Brain and Language 185 (2018) 47–53

Contents lists available at ScienceDirect

Brain and Language

journal homepage: www.elsevier.com/locate/b&l

Short communication

Pragmatic abilities in multiple sclerosis: The contribution of the temporo-parietal junction

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ARTICLE INFO

Keywords:
Pragmatics
Neuropragmatics
Geschwind's area
Language
Social cognition
Multiple sclerosis
Functional connectivity

ABSTRACT

Recent studies showed that multiple sclerosis (MS) patients might experience communicative deficits, specifically in pragmatics (i.e., the ability to integrate the context-dependent aspects of language). A crucial region for pragmatics is the temporo-parietal junction, in particular the so-called Geschwind's area (GA), which is involved in high-level language processes, including the comprehension of narratives, metaphor, and irony. We evaluated the relationship between pragmatic abilities, measured through the Assessment of Pragmatic Abilities and Cognitive Substrates (APACS) test, and the functional connectivity (FC) of the bilateral GAs, assessed through a seed-based analysis of Resting-State fMRI in patients with MS. A positive correlation was observed between APACS scores and the FC for both the right and the left GA and the paracingulate cortex. Our findings suggest that the brain FC for social communication involves connections extending over both hemispheres, including right and left GAs and right and left paracingulate cortex, possibly impaired in patients with MS. This study offers preliminary evidence for future researches enrolling also a control sample to explore the involvement of GA in pragmatics in neurological disorders as well as in healthy conditions.

1. Introduction

Multiple sclerosis (MS) is the most common disabling neurological disease in young adults (Compston & Coles, 2008). Cognitive impairment has been described in 43–72% of patients with MS, affecting processing speed, visual and verbal learning, memory, as well as attention, executive functioning, and working memory (Chiaravalloti & DeLuca, 2008; Rao, Leo, Bernardin, & Unverzagt, 1991). Also language could be impaired in patients with MS (Renauld, Mohamed-Said, & Macoir, 2016), especially high-level linguistic skills, such as understanding ambiguous sentences, non-literal language, and narrative speech (Arrondo, Sepulcre, Duque, Toledo, & Villoslada, 2009). These studies seem to point to a deficit in the dimension of the so-called pragmatics, which allows speakers to understand the context-dependent aspects of meaning, beyond the structural components of language (Bambini & Bara, 2012; Bambini, 2010). Pragmatics is essential when deriving the message that the speaker intends to convey (the so-called speaker's meaning) and when engaging in successful conversation, monitoring discourse and providing adequate information for the exchange (Levinson, 1983; Sperber & Wilson, 2002). In a previous study, we conducted a comprehensive investigation of pragmatic abilities in MS, the first one available in the literature, showing a deficit in 55% of our sample of patients compared to normative data (Carotenuto et al., 2018). Patients fail in conducting an appropriate conversation, as well as in understanding non-literal language such as metaphors and humor. We also showed that in MS pragmatic abilities are relatively independent of cognitive abilities, being the pragmatic deficit equally present in patients with or without cognitive impairment. By contrast, we showed that pragmatics scores were associated with social cognition, another domain that might be impaired in patients with MS

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https://doi.org/10.1016/j.bandl.2018.08.003
Received 25 February 2018; Received in revised form 9 July 2018; Accepted 2 August 2018

(Cotter et al., 2016). Indeed, pragmatics abilities play a pivotal role in social interaction and are strictly connected to social cognition (Sperber & Wilson, 2002), defined as the set of mental operations that underlie social interactions (Green et al., 2008), including the ability to understand the others' mental states and intentions (Theory of Mind [ToM]) and the processes of emotion perception and recognition (Penn, Sanna, & Roberts, 2008).

From the anatomical point of view, the pragmatic aspects of language engage the activity of the temporo-parietal junction (TPJ) in a bilateral fashion (Hagoort & Levinson, 2014), and, specifically, the activity of the so-called Geschwind's area (GA), corresponding to the angular and supramarginal gyri in the inferior parietal lobule (Catani & Bambini, 2014; Catani, Howard, Pajevic, & Jones, 2002; Catani, Jones, & ffytche, 2005; Ruschel et al., 2014). Neuroimaging studies reported the involvement of TPJ in processing a wide array of pragmatic phenomena, from non-literal language to discourse aspects (Bambini, Gentili, Ricciardi, Bertinetto, & Pietrini, 2011; Mason & Just, 2009; Spotorno, Koun, Prado, Van Der Henst, & Noveck, 2012). A recent hypothesis claims that connectivity involving GAs might be key to pragmatic behavior, implementing the most sophisticated level of language and social communication abilities in humans (Catani & Bambini, 2014). Despite abundant research on neuropragmatics in healthy individuals, research on patients is mostly clinical, and no studies investigated the brain connections underpinning pragmatic deficit in patients with pathological changes throughout the brain and specifically in MS, leaving a domain with important impact on social life totally unexplored.

