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Short Communication

Infiltration of the basal ganglia by brain tumors is associated with the development of co-dominant language function on fMRI

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A B S T R A C T

Studies have shown that some patients with left-hemispheric brain tumors have an increased propensity for developing right-sided language support. However, the precise trigger for establishing co-dominant language function in brain tumor patients remains unknown. We analyzed the MR scans of patients with left-hemispheric tumors and either co-dominant ($n = 35$) or left-hemisphere dominant ($n = 35$) language function on fMRI to investigate anatomical factors influencing hemispheric language dominance. Of eleven neuroanatomical areas evaluated for tumor involvement, the basal ganglia was significantly correlated with co-dominant language function ($p < 0.001$). Moreover, among patients whose tumors invaded the basal ganglia, those with language co-dominance performed significantly better on the Boston Naming Test, a clinical measure of aphasia, compared to their left-lateralized counterparts (56.5 versus 36.5, $p = 0.025$). While further studies are needed to elucidate the role of the basal ganglia in establishing co-dominance, our results suggest that reactive co-dominance may afford a behavioral advantage to patients with left-hemispheric tumors.

1. Introduction

During the past decade, functional magnetic resonance imaging (fMRI) has become a mainstay in presurgical planning for brain tumor resection. In addition to providing a way to noninvasively assess the risk of iatrogenic damage, fMRI has proven effective in localizing and lateralizing eloquent areas – e.g. sensory, motor, and language networks – that can be displaced by tumors invading normal tissues (Belyaev, Peck, Brennan, & Holodny, 2013). fMRI is particularly important for planning surgical interventions in putative language regions, given that language is more highly distributed and variable between individuals (Sanai, Mirzadeh, & Berger, 2008).

Beyond serving as a tool in the neurosurgeon's arsenal, fMRI is increasingly being used to elucidate the brain's ability to reorganize following injury. While the literature describing brain plasticity in the context of injury – namely, stroke and epilepsy – is robust, recent neurofunctional imaging studies have demonstrated that major neural reorganizations can also be triggered by tumor invasion (Ius, Angelini, Thiebaut de Schotten, Mandonnet, & Duffau, 2011; Krieg et al., 2013; Petrovich, Holodny, Brennan, & Gutin, 2004; Zheng et al., 2013). To date, four main plasticity patterns have been reported in the study of brain neoplasms: intratumoral, perilesional, ipsilateral hemispheric and contralateral hemispheric reorganization (Desmurget, Bonnetblanc, & Duffau, 2007; Krainik et al., 2003; Meyer et al., 2003; Petrovich et al., 2004). In their review of brain plasticity in the context of slow-growing gliomas, Duffau postulated that these patterns are organized in a hierarchical fashion – that is, local compensations precede remote recruitments (Desmurget et al., 2007). However, the mechanisms underlying such functional reorganization remain enigmatic.

It is reasonable to suggest that there is a "tipping point" where perilesional compensation gives way to an interhemispheric strategy in a hierarchical manner (Duffau, 2011). With respect to the language network, several functional imaging studies have already documented the recruitment of the right (nondominant) hemisphere in patients with tumors in the left hemisphere, where most language typically resides (Partovi et al., 2012; Wang et al., 2013). However, the precise anatomical or functional trigger for the recruitment of the contralateral hemisphere and the alteration in

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language laterality remains to be determined. Thus, we compared two groups of right-handed patients with left hemispheric tumors: in one group, the patients exhibited left-lateralized language function by fMRI and in the other group, the patients exhibited co-dominant language function. We investigated whether certain neuroanatomical structures, when infiltrated by tumor, would correlate with language co-dominance, implying the recruitment of homologous regions in the right hemisphere. Because subcortical injury has been shown to be a predictor of worsening language function in patients subjected to craniotomies (Trinh et al., 2013) and because studies have suggested a critical role of subcortical structures in interhemispheric functional dynamics (Crosson, 1992), we hypothesized that the invasion of subcortical structures would correlate with a greater language deficit and by extension, greater participation of the right hemisphere.

2. Results

2.1. Neuroanatomical correlates of language laterality

Patients with infiltration of the basal ganglia by tumor were significantly more likely than patients without basal ganglia involvement to have co-dominance for language ($p < 0.001$) (Fig. 1). The infiltration of the left precentral gyrus and insula, while approaching significance in a single test ($p = 0.023$ and $p = 0.028$, respectively), did not survive multiple comparisons testing (family-wise type I error rate = 0.005). Neither the involvement of Broca's area (inferior frontal gyrus) nor of Wernicke's area (superior temporal gyrus) correlated significantly with the establishment of hemispheric language co-dominance.

