

Unilateral Neglect after Right-Hemisphere Damage: Contributions from Event-Related Potentials

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Key Words

Brain damage · Unilateral neglect · Event-related potential (ERP) · P_a · N₁ · Mismatch negativity (MMN) · P₃ · N_d · Attention

Abstract

Unilateral neglect is a frequent sequel of right-hemisphere damage. Patients suffering from neglect may fail to detect, orient to, acknowledge or respond to stimuli on their contralesional side, even in the absence of primary sensory or motor loss. Despite the major clinical significance of the phenomenon and its potential implications for our understanding of human cognition, the underlying cognitive deficits are not well understood. We review the relatively few event-related potential studies that attempted to assess the different parts of the cognitive system in neglect patients. We suggest that theories of neglect, based primarily on performance data, may be refined by incorporating these results, and that this line of research may provide information that is not available using traditional performance measures.

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Although motor dysfunctions of patients with focal brain damage are more evident to the eye, cognitive neuropsychological deficits may be at least as disabling. Frequently, cognitive deficits are the major factor impeding the patients' ability to overcome their neural illness and return to their home, family and occupation. Among these deficits, unilateral neglect, a frequent consequence of right-hemisphere damage (RHD), is one of the worst prognostic signs [Denes et al., 1982; Katz et al., 1999]. Despite its frequency and major significance for the patient's outcome, the cognitive and neural deficits underlying unilateral neglect are still debated [Marshall et al., 1993].

Patients suffering from neglect following RHD may fail to acknowledge, respond to, orient to or report stimuli and events occurring on the left side of their personal or extrapersonal space [Heilman et al., 1993]. In extinction, a related disorder, the failure to notice a contralesional stimulus occurs only when a competing stimulus is simultaneously presented more towards the side of the lesion [De Renzi et al., 1984; Heilman et al., 1970; Rapcsak et al., 1987]. Both unilateral neglect and extinction have been dissociated from primary sensory losses such as hemianopsia [Halligan et al., 1990], suggesting that the

source of the disorder is at a higher information-processing level. Although evident primarily in the visual modality, neglect may also be manifested in the auditory and tactile modalities [De Renzi et al., 1984, 1989; Soroker et al., 1997; Gainotti et al., 1989]. Auditory neglect is more difficult to define than tactile or visual neglect, perhaps because the division of the left and right acoustic hemispaces is not as sharp as in the somatosensory and visual domains. This is true both because in natural conditions sounds stimulate both ears and because each ear transmits information to both hemispheres (although with a contralateral predominance [Rosenzweig, 1951]). Nonetheless, auditory neglect and extinction have repeatedly been documented as a consequence of unilateral brain lesions. These phenomena are expressed as failures to detect, identify or localize sounds with a source on the contralesional side [De Renzi et al., 1984, 1989; Soroker et al., 1997].

Theories accounting for the neglect phenomena fall into several broad categories. Early theories suggested that neglect results from a deficit in sensory or perceptual processing of neglected stimuli [Denny-Brown et al., 1952; Denny-Brown and Banker, 1954]. Such theories lost much of their appeal, however, as it became clear that (a) neglect is independent of the existence of primary sensory deficits such as hemianopsia [Halligan et al., 1990], (b) neglect can be demonstrated in the absence of external sensory stimulation [Bisiach and Luzatti, 1978], (c) unlike in the case of primary sensory deficits, neglect can be ameliorated by directing (or cueing) the subject's attention to the neglected side of space [Riddoch and Humphreys, 1983] and (d) the neglected part may be related to an external frame of reference rather than to somatotopic or retinotopic mapping [Behrmann and Moscovitch, 1994; Calamaro et al., 1995; Soroker et al., 1995]. Thus, current opinions of neglect and extinction focus on higher-order functional derangements [for reviews, see Marshall et al., 1993; Riddoch and Humphreys, 1987].

