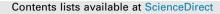
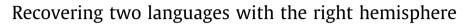
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ABSTRACT

Converging evidence suggests that the right hemisphere (RH) plays an important role in language recovery from aphasia after a left hemisphere (LH) lesion. In this longitudinal study we describe the neurological, cognitive, and linguistic profile of A.C., a bilingual who, after a severe traumatic brain injury, developed a form of fluent aphasia that affected his two languages (i.e., Romanian and Italian). The trauma-induced parenchymal atrophy led to an exceptional ventricular dilation that, gradually, affected the whole left hemisphere. A.C. is now recovering both languages relying only on his right hemisphere. An fMRI experiment employing a bilingual covert verb generation task documented the involvement of the right middle temporal gyrus in processes of lexical selection and access. This case supports the hypothesis that the RH plays a role in language recovery from aphasia when the LH has suffered massive lesions.

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1. Introduction

Language is a complex cognitive function implemented in an extensive array of neural networks (Indefrey, 2014; Vigneau et al., 2006). For long time, the only way to study the neural organization of language relied on the observation of patients with linguistic impairments after focal lesions to the left hemisphere (LH). This approach allowed clinicians to identify areas potentially involved in lexical production and comprehension in the cortical layer of the LH (e.g., Broca, 1865; Geschwind, 1970). Over the past 20 years, converging evidence from both neuropsychological studies on patients with brain lesions and investigations of linguistic processing in healthy individuals suggests that also the right hemisphere (RH), far from being "mute", plays an important role in selective aspects of language processing (Joanette, Goulet, & Hannequin, 1990; Myers, 1993). For example, persons with right

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hemisphere damage may exhibit difficulties involving prosodic, pragmatic, and even narrative abilities (Ferré, Ska, Lajoie, Bleau, & Joanette, 2011; Lehman Blake, 2006; Marini, 2012; Marini et al., 2005). A recent meta-analysis of 128 studies involving right-handed healthy participants found that the involvement of the RH was marginal in phonological and semantic processing but significant in sentence and discourse processing (Vigneau et al., 2011).

A critical issue regards the role potentially played by the RH in aphasia recovery. Generally speaking, the plastic reorganization of the linguistic networks after a lesion requires a complex interplay between the recruitment of neurons in perilesional areas (Heiss & Graf, 1994), the modulation of existing synaptic connections, and the generation of new synapses (Tecchio et al., 2006). As highlighted in a recent critical survey on this topic (Gainotti, 2015), the role of the RH in linguistic recovery after a lesion to the LH is still controversial. Two major hypotheses have been formulated so far: the "interhemispheric inhibition hypothesis" and the "right hemisphere involvement hypothesis". According to the former, a lesion of the language epicenters in the LH (e.g., in the left inferior frontal gyrus) might hypothetically release a transcallosal inhibition on homologue areas in the RH. This might interfere with





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the perilesional reorganization in the LH hampering the process of recovery from aphasia (Turkeltaub, 2015). If this were the case, the inhibition of the RH homologues of language areas in the LH should enhance language recovery in patients with aphasia after lesions to the LH. Over the past 10 years a growing number of studies have tested this hypothesis by applying inhibitory stimulation (i.e., low frequency Transcranic Magnetic Stimulation, TMS or cathodic transcranial direct current stimulation, tDCS) over RH homologues of language areas in such patients. For example, two seminal investigations by Martin et al. (2004) and Naeser et al. (2005) showed that low frequency rTMS over the right pars triangularis improved picture naming in persons with chronic non-fluent aphasia (see also two recent meta-analyses by Ren et al. (2014) and Otal, Olma, Floel, and Wellwood (2015) showing positive effects of RH inhibition on a number of linguistic functions). Critically, most of these studies have focused on the inhibition of a specific region of the RH (i.e., the right inferior frontal gyrus) leaving open the possibility that other areas of the same hemisphere, under specific circumstances, might play an active role in language recovery after a lesion to the LH ("right hemisphere involvement hypothesis"). These circumstances include: (1) the extension of the lesion in the LH, with large lesions more likely to recruit homologue areas in the RH (Anglade, Thiel, & Ansaldo, 2014; Heiss & Thiel, 2006); (2) the time elapsed since the onset of aphasia, with a recruitment of areas in the RH more likely to occur in the acute phase after the lesion and a gradual decrease of such recruitment with time (e.g., Ansaldo, Arguin, & Roch Lecours, 2002; Saur et al., 2006); (3) the speed of the development of the lesion in the LH, with slowly proceeding lesions rather than faster ones more likely to trigger a shift of linguistic functions to the RH (Thiel et al., 2006); (4) the specific linguistic function to be recovered, with a good level of semantic and lexical recovery but a much lower level of phonological and syntactic recovery after reorganization of language areas in the RH (Abel, Weiller, Huber, & Willmes, 2014; Wright, Stamatakis, & Tyler, 2012). The possibility of a right hemispheric involvement in language recovery has been supported by a study by Flöel et al. (2011) where anodal tDCS over the right temporo-parietal cortex improved naming in a cohort of twelve chronic persons with aphasia. Furthermore, this hypothesis is also in line with available evidence suggesting that the right hemisphere might play an active role in language recovery from aphasia (e.g., Barlow, 1877; Basso, Gardelli, Grassi, & Mariotti, 1989; Turkeltaub et al., 2012). For example, Barlow (1877) described the case of a boy with nonfluent aphasia after a stroke in the left inferior frontal gyrus who recovered his linguistic skills over time, but then worsened again after a symmetric stroke in the right hemisphere. This case was taken as evidence that the right hemisphere might assume functions of the left hemisphere in aphasic individuals. More recently, Turkeltaub et al. (2012) described the case of a 72-year-old woman who suffered from chronic non-fluent aphasia following left middle cerebral artery ischemic stroke. In this patient, 10 daily inhibitory TMS sessions over the right pars triangularis improved naming skills. An fMRI scan confirmed the reduction in activity in the target area of the RH (but failed to show any increase in activity in the homologue areas of the LH). This apparently confirmed the "interhemispheric inhibition hypothesis". However, three months after the TMS sessions, the patient suffered a right hemisphere stroke that significantly worsened her linguistic impairments. This supports the possibility that at least some areas of the RH might play a key role in language recovery.

