

# The Neural Correlates of Semantic Feature Analysis in Chronic Aphasia: Discordant Patterns According to the Etiology

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## ABSTRACT

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This event-related functional magnetic resonance imaging (fMRI) study reports on the impact of semantic feature analysis (SFA) therapy on the neural substrate sustaining the recovery from severe anomia in two patients: one participant was diagnosed with primary progressive aphasia (PPA) 2 years before this study; the other participant acquired aphasia 8 years before this study. The participant with PPA showed severe progressive nonfluent aphasia (PNFA), the language profile being similar to a Broca's aphasia; the stroke patient presented with Broca's aphasia and a severe apraxia of speech (AOS).

To examine the neural substrate allowing for recovery, both patients received brief and intensive therapy with SFA; behavioral and event-related (ER)-fMRI measures during oral picture naming were obtained pre- and post-therapy. Both patients benefitted from SFA to improve their naming performance. Functional MRI performances on trained and correct pretraining items were contrasted. Adaptive brain plasticity appeared to operate differently in each patient, despite the similarity of naming recovery profiles.

**KEYWORDS:** ER-fMRI, aphasia, language therapy, stroke, primary progressive aphasia

**Learning Outcomes:** As a result of this activity, the reader will be able to (1) identify positive outcomes in both progressive nonfluent aphasia and chronic aphasia after semantic therapy and, (2) distinguish the differential brain plasticity mechanisms thought to sustain these improvements.

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Treatment of Chronic Aphasia: International Perspectives; Guest Editor, Chris Code, Ph.D.

Semin Speech Lang 2010;31:52–63. Copyright © 2010 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA. Tel: +1(212) 584-4662.

DOI: <http://dx.doi.org/10.1055/s-0029-1244953>.

ISSN 0734-0478.

The term “aphasia” is generally used to refer to an acquired language impairment, which affects language production and/or comprehension, as a result of a stroke. However, aphasia can also be observed as a result of neurodegenerative changes affecting the frontotemporal region, as in the case of primary progressive aphasia (PPA),<sup>1</sup> a neurodegenerative disease characterized by a progressive language impairment, which eventually evolves to dementia.<sup>1</sup> A distinction is made between the fluent and nonfluent variants of PPA. Progressive nonfluent aphasia (PNFA) corresponds to the agrammatic subtype of PPA and is characterized by a progressive deficit in phonology and syntax. At the first stage of PNFA, the language profile resembles that of post-stroke Broca’s aphasia and then gradually develops into global aphasia.<sup>1</sup>

Anomia is observed in both PPA and stroke-induced aphasia. In most cases of aphasia from stroke, a lessening in the severity of anomia is observed. However, the degree of recovery varies from one patient to another. In many cases, major recovery is observed in the subacute phase, shortly after brain injury; however, in other cases very little recovery is observed during that period. It has generally been assumed that early intervention during the acute phase has a positive outcome,<sup>2</sup> whereas improvement in the chronic stage is assumed to be unlikely. However, this idea has recently been challenged by studies showing language improvement resulting from intensive therapy with patients in the chronic phase.<sup>3–6</sup>

## APPROACHES TO ANOMIA THERAPY

Language therapy has been shown to be effective in triggering recovery from anomia in post-stroke aphasia. Essentially, two broad groups of approaches are used to work on anomia in post-stroke aphasia: phonological approaches and semantic approaches. Phonological approaches consist of a series of therapy strategies with a focus on word phonology. Phonological strategies are most frequently used with patients with impairments in the retrieval of phonological forms, at the access or representation levels of the phonological output lexicon.<sup>5,7</sup> Con-

versely, semantic approaches seek to improve word retrieval by stimulating the semantic system with a wide variety of tasks.<sup>2</sup> Some evidence suggests that both approaches can result in improvement of naming ability and also lead to some generalization of therapy effects to untreated items.<sup>2</sup> Among the semantic approaches to therapy, semantic feature analysis (SFA) therapy<sup>8</sup> aims at the activation of semantic representations of a word. This therapy’s approach is based on spreading activation theory,<sup>9</sup> according to which the activation of the semantic features of a target word results in the activation of the target’s semantic network, which itself contributes to the activation of the target’s corresponding phonological information and word production. Thus, stimulation of the semantic network is considered to spread out to all language processing levels, including phonological processing and articulatory planning.