Among the theories assigning the neglect phenomena to levels of processing beyond the sensory system, those involving attention mechanisms are most prevalent. Although these theories may differ in details, they share the notion that neglect is a consequence of a breakdown in a system that normally allocates attentional resources to locations in the neglected hemispace [Halligan and Marshall, 1994; Heilman and Valenstein, 1979; Heilman and Van Der Abell, 1980; Mesulam, 1990]. A related view suggests that attention is constantly attracted to the right side of space by an 'unopposed' left-hemisphere mechanism [Kinsbourne, 1987]. The unilateral attention defi-

cits might be mediated by a failure to execute the disengagement of attention from the right sensory hemifield following damage to the posterior attention system [Posner et al., 1984, 1987]. Theories that do not emphasize disorders of attention suggest that neglect phenomena reflect a failure of the representational system which maps the external space into a neural system. This idea was supported by results suggesting that neglect patients seem to neglect the left parts of space and of objects even in imagery [Bisiach and Luzatti, 1978]. In addition, there are theories suggesting that the neglect syndrome is related to a deficit at specific premotor circuits which have been shown, in primates, to be involved in orienting and reacting to specific regions in space [Rizzolatti and Gallese, 1988].

All the above-mentioned accounts for the neglect and extinction phenomena were primarily based on observation of the patients' behavior and assessment of their performance in formal tests. Recently, these observations have been coupled with direct recording of brain activity using event-related potentials (ERPs). The rest of this paper is dedicated to a review of the latter studies. We start by drawing attention to the major difficulties in using ERPs in brain-damaged patients, which may explain why studies of ERPs in neglect and extinction are scarce despite their potentially important contribution to the understanding of these phenomena.

Difficulties Studying Brain-Damaged Patients with ERPs

Recording ERPs requires considerable cooperation from the subject, both in complying with the task requirements and in minimizing artifacts. Brain-damaged patients may pose difficulties in both directions, especially when studied in relative proximity to the onset of their illness. The difficulties result from several factors. First, it is often difficult to ensure whether the patient fully understood the procedure, aim and significance of the test, especially when there are language disturbances (aphasia), disorientation or confusion. Under these circumstances, the paraphernalia used in an ERP study may be particularly intimidating. Second, with or without psychoactive medications, patients frequently undergo significant fluctuations in their arousal. This may cause problems both in performance and in the interference of slow waves (in the alpha band or slower) in the EEG. Third, (hemi)plegic patients may have difficulties sitting quietly in their chair for the entire test duration, causing excessive artifacts of

muscular activity. Fourth, patients may suffer from general attention deficits making it difficult for them to stay alert, focused and compliant along a prolonged testing session. The latter problem is especially evident in RHD patients who are the main concern of this article.

Although the list is inconclusive, the above difficulties are important enough to require the adjustment of experimental paradigms in an attempt to shorten the testing sessions as much as possible and to minimize the patient's discomfort and apprehension. Unfortunately, even if these precautions are taken, patients are occasionally excluded a priori from ERP studies because of failure to fully cooperate, and considerable parts of data may often need to be discarded due to excessive noise. For example, Angelleli et al. [1996] had to discard data of 12 out of their 60 patients and Deouell et al. [1998b, 2000] have recently had to discard data from 3 out of their 13 patients. This procedure increases, of course, the risk of a selection bias towards less severely affected patients.

Another methodological problem impedes the interpretation of scalp-recorded ERPs in patients who have undergone craniotomy or suffered a significant loss of brain parenchyma. The altered conduction in the damaged tissue may diminish or augment the amplitude of scalp-recorded potentials over the damaged hemisphere even if the underlying generators of a specific ERP component are functioning normally [Aboud et al., 1996].

An additional problem is that the frequently used comparison of patients with normal controls is confounded by many factors other than the phenomenon under investigation. Such factors are, for example, the hospitalization, the use of medications, concomitant affective components and the level of alertness. In fact, even the comparison between patients is complicated by the inescapable variability in lesion sites and sizes, general medical condition and uncontrolled premorbid differences. A possible partial remedy to the latter methodological difficulties is to prefer designs in which each patient is his or her own control. Such designs are relatively easy to implement in neglect, because the interesting contrast is between the hemispaces, within subjects. Thus, the intact side serves as the control for the neglected side.