In this study, we aimed at elucidating patterns of brain activity that might underlie the pragmatic deficit in MS. Specifically, we performed a Resting-State (RS) fMRI study evaluating the correlations of pragmatic abilities with the functional connectivity (FC) of bilateral GA in patients with MS. RS-fMRI is a powerful and non invasive tool to investigate brain functions during rest, with subjects awake but not involved in any specific task (Fox & Raichle, 2007; Lv et al., 2018). Here we investigated possible alterations of RS-fMRI data in patients with MS using a seed-based approach, an analysis that allows for the investigation of the FC of specific brain regions (Fox & Raichle, 2007). We focused our analysis on bilateral GAs, given the robust evidence of their involvement in pragmatics (Catani & Bambini, 2014). In particular, right and left GAs, including anterior and posterior supramarginal gyrus (aSMG and pSMG, respectively) and the angular gyrus (AG), were chosen as seed regions, enrolling a subset of patients whose pragmatic abilities were assessed in the context of a previous study (Carotenuto et al., 2018). Based on the available evidence on the neural correlates of pragmatic abilities in healthy individuals, we speculated that pragmatic deficits in patients with MS could be strongly linked to FC alterations of the GA, and to a disruption of the functional connections encompassing this area. Results would help elucidating the role of FC of GA in pragmatic impairment in MS, offering preliminary evidence for future studies enrolling also a control sample to explore the involvement of this region in the healthy population.

2. Results

2.1. Clinical and demographic data

We enrolled 40 patients with MS. Four of them were excluded from the analysis because of excessive movement artifacts during fMRI scan. Excluded patients were not different from the included ones for age, gender, and Expanded Disability Status Scale (EDSS). A list of demographic and clinical data of the 36 patients included in the study is reported in Table 1.

2.2. Results of pragmatic assessment

Patients obtained an Assessment of Pragmatic Abilities and Cognitive Substrates (APACS) Total score of 0.90 ± 0.08 (mean ± SD), with a mean Pragmatic Production score of 0.96 ± 0.04 and a mean Pragmatic Comprehension score of 0.83 ± 0.1. Compared with normative data (Arcara & Bambini, 2016), 15 (41.7%) out of 36 patients had an impaired performance in the APACS Total score.

Table 1
Demographic and clinical features of multiple sclerosis patients.

Characteristics	Values
Female, N (%)	24 (66.7)
Age [years], mean ± SD	37.4 ± 12.4
Education [years], median (Range)	13 (5–19)
Age at onset [years], mean ± SD	30.6 ± 10.9
Disease duration [years], median (Range)	5 (1–34)
Expanded Disability Status Scale, median (Range)	2.5 (1–6.5)
Relapsing-remitting Multiple Sclerosis, N (%)	32 (88.9)
Secondary-progressive Multiple Sclerosis, N (%)	4 (11.1)

2.3. RS-fMRI data

Mean correlation maps (averaged across all subjects) for the eight tested seeds, superimposed on the cortical surface of a healthy brain in the MNI space, are reported in Fig. 1.

For the left GA, the left aSMG seed showed a correlation with the bilateral supramarginal gyri, along with the ipsilateral insular cortex and the middle temporal gyrus; the left pSMG seed showed correlations with the ipsilateral supramarginal and angular gyri, and the bilateral middle temporal gyrus, along with a cerebellar cluster at the level of the right Crus 1, while the left AG seed showed correlations with the bilateral angular gyri, the left superior and middle temporal gyri, and the right orbitofrontal cortex.

For the right GA, the right aSMG seed showed a correlation with the bilateral supramarginal gyri, along with a cluster located at the level of the left insular cortex; the right pSMG seed showed correlations with a cluster at the level of both the ipsilateral supramarginal and angular gyri, and two right frontal clusters located respectively at the level of the superior and inferior frontal gyri, while the right AG seed showed correlations with the bilateral angular gyri, the right superior and middle temporal gyri, the right orbitofrontal cortex, and the precuneus, along with a cerebellar cluster at the level of the left Crus 1 and 2.

When seeds placed in the Broca's area were tested, the pars opercularis of the left inferior frontal gyrus (op_IFG_l) showed significant correlations with both the right and left IFG, the left frontal orbital cortex, the left inferior temporal gyrus, and a cluster adjacent to the precuneus, along with a cerebellar cluster at the level of the right Crus 1. Finally, the pars triangularis of the left inferior frontal gyrus (tr_IFG_l) seed was significantly correlated with both the right and left IFG.

When testing for correlations of pragmatic abilities scores with RS-fMRI data, a direct correlation between the APACS Total score and a cluster of FC with the paracingulate cortex was found ($p = 0.003$) when evaluating the aSMG_r seed. A similar direct correlation, which however did not survive the correction for multiple comparisons and therefore is reported only as a trend, emerged between the APACS Total score and a cluster located at the level of the paracingulate cortex when testing the aSMG_l seed ($p = 0.009$). No other clusters of significant direct or inverse correlation with the APACS Total score emerged for any of the other tested seeds, in particular no significant correlations emerged when Broca's area seeds were tested. Results of the correlations between RS-fMRI data and the APACS Total score are shown in Fig. 2 and Table 2.

3. Discussion

The main finding of this paper is the association between pragmatics