The only published study of therapy for anomia in PNFA is by Jokel et al,<sup>10</sup> who examined the impact of the computer-based MossTalk Words<sup>11</sup> therapy program in two cases. Although the intensity of therapy differed in each case, both participants showed improvement with trained items, and some generalization of therapy effects were seen at the syntactic level immediately after treatment. However, the score returned to the baseline after 6 months. Considering the impact of PPA on communication abilities, there is a clear need for further studies in this field, particularly given up-to-date, that no specific treatment approach for this population is available in most clinical settings.<sup>12</sup>

## NEUROIMAGING EVIDENCE

Recent advances in neuroimaging provide a new perspective on the study of recovery from anomia; thus, research on therapy-induced brain plasticity in the recovery from anomia has increased considerably in the last decade. Brain plasticity is defined as the brain’s potential to modify neural networks in both healthy and damaged tissue. Most research has approached the issue of brain plasticity with reference to two neurobiological mechanisms: functional reactivation and functional

reorganization. Functional reactivation is observed when after a period of functional inactivity resulting from brain damage, areas enclosed in the language network recover their function.<sup>13</sup> Functional reorganization consists of the activation of neural networks that differ from those that serve processing in healthy participants. Evidence from neuroimaging studies on functional reorganization in post-stroke aphasia has shown that reorganization may engage perilesional areas in the left hemisphere (LH),<sup>14</sup> or it may recruit right hemisphere (RH) areas homologous to the damaged LH areas, particularly when permanent damage to LH areas is observed.<sup>15,16</sup> However, recent neuroimaging studies also suggest that the recovery of aphasia may also be supported by both hemispheres together.<sup>15</sup> Further, some studies suggest that in cases of small LH lesions and mild aphasia, language recovery may be associated with LH activations,<sup>14</sup> whereas in cases of extended LH lesions and severe aphasia, recovery supported by RH activation has been reported.<sup>3,17</sup> Thus, the relative contribution and efficacy of either cerebral hemisphere to the recovery from aphasia is likely to be affected by several factors, including time post-onset, and extent and location of the lesion.

A small number of studies describing the functional network that supports recovered language in the chronic phase of aphasia have been published.<sup>14,16</sup> A few studies have investigated the reorganization process by describing the neural correlates associated with the recovery of naming following specific speech-language therapy.<sup>4-6</sup> For instance, Fridriksson et al<sup>4</sup> studied the effect of therapy focused on 15 words chosen by the patient. These researchers found an increase of bilateral neural activity associated with language performance in the two patients for whom the therapy was effective. However, considering that the analyses were made with both correct responses and paraphasia, it is difficult to discriminate between those areas contributing to recovery and those responsible for error production. Two studies provide evidence for RH contribution to aphasia recovery, and both concern participants with extended LH lesions. Meinzer et al<sup>5</sup> compared correct responses to errors in a naming task during fMRI, with a chronic

Wernicke's aphasia participant. The results showed the activation of homologous areas in the RH with correct responses after 2 weeks of constraint-induced language therapy.<sup>4</sup> These results support the idea that the RH may contribute to recovery from aphasia in the case of extended lesions.<sup>3,17</sup> Similarly, Vitali et al<sup>6</sup> investigated the impact of phonological therapy in two patients with chronic aphasia. The patient with the larger lesion showed less improvement than the one with a smaller lesion; activations in the former patient were observed in the right frontal area, homologous to Broca's area.

Only one neuroimaging study on the neural substrate of naming improvement in PPA patients has been published to date. Finocchiaro et al<sup>18</sup> stimulated the left anterior midfrontal gyrus with a high-frequency repetitive transcranial magnetic stimulation (rTMS) protocol. The authors found a therapy-specific effect (rTMS stimulation) on verb naming. Similar to Finocchiaro et al, Cotelli et al<sup>19</sup> reported improvement in verb naming in a group of 15 participants with anomia following Alzheimer's disease (AD). In line with previous evidence,<sup>20</sup> these results suggest a potential for brain plasticity in the first stages of AD and in cases of PPA.<sup>18</sup>

The present study describes therapy-induced brain plasticity in chronic and severe aphasia. A pre-/post-therapy event-related fMRI design was used to examine the impact of intensive therapy SFA on the neural substrate that is sustaining the recovery from anomia in two patients, one with a PNFA and the other with post-stroke aphasia.