Despite the multitude of problems, several ERP studies made significant contributions to the understanding of the neglect phenomena. The importance of these studies stems from the ERPs' unique virtue of including a series of components that can be selectively associated with sensory, preattentive levels of processing, as well as components associated with higher-level cognitive function. Thus, ERPs may disentangle perceptual and cognitive

processes from their overt outcome and provide a differential index of integrity for each of the probed processing stages.

Sensory-Perceptual (Preattentive) Components

A major question in neglect research is still whether early perceptual processes are really unaltered, as suggested by most contemporary theories that highlight higher-order deficits in neglect. A tentative answer to this question may be provided by examining ERP components such as the N₁/P₁ complex, potentials that, though possibly affected by attention, are mainly associated with early sensory, preattentive processing. Unfortunately only a few studies measured the N₁, P₁ or earlier components in studies of neglect or extinction. In a pioneering study, Watson et al. [1977] produced neglect in monkeys by cortical ablation of the banks of the monkey's arcuate sulcus (in the posterior parts of the prefrontal regions) and measured somatosensory evoked potentials using epidural electrodes before and after surgery. Despite clear signs of neglect performance in these monkeys, the lesion did not significantly affect the P₁, N₁ and P₂ components elicited by electrical stimulation of the median nerve. Vallar et al. [1991a, b] obtained comparable results in humans with focal brain lesions caused by ischemic stroke. In these studies, normal somatosensory evoked potentials (including N₉, N₁₃, P₁₅, N₂₀ and P₂₅) were found in 3 patients with lesions in the right frontotemporoparietal regions and in 1 patient with damage in the right occipital periventricular region, even though the patients were not aware of being stimulated when the electrical shocks were given to the right median nerve. Moreover, in 2 of the patients (whose primary visual cortex was largely spared), the visual evoked potentials (VEPs, including N₇₅, P₁₀₀ and N₁₄₅) also were within the normal range [Vallar et al., 1991b]. In contrast, somatosensory evoked potentials and VEPs were absent or reduced in patients suffering from hemianesthesia or hemianopsia, respectively, following damage in the left primary sensory cortices. Analogous results were reported by Viggiano et al. [1995], who recorded steady-state VEPs in 10 neglect patients, 10 brain-damaged patients without neglect and 6 healthy subjects, and found no right-left amplitude differences related to neglect. Such data were interpreted as supporting the view that the impairment in neglect stems from 'defective access of the output of *preserved* primary sensory analyses to successive processes involved in conscious perception and in overt verbal response' [Vallar et al.,

1991a, p. 1921, our italics]. However, we will now turn to describe a few findings suggesting that more prudence is required in drawing such conclusions.

The possibility that the early sensory processes in neglect may not always be intact is raised by studies showing that early ERPs may be abnormal in patients with neglect and/or extinction. The earliest auditory evoked potential component whose abnormality was associated with extinction is the P_a , a middle-latency component peaking around 35 ms from stimulus onset. Testing patients with lesions involving the auditory cortex or auditory radiation, Ibañez et al. [1989] found that when this component was reduced over the damaged hemisphere, the patients were more likely to suffer from auditory extinction.

An apparent indication of abnormal sensory function in neglect was also found in studies reporting that the visual and auditory N_1 components are smaller over the damaged relative to the intact hemisphere of neglect patients, regardless of the side of stimulation [Deouell et al., 1998b, 2000; Hämäläinen et al., 1998; Verleger et al., 1996]. In contrast, the N_1 in normal subjects is larger over the hemisphere contralateral to the stimulus side [Näätänen and Picton, 1987]. Importantly, the abnormality was found to decrease as a function of recovery [Hämäläinen et al., 1998]. Drawing from the putative association between the N_1 and the orienting response [Luck et al., 1990], Verleger et al. [1996] suggested that the N_1 reduction over the damaged hemisphere reflects the patients' difficulty in orienting towards the contralesional side of space. The enhanced left-hemisphere (relative to right-hemisphere) N_1 , irrespective of the side of the stimuli, may also contribute to the tendency of patients with left-side auditory neglect to err, localizing auditory stimuli as coming more to the right of their true source [Bisiach et al., 1984].