No statistical difference in tumor volume was seen between the two groups ($p = 0.58$ by FLAIR, $p = 0.56$ by contrast enhancement), indicating that co-dominance did not correlate with the lesion size.

2.2. Boston Naming scores

To evaluate the potential behavioral advantages of developing co-dominant language function secondary to tumor, we identified those patients with tumors involving the basal ganglia and analyzed their Boston Naming Test (BNT) scores. Of the patients with documented BNT scores, 10 exhibited co-dominant language function and 10 exhibited left-lateralized language function. Using the Wilcoxon rank sum test, the median BNT score was found to be significantly higher ($p = 0.025$) for the co-dominant group (median = 56.5) than for the left dominant group (median = 36.5), suggesting that co-dominance that is reactive to left hemispheric pathology may afford a behavioral advantage to brain tumor patients.

3. Discussion

The aim of this study was to determine whether pathologic infiltration of certain neuroanatomical structures in brain tumor patients disproportionately contributes to the elicitation of non-dominant language compensation. Our results suggest that the involvement of the basal ganglia factors in the establishment of non-dominant functional language activation. Furthermore, we suggest that in the context of a left hemispheric tumor, co-dominant patients appear to show a behavioral advantage over those who do not elicit right hemispheric support.

To date, the literature regarding language lateralization in the setting of slow-growing tumors remains limited. The few studies that have evaluated the influence of neoplasms on language laterality restricted their analyses to classic language areas like Broca's and Wernicke's areas (Holodny, Schulder, Ybasco, & Liu, 2002; Partovi et al., 2012; Petrovich et al., 2004; Wang et al., 2013). However, studies of patients who suffered acute left-sided ischemic events as well as patients who underwent awake craniotomy procedures in which language function was monitored during cortical and subcortical resection, suggest that subcortical – not cortical – injury is more likely to impart lasting language deficits (Lieberman, 2013; Naeser et al., 1982; Trinh et al., 2013). Thus, we were compelled to evaluate the putative relationship between subcortical damage and the elicitation of right hemispheric language compensation defined as co-dominance on fMRI. While our results chiefly suggest that the involvement of the left basal ganglia by FLAIR and/or contrast is critical for the establishment of co-dominance, the insula and precentral gyrus may also play an essential role. Having survived the first round of statistical testing, these areas failed to pass Bonferroni multiple comparisons testing. However, given our limited sample size ($n = 35$), subsequent studies with a larger cohort of patients may reveal these areas – especially, the subopercular insula with its role in articulatory planning – to be significant (Dronkers, 1996).

In our analysis of those patients whose tumors invaded the basal ganglia, we found that the patients with language co-dominance performed significantly better on the Boston Naming Test, a clinical measure of aphasia, compared to their left-lateralized counterparts. Because this finding is only based on 20 patients, future studies are needed to characterize this effect more completely. However, it is worth noting that this result represents a key difference in the literature regarding brain plasticity induced

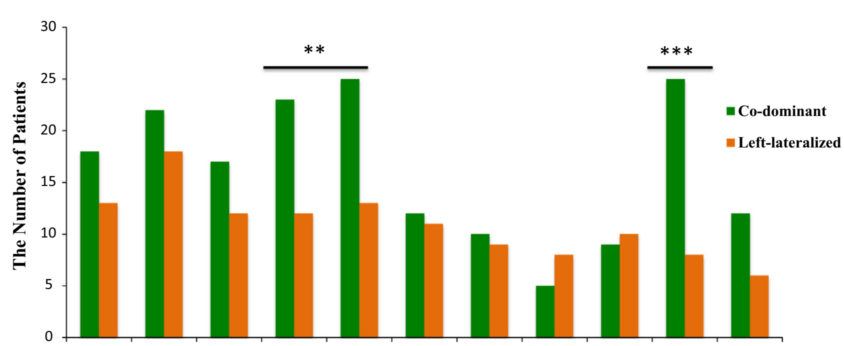

Fig. 1. Relationship between language laterality and tumor location differences in the location of tumor infiltrate in the co-dominant versus the left-lateralized cohort are illustrated. The green and orange bars reflect the number of co-dominant and left-lateralized patients, respectively, whose tumors infiltrated a given neuroanatomical area by FLAIR and/or contrast. While involvement of the insula and left pre-central gyrus approach significance in the co-dominant population, they do not survive multiple comparisons testing ($^{**}p < 0.05$). By contrast, involvement of the basal ganglia is significantly associated with co-dominance ($^{***}p < 0.001$). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)