## MATERIAL AND METHODS

### Participants

CM is a 66-year-old, right-handed man who was ~8 years post-onset from a left frontotemporal stroke, which resulted in severe nonfluent aphasia and apraxia of speech (AOS). He had received individual language therapy intermittently over the previous 8 years. At the beginning of the study, he was not receiving language therapy. Aphasia testing conducted at that point showed severe chronic Broca's

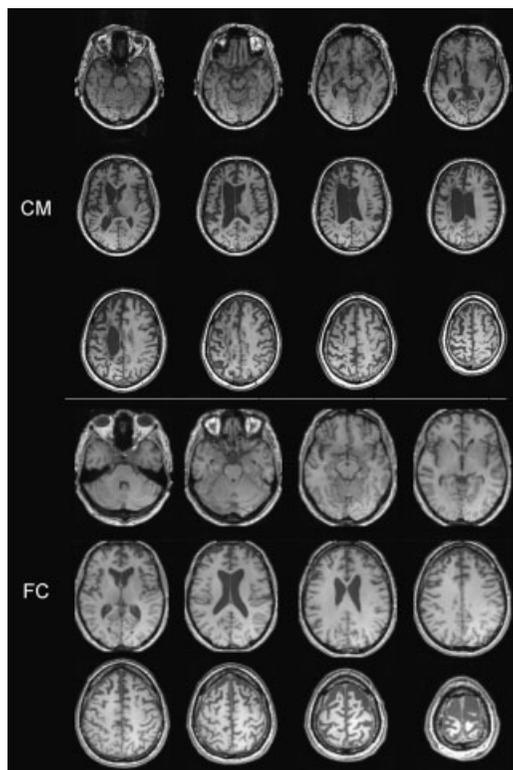
**Table 1** Clinical and Sociodemographic Parameters of CM and FC

Patient ID	Age	Sex	Education (Years)	Handedness	Etiology	Months Post-Onset	Aphasia Syndrome	Aphasia Severity	No. of Treatments
CM	66	M	18	Right	CVA	84	Broca's	Severe	9
FC	60	M	16	Right	Atrophy (PNFA)	24	Broca's	Severe	9

CVA, cerebrovascular accident.

aphasia and AOS. (For both participants, Table 1 contains clinical and sociodemographic information, and Fig. 1 shows structural magnetic resonance imaging [MRI]).

FC is a 60-year-old, right-handed man who was ~2 years post-diagnosis with a non-fluent PPA, which was associated with fronto-temporal degeneration. At the time of the study, FC had severe nonfluent aphasia. He had never received language therapy. Aphasia testing showed a profile similar to a chronic Broca's aphasia (Table 1 and Fig. 2).



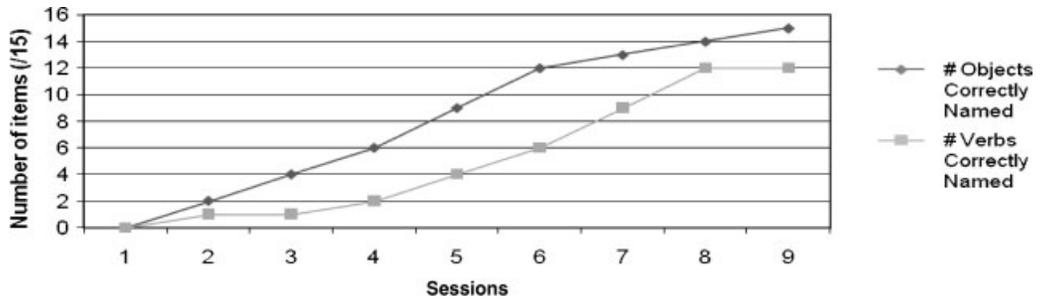
**Figure 1** Anatomical magnetic resonance imaging (MRI) (T1) of stroke patient (CM) (top three rows) and of progressive nonfluent aphasia (PNFA) patient (FC) (bottom three rows).