A caveat in interpreting these results, however, is that neurofunctional impairments are not the only possible account for the N_1 diminution over the damaged hemisphere. As mentioned in the previous section, such a diminution may also result from the reduced conduction of the damaged tissue intervening between the scalp electrodes and the generator of P_a or N_1 , which indeed may be intact [Aboud et al., 1996]. Consequently, drawing strong conclusions from hemispheric asymmetries about the operation of cognitive functions presumably correlated with the N_1 or P_a is risky. Overcoming this potential caveat, Marzi and his colleagues [Marzi, 1998] demonstrated that in their patient suffering from partial visual extinction [extinction was present in 60% of the trials], the

visual N_1 and P_1 components were reduced in those trials in which the left-sided stimulus was extinguished, but not when it was recognized. Other ERP studies also support the possibility that deficits in perceptual processing may indeed exist in neglect patients.

A series of studies reported by Spinelli and her colleagues revealed that there is a latency prolongation of steady-state VEPs elicited by stimulation on the neglected side compared with those elicited by similar stimulation on the intact side [Angelelli et al., 1996; Pitzalis et al., 1997; Spinelli et al., 1994; Spinelli and Di Russo, 1996]. Most importantly, this prolongation was absent in brain-damaged patients who did not show signs of neglect. Even more revealing was the dissociation found between luminance-modulated and chromatically modulated stimuli [Spinelli et al., 1996]. In 10 patients with right-hemisphere damage and visual neglect, the latency of steady-state VEPs was prolonged for stimuli presented on the neglected side, but only when the contrast-reversed sinusoidal stimuli were modulated in luminance at relatively high temporal frequencies (4–10.5 Hz). When the stimuli were equiluminant and hues were modulated within a low temporal-frequency range, no differences were found between the steady-state VEPs elicited by stimuli presented on the neglected and non-neglected sides. The dissociation between the perception of color contrast as opposed to luminance contrast in neglect was further supported by the performance of a frontoparietal patient who neglected low luminance contrast gratings but not high color contrast gratings [Doricchi et al., 1996]. This pattern of performance corresponded with the appearance of unreliable steady-state VEPs for the low luminance contrast stimuli when they were presented in the left (neglected) hemifield, compared with reliable VEPs elicited by low luminance contrast gratings presented to his right side and by high color contrast gratings, regardless of the side stimulated. Interestingly, in this particular patient, even the high color contrast gratings elicited delayed VEPs when the stimuli were on the left, a finding contrasting with that of Spinelli et al. [1996]. The dissociation between the processing of luminance contrast with high temporal frequency and the processing of chromatic contrast with low temporal frequency led Spinelli and her colleagues to suggest that the magnocellular visual system, which is sensitive to luminance and high temporal frequency, is selectively impaired in neglect patients, whereas the parvocellular system, which is sensitive to hues and low temporal frequencies, is largely spared [Spinelli et al., 1996; for the distinction between these parallel visual systems, see Livingstone and Hubel, 1987]. Therefore, some highly spe-

cific deficits in processing incoming information may be influential factors in the failure to overtly respond to neglected stimuli. This possibility was explored in the auditory domain using the mismatch negativity (MMN) component.

The MMN is an electrical brain manifestation elicited by infrequently occurring oddball stimuli interspersed among repetitive stimuli. Since its discovery [Näätänen et al., 1978], it has been investigated in numerous studies and shown to provide a powerful tool for investigating the properties of the central sound representation [Näätänen and Alho, 1997]. Several characteristics of the MMN make it an especially interesting probe in the study of neglect. First, the MMN is assumed to reflect an automatically elicited preattentive process [Alho et al., 1989, 1992; Näätänen 1991; but see Woldorff et al., 1991]. Second, the process underlying the MMN has a potential role in triggering an involuntary attention switch to sound change [Alho et al., 1997; Näätänen, 1990, 1992; Novak et al., 1992; Schröger, 1996; Schröger and Wolff, 1998]. Finally, the MMN paradigm allows one to separately examine the feature-specific processing of auditory stimuli [Aaltonen et al., 1993; Deacon et al., 1998; Deouell et al., 1998, 2000; Schröger, 1995; for a review, see Ritter et al., 1995]. Therefore, it is a suitable method for comparing the preattentive processing of left- and right-sided stimuli, and for evaluating the processing of different dimensions of the auditory stimulus. In a recent study, Deouell et al. [1998b, 2000] took advantage of these characteristics while examining the MMN elicited by tones in 10 RHD patients with auditory neglect or extinction. In 7 patients, visual neglect was also present at the time of the testing. Ten healthy age-matched volunteers were also tested in this study, but the main comparisons were within-subject ones, for the reasons elaborated above. The principal target of the study was to explore the possibility of a specific deficit in encoding spatial information conveyed by left- (neglected-)side stimuli. Three types of deviant tones were mixed within blocks. Deviance was either in stimulus duration, frequency or spatial location of its sound source (probability for each 10%). All stimuli were presented using free-field loudspeakers located 60° to either side of the subject.

