

NAME CALLING IN THE TEMPORAL LOBE

Evidence for Cortical Reorganization of Language in Patients with Hippocampal Sclerosis. Hamberger MJ, Seidel WT, Goodman RR, Williams A, Perrine K, Devinsky O, McKhann GM 2nd. *Brain* 2007;130(Pt 11):2942–2950. Naming is mediated by perisylvian cortex in the left (language-dominant) hemisphere, and thus, left anterior temporal lobe resection for pharmacologically intractable temporal lobe epilepsy (TLE) carries risk for post-operative naming decline. Interestingly, this risk is lower in patients with hippocampal sclerosis (HS) relative to those without HS (non-HS). Although the hippocampus has traditionally been considered a critical structure for memory, without contribution to naming, this pattern might implicate direct hippocampal naming involvement. On the other hand, critical naming sites have been found in anterior, lateral temporal (i.e. extra-hippocampal) neocortex, the region typically removed with 'standard' TLE resection. We, therefore, speculated that the relative preservation of naming in post-operative HS patients might reflect cortical reorganization of language to areas outside this region. Using pre-resection electrical stimulation mapping, we compared the topography of auditory and visual naming sites in 12 patients with HS and 12 patients without structural brain pathology. Consistent with previous work, non-HS patients exhibited post-operative naming decline, whereas HS patients did not. As hypothesized, HS patients had proportionally fewer overall naming sites in anterior temporal cortex, the region typically removed with standard anterior temporal resection, whereas non-HS patients exhibited a more even distribution of naming sites in anterior and posterior temporal regions ($P = 0.03$). Although both groups exhibited the previously reported pattern of auditory naming sites anterior to visual naming sites, auditory naming sites had a significantly more posterior distribution in HS patients ($P = 0.02$). Additionally, non-HS patients exhibited a greater proportion of visual naming sites above the superior temporal sulcus, whereas visual naming sites in HS patients were scattered across superior and inferior temporal cortex. Results suggest that preserved naming ability in HS patients following anterior temporal resection might be attributable, at least in part, to intrahemispheric reorganization of language in response to the likely, early development of sclerosis in the medial temporal region. Furthermore, their more posterior distribution of naming sites is consistent with the more anterior propagation of EEG discharges in TLE. These results hold theoretical implications regarding the role of the dominant hippocampus in determining the cortical representation of semantic and lexical information, and raise questions regarding the specific roles of medial and lateral temporal cortex in targeted word retrieval. The different patterns of naming areas identified in patients with and without HS may also carry clinical implications, potentially improving efficiency during the time-constrained process of stimulation mapping.

COMMENTARY

In this study by Hamberger et al., auditory naming sites in the temporal lobe were found to reside anterior to visual naming sites, which reflect the anatomical locations of multisynaptic pathways that mediate their respective sensory processing. The ventral stream of visual processing involves successive engagement of Brodmann areas 17–21 en route to the lateral aspect of the temporal lobe (1). This pathway corresponds to areas of visual elaboration and ictal experiential phenomena that can be mapped by direct electrical stimulation of the human cortex (2). Auditory processing occurs in first- to third-order association areas of Brodmann area 22 of the superior temporal gyrus, after receiving input from primary auditory cortex (3). However, neurons in the anterior middle and inferior temporal gyri also participate in spoken speech, although these areas lay rostral to areas essential for speech integrity (3). Thus, any one of several verbal functions (i.e., naming, silent speech, reading, and short-term verbal memory) may activate neurons in the aforementioned areas (4). Although auditory and visual naming sites minimally overlapped in non-HS temporal lobe epilepsy

patients in the present study, a previous study demonstrated that evoked potentials between the cortical sites in human disclosed pathways in each direction between anterior and posterior temporal and extratemporal language areas (5).

