# Neural regions essential for writing verbs

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Published online 25 November 2002; doi:10.1038/nn982



Functional imaging data collected during cognitive tasks show which brain regions are active during those tasks, but do not necessarily indicate which regions are essential for those tasks. Here, in a study of two cases of selectively impaired written naming of verbs after focal brain ischemia, we combined imaging and behavioral testing to unambiguously identify brain regions that are crucial for a specific cognitive process. We used magnetic resonance perfusion imaging to show that the selective impairment in each case was due to hypoperfusion (low blood flow) in left posterior inferior frontal gyrus (PIFG) and precentral gyrus (PrG); the impairment was immediately reversed when blood flow was restored to these regions, indicating that parts of the left frontal lobe are crucial for representing and processing verbs.

Stroke[1–7] or focal dementia[8–11] can disproportionately affect the ability to produce either nouns or verbs, indicating that separate neural regions are crucial for producing each word class. The location of these functionally distinct brain regions, however, is unclear. Furthermore, most studies did not test if the impairment was in accessing the meanings, phonological forms or orthographic forms of the affected word class. Cases of impaired written naming of verbs, with relatively spared oral naming of verbs and spared written and oral naming of nouns, can only be due to impaired access to orthographic forms of verbs[3]. Here we report two such cases and identify regions of neural dysfunction responsible for this modality- and word class–specific deficit, using a new technique for identifying brain–behavior relationships.

Case 1 is a 68 year-old woman who was tested 6 hours after onset of writing difficulties. Case 2 is a 48 year-old woman who was tested 12 hours after onset of writing impairment. Both are right-handed and have normal attention, speech production, comprehension, oral reading, repetition and copying. Both were impaired in spelling verbs and pseudowords (such as glamp), and their written narratives contained accurate nouns, but no accurate verbs. To substantiate the clinical impression of disproportionately impaired written naming of verbs relative to nouns, we administered a test of oral and written naming and comprehension consisting of 30 pictures each of pure verbs, pure nouns matched in surface frequency to the verbs, and pure nouns matched in cumulative frequency to the verbs[5]. Informed consent was obtained for the study, using forms and methods approved by the institutional review board of the Johns Hopkins University School of Medicine.

Case 1 correctly wrote the names of only 10/30 (33%) of verbs, but 50/60 (83%) of nouns ($P = 0.0001$, Fisher's exact test). In contrast, she correctly named aloud 28/30 (93%) of verbs and 58/60 (97%) of nouns (not significant, n.s.). Her errors in writing consisted primarily of semantically related words (swing→jump; add→numbers) and a few phonologically plausible misspellings (write→wright). Age-matched control subjects named the nouns and verbs with >97% accuracy (mean, 98.8% for each).

Case 2 correctly wrote 16/30 (53%) of verbs and 56/60 (93%) of nouns in written picture naming ($P < 0.001$). However, oral naming of verbs was relatively spared: 21/30 (70%) for verbs and 48/60 (80%) for nouns (n.s.). Errors in writing were almost exclusively 'don't know' responses. Both patients were 100% correct in comprehension (word/picture verification) with verbs and 98–100% correct with nouns.

Impaired written naming of verbs in these cases cannot be due to impaired access to semantic representations (meanings) of verbs because in each case, oral naming of verbs (which also requires access to semantic representations) was relatively spared, and word/picture verification using the same stimuli was 100% accurate. Impaired written naming of verbs also cannot be due to a general peripheral writing problem, as written naming of nouns was relatively accurate. Our results indicate impairment in accessing orthographic representations of verbs for output in each case.

In an attempt to localize the neural regions responsible for this deficit, we used magnetic resonance diffusion-weighted imaging (DWI) to identify the acute infarct or dense ischemia, and perfusion-weighted imaging (PWI) to identify areas of low perfusion (poor blood flow) that corresponded to impaired tissue function[12,13]. DWI and PWI multi-slice, single-shot, echo planar imaging (EPI) sequences were obtained on a General Electric Signa 1.5-tesla scanner within one hour of language testing. DWI trace images were obtained with $b_{max}$ = 1,000 s/mm$^2$ (TR/TE = 10,000/120 ms). PWI scans (TR/TE = 2,000/60 ms) were obtained with 20 ml of contrast material bolus power injected at 5 ml/s.

In both cases, scans showed a small, acute left subcortical infarct on DWI, and a larger area of hypoperfusion (low blood flow) in frontal cortical regions—including left PIFG and PrG—on PWI (**Figs. 1a** and **2a**). Middle, inferior and superior temporal gyri were not affected.

Both subjects received intervention to improve blood flow to the hypoperfused regions (Case 1, stenting of the left carotid; Case 2, pharmacologically induced blood pressure elevation[14]). In both cases, intervention resulted in both reperfusion of the left PIFG and PrG and immediate reversal of the impairment, indicating that the hypoperfused regions were responsible for

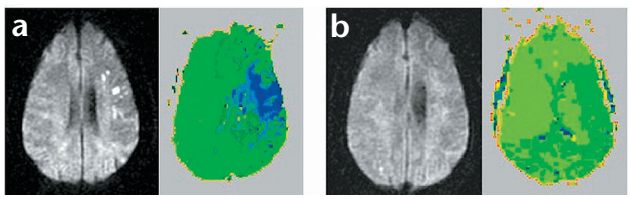


**Fig. 1.** Case 1's DWI (left) and PWI (right) scans before and after intervention to restore blood flow. (**a**) Scans done when written naming of verbs was impaired. (**b**) Scans after intervention, when written naming of verbs had recovered.