In this study, evidence suggesting different functional impediments in the processing of the different dimensions was found. The most robust finding was that the MMN elicited by deviation in sound source location was considerably reduced when the stimuli were on the left (neglected) side. Pitch deviance also tended to exhibit right-side advantage, but this effect was not as robust as

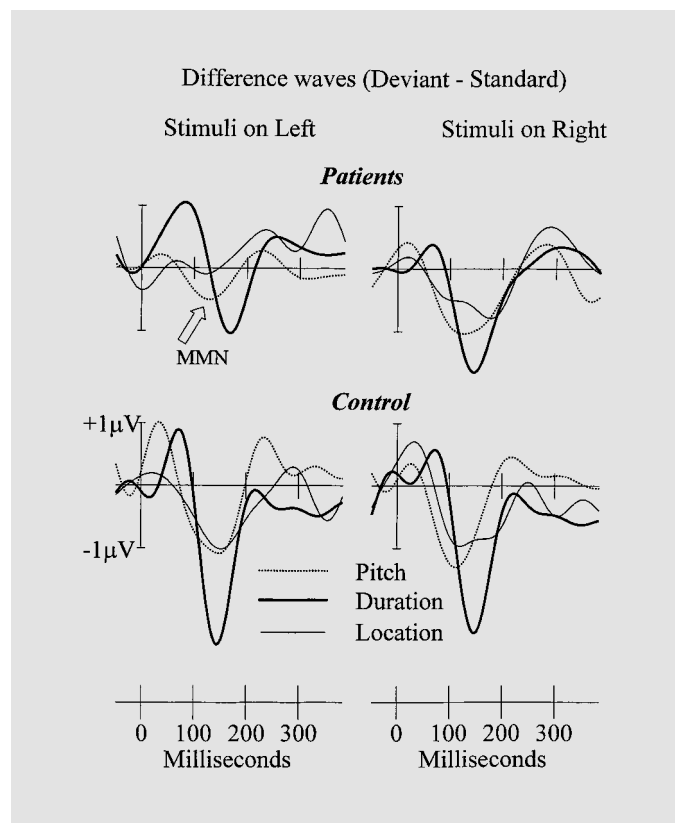


Fig. 1. MMN difference waves at the Fz electrode for deviance in 3 dimensions on either side of 10 RHD patients with neglect and of 10 healthy control subjects. From Deouell et al. [1998b].

for location. In contrast, no right-left difference was found for the MMN elicited by duration deviance (fig. 1). This pattern of results suggests that in audition, like in vision, there is a preattentive and specific deficit in the processing of the spatial attributes of stimuli occurring on the neglected side.

In the only comparable study reported so far, Hämäläinen et al. [1998] obtained MMN to frequency deviance in 7 neglect patients out of 10 RHD patients whose EEG recording had a reasonable signal-to-noise ratio. Surprisingly, however, in 5 of these patients, the MMN amplitude was abnormally large for deviants that occurred on the left (neglected) side and larger than the MMN elicited by deviants occurring on the right side. These unexpected results, which contrast with those of Deouell et al. [2000], may be related to the very early stage after the stroke of the patients of Hämäläinen et al. In line with this possibility, in each of the 3 of these patients who were followed up, the MMN amplitude was reduced to the normal