Several types of data indicate a close anatomical and functional connection between the hippocampus and temporal neocortex. First, anatomical studies have shown that hippocampal projections to the temporal neocortex are mediated through the subiculum and the entorhinal cortex; the anterior part of the superior temporal gyrus and the temporal polar cortex appear to be the principal lateral temporal recipients in primates (3,6). Second, extrahippocampal temporal lobe atrophy has been described in association with hippocampal sclerosis (HS) in patients with temporal lobe epilepsy (7). Third, PET studies in patients with mesial temporal epilepsy have revealed that temporal lobe hypometabolism extends over both its mesial and lateral aspects (8). Additionally, combined depth and subdural EEG recordings of hippocampal-originating seizures in humans found principal spread to temporal neocortex (9).

Some studies of verbal memory deficits after left temporal lobectomy correlate verbal memory loss with the extent of lateral temporal removal, while other studies correlate it with the amount of mesial temporal resection (3). Evidence is similarly mixed for naming. As in the current study, multiple prior

reports have linked pathology and reduced function in the hippocampus to poor naming (10). Others have found postoperative naming changes associated with resection of larger volumes of neocortical tissue, regardless of whether or not surgery involved sparing of language eloquent cortex, as determined by stimulation mapping or anatomy (i.e., superior temporal gyrus) (11). Further, although strict damage to mesial structures from herpes simplex encephalitis often results in specific amnesia without deficits in naming or other measures of semantic memory, naming may be affected if lateral temporal cortex also is compromised (12).

The foregoing data suggest that naming and other verbal memory functions are the product of concerted mesial and lateral temporal activity. Hamberger et al. discuss further evidence of this hypothesis, which melds well with a more recent model of memory, called multiple trace theory, which emphasizes different strengths in the interactions and connections between these brain areas depending on whether the information was learned recently or more remotely. The multiple trace theory asserts that hippocampal regions may be involved in retrieving certain aspects of semantic memory (including object names), even if they are stored primarily in extrahippocampal cortex (13). This interactionist view helps interpret an interesting pattern reported in this and other studies (14), that is, the apparent greater sensitivity of the Boston Naming Test to postlobectomy changes compared with other visual naming measures. Hamberger et al. suggested that the greater proportion of low-frequency words in the Boston Naming Test might partly explain this finding. This theory is consistent with hypotheses in multiple trace theory and with the finding that words learned later in life are more susceptible to loss after anterior medial temporal lobectomy (15).

The current study found better post-temporal lobectomy naming among HS patients with as compared with non-HS patients, which correlated with a preoperative displacement of auditory naming posterior to usual dominant temporal lobe resections, as shown by preoperative or intraoperative mapping. No such displacement occurred among non-HS temporal lobe epilepsy patients. This finding is in alignment with the possibility that the persistent dysfunction associated with HS epilepsy will more effectively engender cortical reorganization than will intermittent disruptions associated with non-HS focal epilepsy. Furthermore, despite a greater total number of neocortical temporal naming areas in patients with HS, including anterior regions, naming was less affected by temporal resection. It has been suggested that cortical reorganization may produce a protective factor against postoperative decline, possibly because those additional language sites are redundant (11); however, cortical reorganization possibly may represent migration of functions normally mediated by nonsclerotic hippocampal

tissue. Further investigation is necessary to better understand this apparent greater neuroplasticity.

Despite the lack of any study specifically linking post-temporal lobectomy naming ability with quality of life, the displacement of auditory naming sites to a more posterior distribution is good news for HS patients and their caregivers. The presence of HS is the most consistently demonstrated predictor of a good seizure outcome (16), substantially better than that for temporal lobectomy for which no lesion has been identified (17) and often predicts lower risk of postsurgical memory decline (18). Thus, HS may be the major factor linking the presence of three beneficial outcomes to left temporal lobectomy: 1) seizure freedom, 2) minimal change in verbal memory or naming, and 3) satisfactory quality of life (19,20). Results of the current study may underlie this favorable constellation.