## Procedure and Design

Before treatment, both participants were examined with the Montreal-Toulouse 86 Beta version<sup>21</sup> to describe their aphasia profile, and the Edinburgh Inventory<sup>22</sup> to assess handedness. They underwent two baseline naming assessments with Snodgrass and Vandewar<sup>23</sup> 260 object images within a 1-week interval; both participants showed a stable oral naming performance. From the pretherapy scanning results, a list of 30 correctly and 30 incorrectly named items was built for both nouns and verbs. Thirty numerically distorted images served as the control condition. Participants were instructed to name the randomly presented pictures of nouns and verbs, and to say 'baba' to distorted pictures. Oral responses were audio recorded.

## Therapy

Both patients attended three 60-minute sessions per week for 3 weeks. Training stimuli, 15 objects and 15 verbs chosen from the incorrectly named pictures prior to therapy from the Snodgrass and were presented individually and in random order, and patients were asked to name each picture. If they accurately named the picture, the speech-language pathologist (SLP) moved on to another stimulus. When the participant was unable to name the picture, he was prompted with semantic features from SFA to activate a semantic network and thereby facilitate word retrieval. Thus, if the participant gave an incorrect response that was related to the picture, prompts were generated based on what he said. After three prompts, the target word was presented orally to the patient, who was then asked to repeat the word. After 3 weeks, both CM and FC reached a criterion level of 80% correct for both nouns and verbs.



**Figure 2** Number of trained nouns and verbs correctly named in each session by stroke patient (CM).

### Functional Imaging

For the functional images, 28 contiguous 1-mm slices were obtained using a 3T Magnetom TRIO (Siemens, Germany). A standard T1 was also acquired during each session for high-resolution anatomical images of the patients' brains. The functional MRI (fMRI) data were analyzed using a conventional statistical parametric mapping (SPM) analysis (SPM-2, Wellcome Department of Imaging Neuroscience, London, UK). A single statistical analysis combining the data from the first and second fMRI sessions was performed for both participants. Effects of interest (successful naming with treated/untreated/correctly named items pretherapy) were independently modeled in the statistical analysis.

## RESULTS

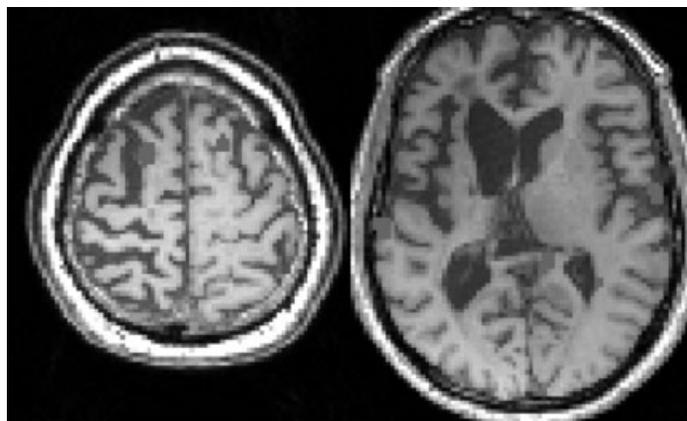
### Stroke Patient: CM

By the end of the therapy period, CM was able to name all 15 trained objects and 12 out of 15 verbs. During post-therapy scanning, however, he performed less well compared with his last therapy session (Fig. 2). Thus, during scanning, CM correctly named 12 trained objects and 10 trained verbs. He also named four untrained objects and verbs, which he was unable to name before therapy. Similarly, CM improved his naming ability on the Snodgrass and Vandewart set<sup>23</sup> mainly with the trained items.

Compared with correctly named objects before therapy, trained objects revealed activations in the right precentral gyrus (preCG), the

superior frontal gyrus (SFG) bilaterally, the inferior occipital gyrus (IOG) bilaterally, and the left globus pallidus. Thus, post-therapy activation maps with objects were larger in the LH (Fig. 3). With trained verbs, however, post-therapy activations were bilateral and specifically included the left inferior temporal gyrus (ITG), the superior temporal gyrus (STG), the middle temporal gyrus (MTG), the left middle occipital gyrus (MOG), the right cuneus, the right PreCG, the right middle frontal gyrus (midFG), the right dorso-lateral prefrontal cortex, the right cingulate gyrus, and the right parahippocampal gyrus (PHipG) (Fig. 4).

