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Inhibition of return in spatial attention: direct evidence for collicular generation

Ayelet Sapir[1], Nachum Soroker[2], Andrea Berger[1] and Avishai Henik[1]

[1] *Department of Behavioral Sciences and Zlotowski Center for Neuroscience, Ben-Gurion University of the Negev, Israel*

[2] *Loewenstein Rehabilitation Hospital and Sackler School of Medicine, Tel Aviv University, Israel*

Correspondence should be addressed to A.H. (henik@bgumail.bgu.ac.il)

Visuomotor pathways in the vertebrate midbrain mediate rapid, reflexive orienting to abrupt changes. Using the 'inhibition of return' (IOR) mechanism, the attentional system favors novel spatial locations by inhibiting already scanned ones[1]. In a rare patient with a unilateral lesion restricted to the dorsal midbrain, we demonstrate that IOR is generated within the midbrain superior colliculus.

Midbrain visuomotor pathways provide all vertebrates with mechanisms for rapid, reflexive orienting to abrupt environmental changes. Through evolution, visual pathways have become integrated with cortical mechanisms involved in strategic search under endogenous control. Demands of the external environment constantly compete with those of internally generated goals; and coherent behavior requires control mechanisms to arbitrate between them and to coordinate their actions. Thus, although there are adaptive advantages to orienting automatically to new sensory signals in the visual periphery, it is important that the organism limit the duration of attention to stimuli so that it maintains the ability to scan and detect potentially meaningful events at other spatial locations. IOR is a mechanism by which attention is temporarily inhibited from returning to a recently scanned location. By integrating attention with eye movements, IOR is thought to promote an efficient visual-search strategy that favors novelty[2]. Recent work confirms that IOR provides a mechanism for efficient foraging[3].

The superior colliculus (SC) has been implicated as the neural substrate for IOR through four converging, but indirect, lines of evidence. First, 10R is abnormal in patients with midbrain degeneration due to progressive supranuclear palsy (PSP)[4]. Second, it is preserved in patients with hemianopia, a condition in which only extrageniculate pathways are available to process visual information[5]. Third, it is present in newborn infants, in whom the geniculostriate pathways are not yet developed[6]. Fourth, it is generated asymmetrically in temporal and nasal visual fields[7], suggesting retinotecal mediation[8,9,10].

Although each of these observations is consistent with midbrain mediation of IOR, the evidence remains indirect. PSP is a heterogeneous degeneration involving many subcortical struc-

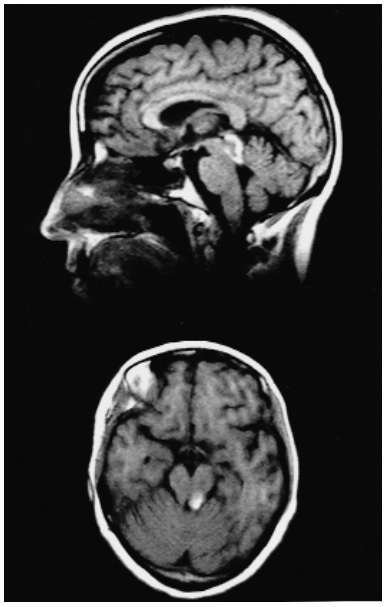

Fig. 1. Neuroimage of a 46-year-old patient, SG. Midsagittal (**a**) and axial (**b**) MRI seven days after onset showing bleeding in the dorsal mesencephalon, mainly in the right superior colliculus (SC). Blood is also seen in the cerebral aqueduct. CT-scans in the first and third days also revealed blood in the ventricles, mainly in the fourth ventricle. Two months after onset, the CT scan was normal except for a small hypodense area in the right SC. Clinical evaluation at the time of testing was normal except for slight limitation of upward gaze and abduction of the right eye, and diminished hearing in the left ear.

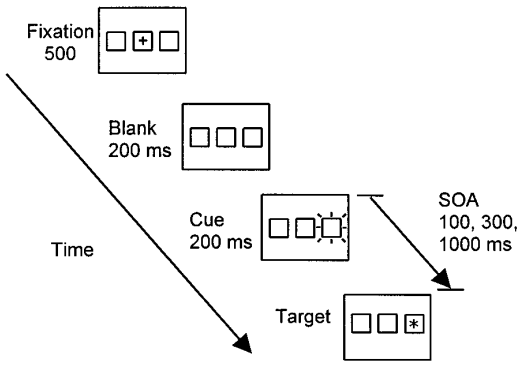

Fig. 2. Experimental procedure. Reaction time (RT) was measured for key press responses for detecting a target at a peripheral location. The target was preceded by a cue, which directed attention either to the target location (valid cue) or to the wrong location (invalid cue), or provided no spatial information (neutral cue; presented in the middle box). Reflexive orienting produced an early advantage at the cued location, superseded after a few hundred ms by inhibition at the same location, resulting in longer reaction times (IOR). In each trial, a fixation cross was presented for 500 ms, followed by a 200-ms blank interval, a 200-ms cue (brightening of one of three boxes with equal probability) and a target 100, 300 or 1000 ms after cue onset (stimulus–onset asynchrony; SOA). The target remained in view until the patient responded. Within each of six sessions, each eye was examined in separate blocks of 210 trials each. Stimulus-onset asynchrony, validity and hemifield were manipulated within blocks.

