Spatial neglect and paradoxical lesion effects in the cat — A model based on midbrain connectivity

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Abstract

Spatial visual attention in humans and mammals is severely disrupted after deactivation of specific cortical or subcortical regions. Such dysfunction has frequently been associated with impaired unilateral cortical mechanisms. Alternatively, I propose that essential mechanisms of spatial attention are based on the bilateral competition between subcortical midbrain structures. Consequently, visuospatial hemineglect and hemi-extinction arise from unbalanced bilateral competition. I present a simple mathematical model, based on known connectivity of the cat midbrain, that exemplifies the principle of competition through mutual inter-hemispheric inhibition. The model represents a linear, topographic integration of several cortical and subcortical inputs in the two halves of the feline superior colliculus. Such a system reproduced a variety of neglect symptoms and also explained the paradoxical effects observed in some lesion experiments where the consequences of a primary lesion could be reversed through a secondary lesion in structures of the contralateral hemisphere. The model generated predictions for future experiments. © 2000 Elsevier Science B.V. All rights reserved.

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1. Introduction

Intriguing effects of damaged attentional systems have been observed in humans as well as in other mammalian species, such as the cat. As the connectivity and
physiology of the cat brain have been well explored over the last decades, this system provides a good model for studying the mechanisms of intact and impaired spatial attention.

Cats with unilateral lesions of the junction of left or right temporo-occipito-parietal (TOP) cortices fail to orient to visual stimuli presented to them in the contralesional hemifield [13,16,17]. The same deficit follows unilateral lesions or inactivation of the superior colliculus [16,8]. These results implicate unilateral cortical and midbrain structures in mediating spatial attention in the cat. Symptomatically similar attentional deficits have been observed in human patients with brain lesions mainly in parietal, medial frontal and premotor cortices (e.g. [18] for review).

A further puzzling and illuminating set of effects is related to the mechanisms of spatial orienting in the cat. In a classic experiment, Sprague [17] demonstrated that the visual hemineglect induced by removing large portions of occipital–temporal cortex in one hemisphere could be paradoxically reversed by subsequently damaging even more brain tissue. Secondary lesions that led to a recovery of spatial attention included destruction of the superior colliculus on the contralesional side, or sectioning the commissure of the superior colliculus [17]. Similar restoration of function was, moreover, produced by secondary lesions to the contralesional substantia nigra pars reticulata [20], or by destruction of non-tectal fibers in the commissure of the superior colliculus [19]. These surprising results appear to suggest that the initially lesioned unilateral structures were not essential to the orienting behavior.

In a more recent series of experiments, Payne and Lomber confirmed and extended these results by reversibly cooling TOP cortical and collicular locations [13,8]. Their experiments produced contralateral hemineglect for unilateral cooling of either cortical or subcortical sites, as well as paradoxical restoration of attention after bilateral inactivation of the TOP cortex, or the colliculi, alone. These results demonstrated that performance could be restored by subsequent inactivation at the same level as the primary lesion.

Notwithstanding a large amount of experimental work, the precise mechanisms of spatial attention, its disruption by unilateral lesions, and its paradoxical restoration remain poorly understood [8,2]. The described results suggest that intact, lesioned and paradoxically restored orienting behavior in the cat arises from interactions between a potentially large set of cortical and midbrain structures. As the anatomical connectivity between these structures is confusingly complex, e.g. [5], I attempted to explain the main experimental findings with the help of a simple mathematical model comprising only the most basic structural aspects of the cat’s attentional system.

2. Methods

Spatial orienting in the cat is likely to be mediated by a wide-ranging network of several cortical and subcortical stations. A survey of some of these pathways is provided elsewhere [6]. For the design of a first basic model I concentrated on the set of structures implicated in the most robust results, namely the superior colliculi and their cortical and subcortical inputs.
The model represents the gross neuronal activity in two competing ‘midbrain structures’, $M_L$ and $M_R$, one in either half of the brain. The description of these stations was largely based on anatomical data for the SC [6], however, some of the assumed mechanisms might also apply to other brain structures. $M_L$ and $M_R$ are topographically organized into sectors that represent specific visual field eccentricities, and which receive topographically mapped inputs. Topographically mirror-symmetric sectors in the two structures (e.g., $M_{L-15}$ and $M_{R15}$) mutually inhibit one another via reciprocal commissural connections. The basic structure of the model is shown in Fig. 1.

The different sectors in $M_L$ and $M_R$ were described as dynamical variables in a system of coupled ordinary differential equations, and their respective neural activity was determined as a linear superposition of all different excitatory and inhibitory inputs. The representation of attention to the regions of the visual field was assessed by averaging the steady-state values of the variables that correspond to matching sectors from both midbrain structures (e.g., the activity of $M_{L45}$ with that of $M_{R45}$). Such a read-out would provide a very simple directional signal mechanism for downstream motor or sensory systems.
3. Results

The model was tested for stimuli presented at different eccentricities, given intact, unilaterally lesioned or multiply lesioned pathways. A detailed demonstration of the model’s behavior is presented in [6]. The model reproduced correct orienting of the intact system. For unilaterally lesioned cortical inputs (simulated by reducing the left or right input pathways to a residual 10% of their intact strength values), it displayed significantly reduced activity in the ipsilesional midbrain structure, agreeing with findings from electrophysiological experiments [9,4]. In this unilateral lesion condition, the system moreover failed to respond to visual stimuli presented in the contralesional hemifield (unless the stimuli were very close to the vertical meridian), thus reproducing the experimental effects of spatial hemineglect in the cat [13,16,17]. If the unilateral lesions had only a moderate impact (e.g., if they left 30% rather than 10% of the input pathways intact), the model exhibited symptoms of (hemi-) extinction. Under this condition, the system did respond to unilateral stimuli presented in the contralesional hemifield; for bilaterally presented stimuli, however, it orientated only towards the ipsilesional stimulus, while the contralesional stimulus was ignored.

