This scientific commentary refers to ‘How right hemisphere damage after stroke can impair speech comprehension’, by Gajardo-Vidal et al. (doi:10.1093/brain/awy270).

Traditionally it has been assumed that most people are left hemisphere dominant for language, and yet several studies have reported cases of language impairment following a right hemisphere stroke. What could cause this impairment? One hypothesis is that anyone who experiences disruption to language processing following a right hemisphere stroke must have atypical impairment? One hypothesis is that anyone who experiences disruption to language processing following a right hemisphere stroke must have atypical language lateralization (Mariën et al., 2004). An alternative account is that a non-linguistic cognitive impairment underlies these deficits. Accumulating evidence suggests that the right hemisphere has essential roles in the processing of language. The right hemisphere is critical for perceiving sarcasm (Davis et al., 2016), integrating context required for understanding metaphor, inference, and humour, as well as recognizing and expressing affective or emotional prosody—changes in pitch, rhythm, rate, and loudness that convey emotions (Ross and Monnot, 2008; Wright et al., 2018). We regularly use prosody to change the meaning of sentences. A sentence like ‘it’s so good to see you’ can take on several different meanings if it is spoken with cheerful surprise, boredom, or sarcasm. The inability to understand humour, emotions, and sarcasm can wreak havoc on a patient’s friendships and relationships if his or her friends and family are not aware that this impairment can result from a stroke. Some specific brain regions have been implicated in these impairments. For example, damage to right posterior superior temporal gyrus has been found to impair emotional prosody comprehension (Ross and Monnot, 2008; Witteman et al., 2011), while damage to right inferior frontal cortex impairs expression of emotion (Ross and Monnot, 2008; Patel et al., 2018). Damage to the right sagittal stratum predicted an impaired ability to understand sarcasm (Davis et al., 2016). In this issue of Brain, Gajardo-Vidal and colleagues examine the contribution of right hemisphere regions to language functions that are more traditionally thought to depend on the left hemisphere, such as comprehension of the explicit content of sentences (Gajardo-Vidal et al., 2018).

The authors established a role of the right hemisphere in sentence comprehension through a series of experiments combining behavioural testing and voxel-based morphometry in stroke survivors and functional imaging in neurologically normal participants. In their first experiment they sought to determine which specific language impairments were most common in participants with right hemisphere stroke (n = 109) versus left hemisphere stroke (n = 369). Right hemisphere patients were most likely to be impaired in auditory sentence-to-picture matching, while left hemisphere patients were most likely to have difficulty with a spoken picture description task. After excluding participants with visual perception deficits, they found that 12/93 right hemisphere stroke patients were impaired on auditory sentence-to-picture matching. Furthermore, 9/12 of these patients had deficits that could not be explained by difficulties with speech perception, semantics, phonological memory, syntactic processing, or the integration of syntactic and semantic information in a sentence. These patients had particular difficulty comprehending more complex semantically reversible sentences in which the most common subject-verb-object relationship had been reversed (e.g. ‘The singer hits the soldier’ and ‘The shoe under the pencil is blue’). Difficulty comprehending these kinds of complex sentences could have serious real-world consequences for patients. For example, a right hemisphere stroke survivor might misunderstand a sentence like, ‘The pill under the bottle is for you’ as meaning the whole bottle is for him to take.

In their second experiment, Gajardo-Vidal et al. used voxel-based morphometry to determine which right hemisphere brain regions were associated with impairment of auditory sentence comprehension. They found that the nine patients with deficits had significantly more damage to the dorsal parts of the right superior longitudinal fasciculus and the right inferior frontal sulcus when compared to 75 control
patients with right hemisphere stroke who did not have impaired sentence comprehension. Damage was found in two-thirds (6/9) of the patients with sentence comprehension impairments, compared to only 4% (3/75) of the control patients. The other three patients with deficits had small lesions impacting the putamen, thalamus, caudate, or right temporal lobe.