Because the goal of the present study was to look at therapy-induced brain plasticity with SFA, we wanted to compare the network for spontaneous correct naming before therapy with the one observed post-therapy. Before therapy, activation maps of accurate object naming included the bilateral PHipG, the right MTG, the superior parietal lobule (SPL) and STG bilaterally, the left cuneus, the right fusiform, right postcentral gyrus (postCG), and the right cerebellum (Fig. 3). Thus, most activations were in the RH; this was also the case with accurately named verbs before therapy, which significantly activated the right ITG, the MTG, the STG, the postCG, the PHipG, and the cerebellum. The LH activations included the thalamus, the postCG, and the SPL (Fig. 4). After therapy, fewer areas were recruited with trained nouns and verbs compared with pretherapy activation maps for spontaneously named items. Moreover, post-therapy significantly activated more naming-specific areas, compared with those recruited before therapy.

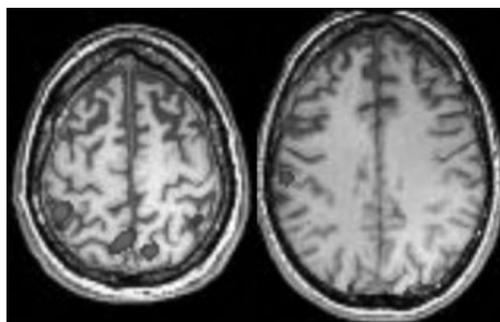


**Figure 3** Significant blood oxygenation level-dependent (BOLD) signal increase with trained objects (left panel) and spontaneously named objects before therapy (right panel) in CM.

### Nonfluent Primary Progressive Aphasia: Patient FC

After nine SFA therapy sessions, FC could name 14 trained objects and 14 trained verbs. Like CM, his performance in the scanner was less accurate compared with the last therapy session. Thus, FC correctly named 10 trained objects and 10 trained verbs during the fMRI scan, but could not name any untrained items, which shows a training-specific therapy effect (Fig. 5).

Correctly named trained objects recruited mostly RH areas. These included the SPL and the IPL bilaterally, the precuneus, the right PHipG, and the paracentral gyrus. Significantly activated LH areas were subcortical and included the thalamus, the putamen, and the lateral globus pallidus. The left STG and



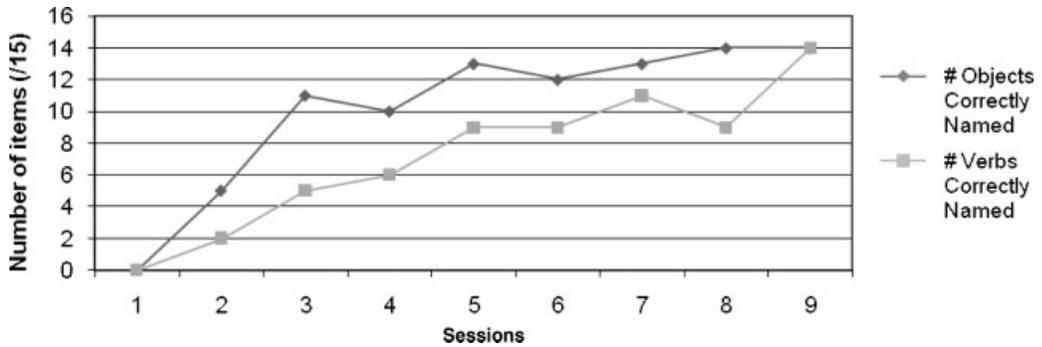
**Figure 4** Significant blood oxygenation level-dependent (BOLD) signal increase with trained verbs (left panel) and spontaneously named verbs before post to therapy (right panel) in CM.

MTG were also recruited with trained objects after therapy (Fig. 6). With verbs, the activations were slightly larger in the LH, although RH areas were also recruited. In particular, trained verbs recruited bilateral inferior parietal areas, the MFG, the IFG, the left ITG and fusiform gyri, the right MTG, the left SPL, the left lingual gyrus, the left MOG, and the right precuneus (Fig. 7).