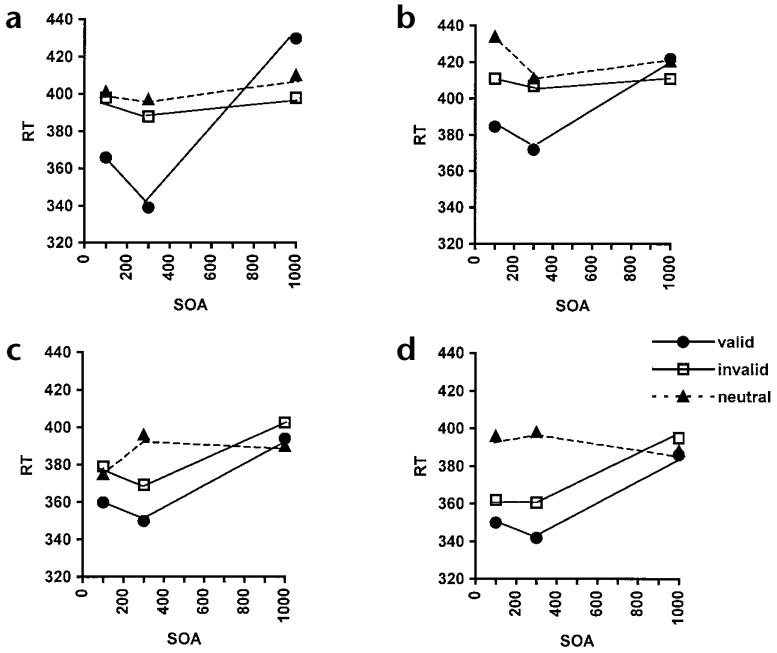

Fig. 3. Median detection RTs. (**a**, **b**) Results for the ipsilesional hemifields (temporal hemifield of the right eye and nasal hemifield of the left eye, respectively). The interaction between stimulus-onset asynchrony and validity in each ipsilesional hemifield was significant ($F_{2,10}$ = 19.8, $p < 0.0005$ and $F_{2,10}$ = 12.05, $p < 0.005$, respectively). (**c**, **d**) Results for the contralesional hemifields (temporal hemifield of the left eye and nasal hemifield of the right eye). The two-way interactions between stimulus-onset asynchrony and validity were not significant ($F < 1$ for both).

tures, including the basal ganglia and reticular formation, as well as the peritectal region. The generation of IOR in newborns[6] and within the hemianopic field of one patient[5] implicates extrageniculate pathways, but not specifically those projecting from retina to dorsal midbrain. Similarly, interpretation of anatomical evidence suggesting temporonasal asymmetries as markers for the retinotectal pathway[11,12] in monkeys is controversial[13]; therefore, extrapolation to humans is problematic.

Here we report a single patient with a small spontaneous hemorrhage in the right side of the posterior midbrain (**Fig. 1**). Unilateral involvement of the SC enabled us to observe an IOR asymmetry that directly demonstrated a role of this structure in the generation of IOR.

Our experimental protocol employed was a variant of Posner's spatial-cueing task[3] (**Fig. 2**). To measure responses to stimuli appearing in the temporal and the nasal visual hemifields of each eye separately, we used monocular presentation. It was predicted that IOR would be less efficiently activated by signals in the hemifields corresponding to the damaged right SC (temporal hemifield of left eye and nasal hemifield of right eye), and would be normally activated by signals in the hemifields corresponding to the intact left SC (temporal hemifield of right eye and nasal hemifield of left eye). In addition, because anatomical data suggests that the retinotectal pathway has more crossed fibers (from the medial hemiretina/temporal hemifield of the contralateral eye) than uncrossed fibers (from the lateral hemiretina/nasal hemifield of the ipsilateral eye), we also tested the hypothesis that temporonasal asymmetry could reveal retinotectal mediation of the IOR in humans. This was accomplished by determining if the intact, left SC would generate a larger IOR in response to crossed than uncrossed presentation (that is, a larger IOR in the temporal hemifield of the right eye than in the nasal hemifield of the left eye).

Median reaction times for each experimental condition were subjected to a four-way repeated measures analysis of variance (ANOVA) with the following factors: eye (right, left), hemifield (nasal, temporal), stimulus-onset asynchrony (100, 300, 1000 ms) and cue validity (valid, invalid, neutral). The four-way interaction between eye, hemifield, stimulus–onset asynchrony and validity was significant ($F_{4,20} = 5.92$, $p < 0.005$). The relationships between eye, stimulus–onset asynchrony and validity are presented separately for the temporal and nasal hemifields (**Fig. 3**). IOR developed only in the hemifields projecting to the intact left SC (temporal hemifield of the right eye and nasal hemifield of the left eye). No IOR was found in the hemifields projecting to the damaged right SC (temporal hemifield of the left eye and nasal hemifield of the right eye). Planned comparisons showed that the intact left SC generated a larger IOR in crossed (temporal hemifield of right eye) than in uncrossed (nasal hemifield of left eye) presentation (32 ms and 11 ms, respectively; $F_{1,5} = 65.33$, $p < 0.0005$).

This investigation of an extremely rare patient provides direct evidence for collicular generation of IOR, supporting the view that the evolutionarily older retinotectal visual system has an inhibitory tagging mechanism (IOR) that enables the coordination of reflexive visual orienting by the voluntary attentional system.

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