For three different secondary lesions in addition to the primary, unilateral cortical lesion (lesioning either the contralesional cortical input pathways, or the contralesional midbrain structure, or sectioning the commissural fibers linking the midbrain halves), the model reproduced the experimental results of paradoxical recovery [17,8]. The model also agreed with the experimental observation that the recovery of orienting was least efficient for the commissurotomy as a secondary lesion [17].

The model moreover replicated the experimental finding that the paradoxical recovery of spatial attention was not complete in the far periphery of the cat’s visual field [17,8]: For bilateral lesions of the input paths, the activity in the midbrain sectors that represented the peripheral stimuli did not exceed the baseline activity of those sectors representing the center of vision. Consequently, the midbrain would compute only ambiguous signals for the perceived stimulus location.

Finally, the activity distribution in the modeled midbrain structures showed remarkable similarities with the distribution of spatial exploration by human neglect patients and healthy control subjects, see Fig. 2.

4. Conclusions and predictions

This model demonstrates that topographically organized connectivity together with competition between bilateral brain structures can readily explain intact and impaired visuospatial orienting in the cat, as well as apparently paradoxical effects of certain multiple lesions. The known connectivity of the cat brain suggests that an important component of the competition mechanism is based on interactions between subcortical midbrain structures, with cortical stations shaping their input. As the seemingly paradoxical lesion effects demonstrate, any attempts to assign functional properties of the brain to specialized brain regions have to take into account the potential distribution of neural functions across wide-ranging networks [21].
Fig. 2. Representation of visual space in the cat midbrain model (a) and in human spatial exploration (b). The resting state activity in the intact midbrain model (solid line in panel (a)) is determined mainly by the Gaussian distributions of input strengths into the bilateral structures. On the other hand, resting activity in the unilaterally lesioned model (panel (a), dashed line) is strongly depressed for the contralesional (‘neglected’) left field, and the peak of activity is shifted off the midline into the ipsilesional (‘intact’) field by about 20°. This modeled representation of attentional space shows similarities to the unstimulated exploration of visual space by healthy volunteers (panel (b), solid line) and human hemineglect patients (panel (b), dashed line); diagram redrawn from [7]. Note in particular that the peak of attentional activity or visual search activity is higher for the unilaterally lesioned model system or the unilateral neglect patients, compared to the intact system or healthy controls. This indicates the desinhibition resulting from a unilateral lesion.

The results of this study allow making predictions for future experiments. The model suggests that the phenomena of neglect and extinction are based on the same basic neural mechanism. This hypothesis could be tested experimentally by producing extinction symptoms in the cat, using the scalable and reversible cooling technique [14] to create a more moderate deactivation of tissue than that leading to neglect [13].

The model further suggests that the impairment underlying hemi-extinction produces differential effects for the attention towards stimuli presented at central and at
peripheral eccentricities in the visual fields. Some experimental support already exists for this hypothesis [12].

Since the proposed model for spatial attention relies on competitive bilateral interactions, unilateral lesions of the system can be expected to create disinhibition of the contralateral hemisphere (see Fig. 2). Consequently, unilateral lesion conditions may actually produce a better-than-normal performance in the intact hemifield.

The similarity of some effects in cats and humans suggests that spatial attention in the two species might also be mediated by similar neural mechanisms. For instance, Fink et al. [3] showed that bilateral visual stimulation led to a reduction of cortical metabolic activity in humans compared to the activity induced by unilateral stimuli. This observation, on the other hand, also allows for the possibility that an important part of the inter-hemispheric competition in the human brain is realized on the cortical level. A cortical stage of attentional competition may also be the basis of effects observed by Brefczynski and DeYoe [1], who investigated the representation of the ‘attentional spotlight’ in topographically organized human visual cortex. Apart from strongly activated cortex that represented the given unilateral stimulus, they also found weak to moderate activity in the cortical representation of an eccentricity exactly opposite to the presented stimulus. Such activity may reflect the activity of inhibitory interneurons in an inter-hemispheric competition mechanism for spatial attention. More details of these competition mechanisms in humans will certainly be unraveled by the systematic application of reversible deactivation techniques such as transcranial magnetic stimulation [11,10].

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References


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Claus C. Hilgetag studied Biophysics in Berlin and Neuroscience in Edinburgh, Oxford and Newcastle, and has worked on the computational analysis of complex metabolic and complex neural networks. He is currently a Wellcome Trust Prize International Fellow in the Department of Anatomy and Neurobiology of the Boston University School of Medicine, where, together with Prof. Bertram R. Payne, he is investigating the mechanisms for spatial attention in mammals, using reversible lesion techniques, behavioral testing and mathematical modeling.