Correct object naming before therapy recruited the inferior parietal lobule (IPL), the preCG, the MOG, and the cuneus—all in the RH—and the cerebellum bilaterally (Fig. 6). With verbs, FC significantly activated the right SFG and STG; further, smaller clusters were observed in the left precentral and cingulate gyri (Fig. 7). Hence, before therapy, recruitment was slightly larger in the RH, both with nouns and verbs. Unlike CM, FC showed larger post-therapy activation maps compared with pretherapy ones, and more significantly activated semantic processing areas. (Detailed imaging data for both participants may be obtained from the authors.)

## DISCUSSION

This study examined the neural correlates of efficient SFA therapy in two cases of chronic aphasia. This is the first study to show the efficacy of SFA in a case of chronic anomia resulting from degenerative brain lesion. Concurrently with behavioral improvement, changes in the neural substrate of naming



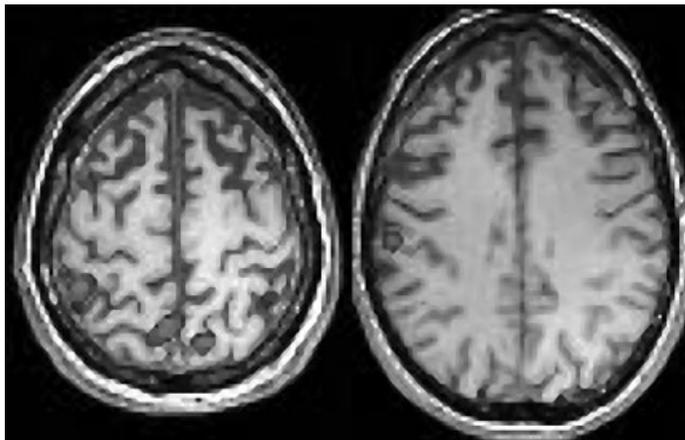
**Figure 5** Number of trained nouns and verbs correctly named in each session by progressive nonfluent aphasia (PNFA) patient (FC).

were observed in both participants. In line with previous longitudinal studies,<sup>24</sup> these results show that brain plasticity is still possible even several years after aphasia onset. Further, our results show different spontaneous and therapy-induced brain plasticity mechanisms in both participants. In the case of post-stroke aphasia (CM), compensation mechanisms developed before the present study resulted in predominantly RH recruitment. Conversely, pretherapy activations were bilateral in the participant with PNFA (FC). These results suggest that spontaneous brain plasticity mechanisms could differ depending on aphasia etiology; thus the progressive nature of PNFA may have allowed for gradual bilateral compensation. Differences across participants were also observed in the therapy-induced brain plasticity activation patterns. Thus, the post-stroke par-

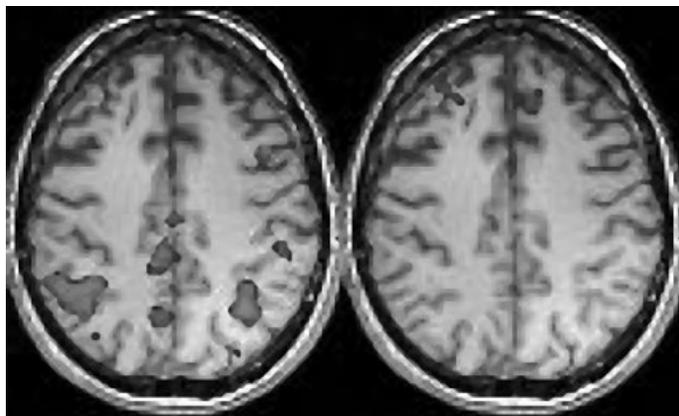
ticipant showed contraction of the network, specifically recruited phonological processing, and speech programming areas, whereas the PNFA participant showed network expansion and mostly recruited semantic processing areas. Interestingly, despite the differences in the spontaneously developed neural networks across patients, both of them showed bilateralization of efficient naming networks following SFA.

#### Stroke Patient: CM

In the case of CM, post-therapy activations included the right preCG and the SFG bilaterally, both of which are known for being involved in speech production and articulatory planning.<sup>25</sup> Interestingly, CM showed no significant activation in semantic processing areas,



**Figure 6** Significant blood oxygenation level-dependent (BOLD) signal increase with trained objects (left panel) and spontaneously named objects before therapy (right panel) in FC.