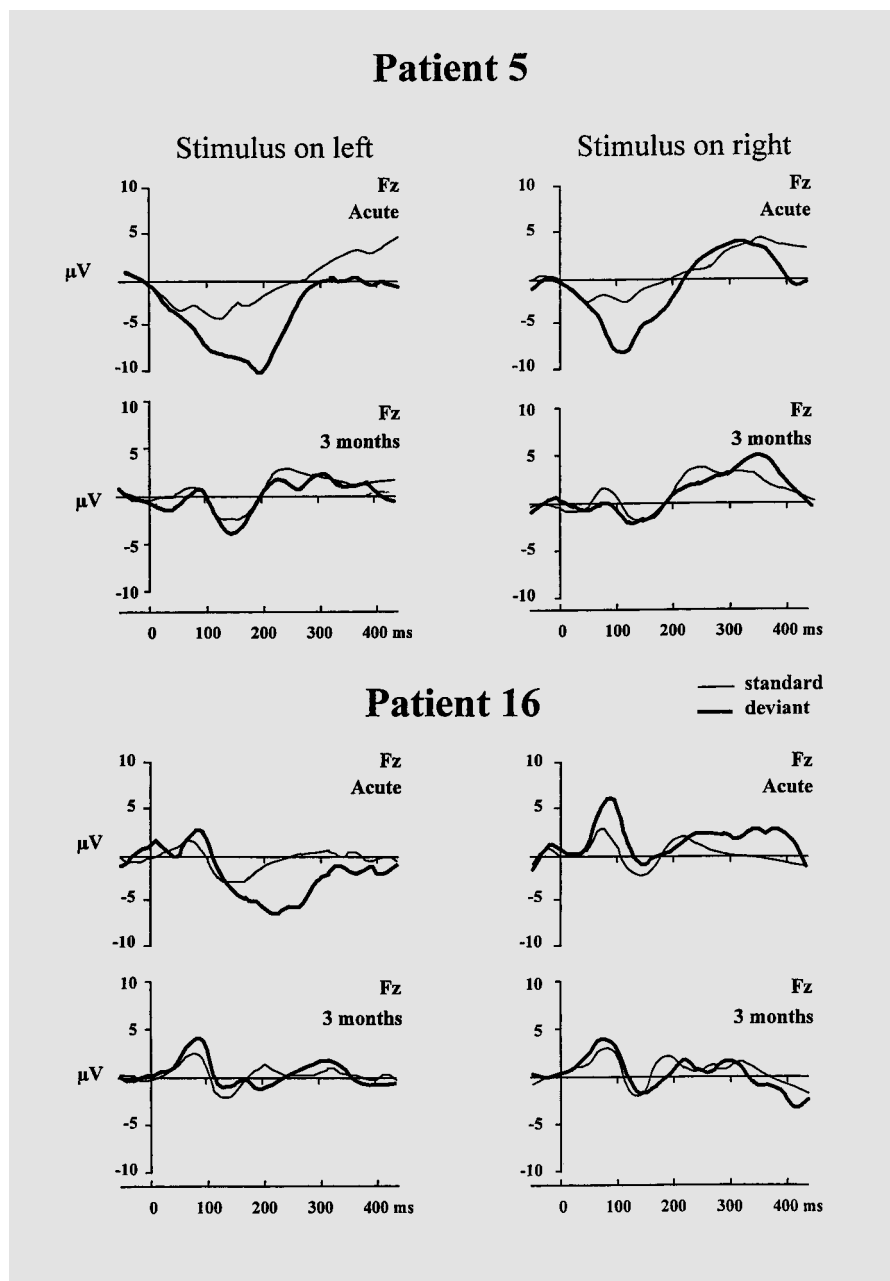


Fig. 2. ERPs at the Fz electrode of 2 RHD neglect patients to standard (thin lines) and deviant (thick lines) tones delivered via loudspeakers positioned on the left or right side of the patient. For patient 5, the measurements in the acute phase were performed 17 days after stroke (severe neglect) with a follow-up after 3 months (no neglect); for patient 16, the measurements were performed 12 days after stroke (severe neglect) and at 3 months (no neglect). From Hämäläinen et al. [1998].

range 3 months later (fig. 2). There are several methodological differences between this latter study and that of Deouell et al. [in press]. However, taken together, both MMN studies of neglect patients suggest that the MMN may be elicited in most neglect patients, that the MMN amplitude in neglect patients may be related to the side of stimulation and to the dimension of deviance in a complex way, and that these differences may be used to explore the mechanisms underlying neglect and recovery from it.

