hypothesis 1a). More specifically, we expected that regions within the ventral stream of language processing, namely the middle temporal gyrus and inferior temporal sulcus, and underlying white-matter structures (i.e., the extreme capsule fibre system and the uncinate fascicle) would be the most relevant in driving reorganization of language comprehension (Hypothesis 1b). For language production, we expected that lesions within the dorsal stream of language processing, namely the temporo-parietal junction, premotor cortex, inferior frontal gyrus and anterior insula, and underlying white matter structures would be predictive for reorganization (Hypothesis 1c). Since language production and language comprehension usually recruit overlapping networks of the same hemisphere, we also expected a significant correlation between lateralization of language production and language perception (Hypothesis 2).

Since our sample also contained patients with epilepsy, we were able to test also an alternative hypotheses, namely that language reorganization will be more frequent in patients with epilepsy as compared to patients without epilepsy, irrespective of lesion location or lesion type (Alternative hypothesis 1a*).