**Figure 7** Significant blood oxygenation level-dependent (BOLD) signal increase with trained verbs (left panel) and spontaneously named verbs before to therapy (right panel) in FC.

which is surprising given that SFA focuses on the stimulation of the semantic features of words. However, considering that CM's comprehension abilities were relatively preserved in comparison with his phonological processing and speech and motor programming abilities, it is possible that the activation seen in the post-therapy fMRI session reflect the speech programming processing, which was in fact the most disrupted, as a result of spreading activation from the semantic system. Interestingly, SFA therapy appears to have had a different impact with verbs, with greater activity for trained verbs observed in the MTG and STG in the LH, including Wernicke's area. Activation in the left MTG has been reported in a wide range of semantic tasks,<sup>26</sup> whereas the activation of Wernicke's area is generally associated with access to the lexical word form.<sup>27</sup> Before therapy, activations were observed in the ITG, MTG and STG, but in the RH rather than the LH. Reactivation of perilesional LH areas is considered to result in better aphasia recovery.<sup>5</sup> Thus, the results of the present study suggest that intensive training with SFA may lead to the reactivation of perilesional brain areas, in patients with chronic aphasia.<sup>3,17</sup> It is plausible that the semantic nature of SFA contributed to the reactivation of the LH semantic network, particularly with verbs; thus, it is possible that the severe verb naming deficits observed before therapy included some semantic processing component. A pre-/post-therapy de-

scription of semantic versus phonological components of CM's anomia with nouns and verbs could have provided some cues to better understand the distinct impact of SFA with verbs and nouns.

Significant activation occurred in the right dorsolateral prefrontal cortex with trained verbs only; this is consistent with previous studies on naming in healthy populations,<sup>28</sup> as well as with lesion studies<sup>29</sup> that report an RH takeover in cases of permanent damage to LH language processing areas. As proposed by Hécaen<sup>30</sup> and Sergent,<sup>31</sup> it is likely that this takeover is facilitated by anatomical and neuro-functional similarity between the damaged areas and their contralateral equivalents.

Finally, CM showed a post-therapy contraction of the activation pattern; thus, specifically with nouns, the number of voxels and brain areas significantly activated following therapy was much smaller than before therapy. With verbs, the number of significantly activated areas was also smaller, but activation clusters were larger. Previous studies have shown that motor overtraining<sup>32</sup> and improved performance on language tasks<sup>33</sup> result in a concentration of activation maps. In line with this evidence,<sup>32,33</sup> the results of the present study suggest that the naming strategy induced by SFA considerably reduced naming effort in CM, which resulted in lesser recruitment needs to support word retrieval. It is possible that verbs remained more effortful to produce than nouns.

### Nonfluent Primary Progressive Aphasia: Patient: FC

Following SFA, FC's efforts to name trained objects resulted in the recruitment of temporal areas. Specifically, the left MTG and STG were recruited, both of which have been shown to be active in a variety of picture naming tasks.<sup>34</sup> The bilateral activation of the IPL, which has been related to semantic integration,<sup>34,35</sup> was observed as well following SFA. Moreover, trained verbs also recruited semantically related areas, more specifically the left ITG and the right MTG, as well as the fusiform gyrus bilaterally. These activations are consistent with the semantic nature of SFA and therefore are likely to have been therapy-induced.

As discussed earlier, previous studies have found evidence that verb naming is associated with activations in the frontal lobes.<sup>28,29</sup> Martin et al<sup>36</sup> observed selective activation in the left IFG with action naming, which is also true in the case of FC. Accordingly, the post-therapy naming network showed a more "normalized" pattern, as opposed to what was observed in case of the stroke patient, CM. As discussed by Fridriksson et al<sup>4</sup> and Musso et al,<sup>37</sup> a stroke may lead to compensatory cortical adaptation of areas not specific to language processing. This does not appear to be the case with FC, who has a degenerative disease. In fact, the evidence shows that SFA therapy worked well with FC and led to the activation of semantic processing areas that were not activated before therapy. Further, the present results concur with previous reports on the reactivation of preexisting networks in participants with PNFA, whereas a reorganization factor seems to be underlying adaptive plasticity mechanisms observed in the post-stroke participant, CM.