Overall, these findings provide both indirect and direct evidence of the role played by the right hemisphere in language recovery from aphasia. In the current study we provide an accurate description of the neurological, cognitive and linguistic profile of A.C., a bilingual with parallel aphasia after severe traumatic brain injury. Most importantly, a large ventricular dilation affecting left fronto-temporo-parietal regions has devastated his left hemisphere over a period of four months in which the left lateral ventricle kept dilating (from April until August 2009). Since then no further ventricular dilation was observable and only three months later (since November 2009) the patient initiated a gradual and very slow linguistic recovery of his two languages relying only on his RH. We believe that this case provides an opportunity to significantly contribute to the ongoing debate on the role played by the RH on language recovery.

2. Materials and methods

2.1. Case history

A.C. is a 24 years old right-handed male who was born in Romania. His limb dominance was determined according to the Edinburgh Handedness Inventory (Oldfield, 1971). At the age of 7 he moved with his family to Italy where he completed his instruction and was hired as mechanic. Before the insult, A.C. was a sequential bilingual with comparable levels of exposure to his two languages (L1 at home with family and relatives; L2 at work and with friends) and similar levels of proficiency in both Romanian (L1) and Italian (L2). His bilingual history was explored by administering the questionnaire contained in the first section of the Bilingual Aphasia Test (BAT; Paradis, 1987; see Table S1).

In April 2009, at age 19, A.C. was involved in a car accident and reported a severe traumatic brain injury (Glasgow Coma Scale = 4; post-traumatic amnesia > 1 month) resulting in a coma (20 days). Immediately after the accident, a first CT scan showed cerebral edema, subarachnoid hemorrhage (SAH), and a compression of the lateral ventricle in the left cerebral hemisphere (see Fig. 1a). A.C. received frontal-temporal craniotomy, followed by removal of necrotic brain tissue. After three months (July 2009), a second CT scan showed malacia in the left hemisphere, global dilation of the entire left ventricular system, and focal dilation ex vacuo of the left lateral ventricle. The global dilation was likely the consequence of the SAH, whereas the focal dilation of the lateral ventricle was determined by the left hemisphere malacia (see Fig. 1b). A third scan (August 2009) showed a further dilation of the left lateral ventricle that was particularly evident in the frontal, parietal and occipital lobes (see Fig. 1c). After this period, no further ventricular dilation was observable (see Fig. 1d). Immediately after the coma, A.C. was diagnosed with spastic tetraparesis, mostly right lateralized. In September 2009 his motoric impairment was still characterized by marked right hemiparesis that forced him to the use of a wheelchair. A.C. had been hospitalized for 18 months at the "Santa Croce" Hospital in Cuneo (Italy). During the hospitalization, he was mostly exposed to Italian, the language used by the medical staff. In October 2009 it was still not possible to perform a neuropsychological assessment and his linguistic skills were severely affected. He could not speak because of massive orofacial apraxia. In November 2009, A.C. could understand simple requests in Italian and in the same language could name colors but still not verbs and objects. His speech contained semantic paraphasias and perseverations. A first, still incomplete, neuropsychological assessment performed in May 2010 in Italian showed major difficulties as attested by his inability to complete several tests and the low scores obtained on the Mini-Mental State Examination (MMSE: 23/30) and on tests assessing attention (trail making A z-scores: -3.52; trail making B z-scores: -14; visual search test: z-scores: -3.33). In October 2010, A.C. eventually left the Hospital and began an intensive rehabilitation program at the Rehabilitation Center "Puzzle" in Turin, where his cognitive and linguistic skills were thoroughly assessed in different periods (see Table 1) and where he is still receiving cognitive and linguistic rehabilitation in Italian (his L2) twice a week in sessions of

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