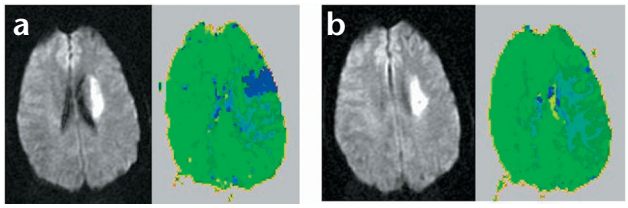


**Fig. 2.** Case 2's DWI (left) and PWI (right) scans before and intervention to restore blood flow. (**a**) Scans done when written naming of verbs was impaired. (**b**) Scans after intervention, when written naming of verbs had recovered.

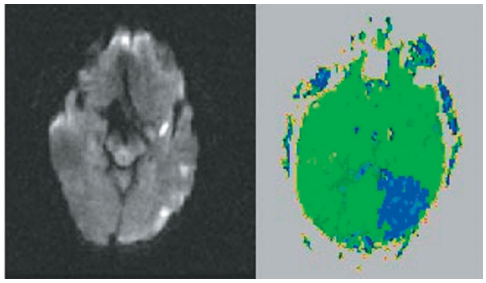

**Fig. 3.** Case 3's DWI (left) and PWI (right) scans performed within 1 h of the naming tests (without intervention), when written naming of nouns was impaired.

the deficit (**Figs. 1b** and **2b**). Within 12 hours after intervention that restored blood flow, written naming of verbs improved to >90% correct in each case.

The disproportionate impairment of verbs in Cases 1 and 2 cannot be explained by greater 'difficulty' of verbs in the battery used, as other patients have shown more errors naming the nouns than the verbs in this battery, at least in oral naming[2,3,5,11]. Furthermore, a third patient with acute stroke who was administered this battery showed greater impairment in written (and oral) naming of nouns than verbs. This 66 year-old, right-handed man, who was tested within 12 hours of stroke symptoms, correctly wrote the names of 90% (27/30) of the verbs and 47% (28/60) of the nouns ($P < 0.0001$). Word/picture verification was completely accurate for both word classes. DWI showed small infarcts in posterior inferior and middle temporal gyri and insula, and PWI showed hypoperfusion of a large portion of posterior middle and inferior temporal gyri (**Fig. 3**). Left PIFG and PrG, which were hypoperfused in Cases 1 and 2, were normally perfused in this patient.

Although a few previous studies have documented selective impairment in accessing the names of verbs in only one modality of output, the neural basis for this has remained elusive. Previously described patients had very large strokes from which they had recovered language skills except naming verbs[3], or had degenerative disease (in which it was impossible to determine the precise areas of neural dysfunction)[11]. In the present cases, the modality-specific impairment in written verb naming was documented in the acute stage of stroke, before the opportunity for extensive reorganization, or before any therapy that might have focused on a single class of words or modality of output. The crucial role of left PIFG and PrG in written verb naming was demonstrated by showing that written naming of verbs was impaired when left PIFG and PrG were hypoperfused, and recovered when this region was reperfused. Furthermore, written naming of verbs was disproportionately spared in Case 3, who had normal perfusion of these frontal regions.

In summary, these cases shed new light on the organization of language in the brain by showing that the left PIFG and PrG are crucially involved in representing and processing orthographic word forms of verbs. We were able to identify areas of dysfunctional brain tissue associated with selective impairment in accessing verbs for written production and to demonstrate that restoration of tissue function in these areas, by restoring blood flow, successfully restored the ability to access those word forms. This study shows a clearly localized neural correlate of a highly specific deficit at the onset of the deficit (before the opportunity for reorganization of structure/function relationships or rehabilitation) in subjects with previously normal neurologic function. These results illustrate the remarkable organization of cognitive functions in the cortex, as well as the use of a powerful new tool for documenting brain–cognition relations.

**Acknowledgments**

*This work was supported by National Institutes of Health grants RO1 DC05375 and P41 RR15241 and by the Charles A. Dana Foundation.*

**Competing interests statement**

*The authors declare that they have no competing financial interests.*

RECEIVED 13 JULY; ACCEPTED 30 OCTOBER 2002

1. Miceli, G., Silveri, M.C., Villa, G. & Caramazza, A. *Cortex* **20**, 217–220 (1984).
2. Zingeser, L.B. & Berndt, R.S. *Brain Lang.* **39**, 14–32 (1990).
3. Caramazza, A. & Hillis, A.E. *Nature* **349**, 788–790 (1991).
4. Damasio, A.R. & Tranel, D. *Proc. Natl. Acad. Sci. USA* **90**, 4957–4960 (1993).
5. Hillis, A.E. & Caramazza, A. *J. Cogn. Neurosci.* **7**, 396–407 (1995).
6. Berndt, R.S., Mitchum, C.C., Haendiges, A.N. & Sandson, J. *Brain Lang.* **56**, 68–106 (1997).
7. Tranel, D., Adolphs, R., Damasio, H. & Damasio, A.R. *Cogn. Neuropsychol.* **18**, 655–670 (2001).
8. McCarthy, R.A. & Warrington, E.K. *Neuropsychologia* **23**, 709–723 (1985).
9. Daniele, A., Giustolisi, L., Silveri, M.C., Colosimo, C. & Gainotti, G. *Neuropsychologia* **32**, 1325–1341 (1994).
10. Bak, T.H., O'Donovan, D.G., Xuereb, J.H., Bonifcae, S. & Hodges, J.R. *Brain* **124**, 103–120 (2001).
11. Hillis, A.E., Tuffiash, E. & Caramazza, A. *J. Cogn. Neurosci.* **14**, 1099–1108 (2002).
12. Barber, P.A. *et al. Neurology* **51**, 418–426 (1998).
13. Hillis, A.E. *et al. Ann. Neurol.* **50**, 561–566 (2001).
14. Rordorf, G. *et al. Stroke* **28**, 2133–2138 (1997).