To further evaluate the role of the brain regions identified in Experiment 2 in auditory sentence comprehension, the authors conducted a third experiment involving functional neuroimaging of neurologically healthy participants ($n = 25$) during an auditory sentence-to-picture matching task, as well as several other tasks including sentence processing, phonological retrieval, and verbal short-term memory. Their results confirmed that the right inferior frontal sulcus and right mediodorsal thalamus are activated during auditory sentence-to-picture matching in healthy controls. In fact, these regions were activated by many language tasks. These results led the authors to complete a fourth experiment in a second group of neurologically healthy participants ($n = 25$) in order to determine whether these areas are specifically important for language processing or whether they serve a more domain-general role. In a functional neuroimaging experiment in which participants were presented with a one-back working memory task using both linguistic and non-linguistic stimuli, Garjardo-Vidal et al. found significantly more activation during the non-linguistic task in the right inferior frontal and right thalamic regions. Thus, the combined results of Experiments 3 and 4 suggest that the right inferior frontal and mediodorsal thalamic regions do not play an exclusive role in auditory sentence comprehension, and instead are important for domain-general working memory, an important executive function that appears to subserve auditory sentence comprehension.

**Figure 1** A schematic representation of some cognitive processes that support performance on the sentence-picture matching task, and their lateralization to right or left hemisphere. Note that the figure is oversimplified, as left hemisphere regions are also involved in working memory, and some cognitive-linguistic processes underlying sentence comprehension are not depicted. Red dashed lines represent input to a cognitive process from another cognitive process. Black dashed lines represent activation of a concept that allows selection of the correct picture. Note that the target concept is the one that receives the greatest activation (from both word comprehension or lexical semantics and from thematic role assignment or morphosyntactic processing).
The authors’ results complement the literature describing impairments of sarcasm, emotional prosody, and abstract or contextual meaning in patients with right hemisphere damage. They demonstrate that language comprehension impairments in this population can in fact closely resemble those seen in patients with left hemisphere damage because right hemisphere damage can impair domain-general working memory essential for language processing. A schematic representation of the proposed role of working memory in the sentence comprehension task is shown in Fig. 1.

The findings of Garjardo-Vidal and colleagues, combined with results from other studies examining language comprehension in patients with right hemisphere damage, indicate that many patients are living with language comprehension deficits that remain unrecognized and untreated. In the future, patients with right hemisphere stroke should be routinely assessed for language, sarcasm, and emotional prosody deficits. Furthermore, providing education about these comprehension deficits can help stroke survivors and caregivers use compensatory strategies. These strategies could include caregivers and family explicitly stating the emotions they are feeling, and using simpler sentences rather than complex ones to help improve communication. Garjardo-Vidal and colleagues’ work provides a foundation for future studies examining the specific executive functions that underlie language comprehension, and potentially for developing treatments that target these deficits.

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In search of lost trafficking

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Frontotemporal dementia (FTD) is a neurodegenerative syndrome characterized by atrophy of the frontal and temporal lobes, leading to alterations in behaviour, personality and language. Early symptoms can manifest as mildly as inappropriate comments, word-finding difficulty and apathy towards loved ones, or as more severe changes such as criminal behaviours (e.g. theft, sexual disinhibition) and reckless financial decisions, which can tragically lead to alienation of friends and family. FTD is one of the leading causes of early-onset dementia and is the third most common cause of dementia overall. Although historically observed to co-occur with amyotrophic lateral sclerosis (ALS), recent studies showing overlap of several genetic and neuropathological features have helped to reframe FTD and ALS as existing on a spectrum with features of motor neuron disease in up to 40% of patients with FTD. Mutations in the genes C9orf72, MAPT and GRN account for about 60% of inherited FTD cases, while rarer mutations occur in other genes such as VCP, TBK1, CHMP2B, TARDBP and FUS (Bang et al., 2015). Although rare, mutations in

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