by Warren T. Blume, MD, and Brent Hayman-Abello, PhD

References

1. Jones EG, Powell TPS. An anatomical study of converging sensory pathways within the cerebral cortex of the monkey. *Brain* 1970;93:793–820.
2. Penfield W. Functional localization in the cerebral cortex. In: Penfield W, Jasper H, eds. *Epilepsy and the Functional Anatomy of the Human Brain*. Boston: Little Brown, 1954:41–155.
3. Gloor P. The temporal isocortex. In: Gloor P, ed. *The Temporal Lobe and Limbic System*. New York: Oxford; 1997: 202–205.
4. Ojemann GA, Creutzfeldt O, Lettich E, Haglund MM. Neuronal activity in human lateral temporal cortex related to short-term verbal memory, naming and reading. *Brain* 1988;111:1383–1403.
5. Matsumoto R, Nair DR, LaPresto E, Najm I, Bingaman W, Shibusaki H, Ludors HO. Functional connectivity in the human language system: A cortico-cortical evoked potential study. *Brain* 2004;127:2316–2330.
6. Kosel C, van Hoesen GW, Rosene DL. Non-hippocampal cortical projections from the entorhinal cortex in the rat and rhesus monkey. *Brain Res* 1982;244:201–213.
7. Moran NF, Lemieux L, Kitchen ND, Fish DR, Shorvon SD. Extrahippocampal temporal lobe atrophy in temporal lobe epilepsy and mesial temporal sclerosis. *Brain* 2001;124:167–175.
8. Henry TR, Engel J Jr, Mazziotta JC. Clinical evaluation of interictal fluorine-18-fluorodeoxyglucose PET in partial epilepsy. *J Nucl Med* 1993;34:1892–1898.
9. Spencer SS, Williamson PD, Spencer DD, Mattson RH. Human hippocampal seizure spread studied by depth and subdural recording: The hippocampal commissure. *Epilepsia* 1987;28:479–489.
10. Sawrie SM, Martin RC, Gilliam FG, Faught RE, Maton B, Hugg JW, Bush N, Sinclair K, Kuzniecky RI. Visual naming and hippocampal function: A neural network study using quantitative 1H magnetic resonance spectroscopy. *Brain* 2000;123:770–780.
11. Hermann BP, Chelune GJ, Loring DW, Trenerry MR, Perrine K, Barr W, Strauss E, Westerveld M. Visual confrontation naming following left anterior temporal lobectomy: A comparison of surgical approaches. *Neuropsychology* 1999;13:3–9.

12. Levy DA, Bayley PJ, Squire LR. The anatomy of semantic knowledge: Medial vs. lateral temporal lobe. *Proc Natl Acad Sci* 2004;101:6710–6715.
13. Moscovitch M, Rosenbaum RS, Gilboa A, Addis DR, Westmacott R, Grady C, McAndrews MP, Levine B, Black S, Winocur G, Nadel L. Functional neuroanatomy of remote episodic, semantic and spatial memory: A unified account based on multiple trace theory. *J Anat* 2005;207:35–66.
14. Davies K, Bell B, Bush A, Hermann B, Dohan FC, Japp AS. Naming decline after left anterior temporal lobectomy correlates with pathological status of resected hippocampus. *Epilepsia* 1998;39:407–419.
15. Bell BD, Davies KG, Hermann BP, Walters G. Confrontation naming after anterior temporal lobectomy is related to age of acquisition of the object names. *Neuropsychologia* 2000;38: 83–92.
16. Berg AT, Langfitt JT, Vickrey BG, Wiebe S. Outcome measures In: Engel J Jr, Pedley TA, eds. *Epilepsy a Comprehensive Textbook*. Philadelphia: Lippincott Williams & Wilkins; 2007:1929–1937.
17. Blume WT, Ganapathy GR, Munoz D, Lee DH. Indices of resective surgery effectiveness for intractable nonlesional focal epilepsy. *Epilepsia* 2004;45:46–53.
18. Stroup E, Langfitt J, Berg M, McDermott M, Pilcher W, Como P. Predicting verbal memory decline following anterior temporal lobectomy (ATL). *Neurology* 2003;60:1266–1273.
19. Helmstaedter C, Kurthen M, Lux S, Reuber M, Elger CE. Chronic epilepsy and cognition: A longitudinal study in temporal lobe epilepsy. *Ann Neurol* 2003;54:425–432.
20. Tellez-Zenteno JF, Dhar R, Hernandez-Ronquillo L, Wiebe S. Long-term outcomes in epilepsy surgery: Antiepileptic drugs, mortality, cognitive and psychosocial aspects. *Brain* 2007;130: 334–345.