Before therapy, the activation obtained with objects was less specific to the naming task than that observed post-therapy, for both objects and verbs. Interestingly, activation in the right preCG, which is implicated in speech production and articulatory planning, and in the right IPL, which is involved in the phonological loop of verbal working memory, suggest that FC was relying more on a phonemic strategy than on a semantic strategy to retrieve

words. Thus, following therapy, FC may have changed his word retrieval strategy with verbs from a phonologically based to a semantically based strategy. This claim is further supported by the activation encountered with correctly spontaneously named verbs before therapy. Hence, FC showed significant activation of the preCG and the cingulate, which have been previously associated with articulatory planning<sup>38</sup> and persistent effortful articulatory processing of phonological sequences in lexical learning<sup>39</sup>; he also showed significant activation in the right MFG and IFG (Brodmann area 8), both of which have been reported to occur during articulatory processing.<sup>6</sup>

Contrary to CM, FC recruited larger network after therapy. With objects, more voxels were activated after therapy, but the number of areas did not increase. With verbs, both number of voxels and number of areas were larger after therapy. Previous evidence showed greater recruitment of the same brain regions in patients with Alzheimer's disease as a means of compensation.<sup>40</sup> This greater need for recruitment was associated with improved performance, which in the present case consists of improved naming abilities. Thus, SFA appears to induce brain plasticity changes in stroke patients, but also triggers compensatory brain plasticity mechanisms in degenerative disease. Further, this evidence suggests that degenerative diseases do not preclude adaptive brain plasticity, at least in the short term following intensive intervention. The efficacy of SFA to trigger adaptive plasticity in cases of degenerative disease should be further explored.

In general, recent studies of motor and language recovery have suggested that RH activation may reflect maladaptive brain plasticity mechanisms, unrelated to functional performance.<sup>41</sup> More specifically, Naeser et al<sup>41</sup> showed that the inhibition of the RH areas with repetitive transcranial magnetic stimulation resulted in improved language. The present findings do not appear to support this point of view; only good responses were associated to RH activations, suggesting that they support efficient language performance. Our results agree with previous studies reporting RH activation in association with language improvement.<sup>25</sup>

Heiss et al<sup>42</sup> demonstrated that better recovery was observed in the case of a reactivation of left temporal regions. Cardebat et al<sup>43</sup> also showed that with improved performance, less activation was observed in normal participants, whereas the patterns tend to “normalize” in patients. Accordingly, because naming tasks normally recruit the LH predominantly,<sup>43</sup> normalization of the activations patterns in patients who recruited the RH before therapy should lead to larger LH recruitment with improved performance following therapy, as shown by CM with object naming.

Regarding therapy intensity, in a recent meta-analysis, Bhogal et al<sup>3</sup> claim that positive treatment effects are associated with at least 8.8 hours of therapy per week. In our study, both CM and FC showed positive outcomes with 3 hours of therapy per week. Although it is possible that the outcome could have been even better with more intensive therapy, we chose this frequency because it is relatively close to the amount of speech-language therapy patients receive from external services, at least in Quebec. The implementation of more than 8.8 hours of treatment per week appears to be expensive and difficult to put into practice, largely because it requires patients to stop their daily activities during the duration of the therapy.<sup>44</sup> Further, Bhogal et al<sup>3</sup> did not consider the type of the therapy provided or whether it was delivered on an individual or group basis. Thus, the fact that both of the participants in the present study received individual therapy, with intensive training of a limited number of items over the course of the entire therapy, contributed to their achieving improvement; however, that may be a function not only of the number of weekly hours provided, but also of the number of items trained during those hours.

It is interesting to note that therapy-induced activation varied across participants, despite equivalent behavioral improvement. It is possible that these differences arise from their differing etiologies. This working hypothesis should be further explored by multiple single-case studies, with a larger number of post-stroke Broca’s aphasia and PNFA subjects.

Research on the neural correlates associated with specific aphasia therapy effects may

provide a better understanding of which aphasia profiles are likely to benefit from a given therapy approach.<sup>44</sup> Multiple single-case studies may provide insights into brain plasticity, which will contribute to better design group studies. However, because brain damage may disrupt the cognitive system in multiple ways,<sup>45</sup> averaging over a group of patients has to be done carefully, with very precise hypotheses.<sup>46</sup>

#### ACKNOWLEDGMENTS

This study was possible thanks to a Canadian Institute in Health Research Doctoral grant to KM and a Fonds de recherche en santé du Québec grant to AIA.

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