Components Related to Attention and Higher-Level Functions

In the neuropsychological literature, neglect phenomena are frequently related to the disruption of attention mechanisms. Although, as reviewed above, the attention theories of neglect vary, the crux of all of them seems to be a failure to select contralesional objects or events and to shift attention towards them. The literature includes very

few studies that attempted to assess attention, selection or action processes in neglect patients using ERPs.

In their above-mentioned study, Watson et al. [1977] found no deficit in the somatosensory N_1 in monkeys with postoperative neglect but found a delayed N_2 and P_3 in response to the stimulation of the contralesional median nerve, accompanied by an *increase* in the P_3 amplitude. The delay of the P_3 peak was replicated in the study of Lhermitte et al. [1985] on visual neglect, using a somatosensory oddball paradigm, but a tendency for a reduction rather than augmentation of the P_3 amplitude was reported. Interestingly, the auditory P_3 was normal in these patients, which may have reflected the fact that 7 out of the 9 patients showed no sign of auditory neglect. The 'Posner paradigm' [Posner et al., 1984] was used to further explore the effect of neglect on the allocation of attention, as reflected by the P_3 and N_d [Verleger et al., 1996]. In Posner's cueing paradigm, the subject is required, without moving his/her eyes, to press a button in response to a visual target randomly appearing on the left or right of a fixation point. Shortly before the appearance of the target, a visual cue is flashed either where the target is about to appear (the so-called 'valid cue') or on the other side of the fixation point ('invalid cue'). Valid cues shorten the reaction time (RT) while invalid cues prolong it (relative to the RT following a neutral cue appearing at the fixation point). Enhanced attention to the cued location is reflected in the elicitation of the N_d , presumably an electrophysiological manifestation of the enhanced processing of the cued stimuli [Eimer, 1994; Schröger, 1994]. In right parietal patients, an invalid cue on the ipsilesional side dramatically slowed down the RT to contralesional targets, more than the normal effect of such a cue and more than the effect of a contralesional invalid cue on the RT to an ipsilesional target [Posner et al., 1984]. This pattern led the authors to suggest that patients with parietal lesions fail to 'disengage' from stimuli (e.g., the invalid cue) on the ipsilesional side and therefore they cannot adequately attend to the ensuing left-sided targets. The latter suggestion was corroborated by the finding that in right parietal patients, the N_d to left-side targets was significantly smaller following right-sided (invalid) cues than any other cue-target combination [Verleger et al., 1996]. This effect was evident as early as 200 ms from target onset, suggesting that even if the underlying deficit may be in the higher-order attention mechanism, it affects 'the very processing of perceptual input' [Verleger et al., 1996, p. 455].

A more complex pattern of results was obtained by Verleger et al. [1996] regarding the patients' P_3 component in the Posner paradigm. The late positive potential

(or P_{3f} , denoting a P_3 recorded at Fz [Donchin et al., 1978]) was largest for the critical combination of right cue and left target. This pattern resembles the enhanced P_3 in monkeys of Watson et al. [1977]. Post hoc, the P_{3f} enhancement was interpreted as reflecting an attempt of the patient to reorient his/her attention towards the left-side target which presumably was late to be detected, but this interpretation awaits more critical validation. In contrast to the P_{3f} , the P_{3b} (recorded at Pz) was reduced in patients, relative to controls, irrespective of the cue and target location. This general reduction was ascribed to damage to P_3 generators especially at the temporoparietal junction. At this point, it is evident that additional studies of endogenous ERP components in neglect await to be conducted.

The distribution of the MMN across and within hemispheres may also be informative regarding the neuroanatomy of attention mechanisms related to neglect. One of the theories explaining the prevalence of neglect after right- rather than left-hemisphere damage suggests that the right side of space is attended by both hemispheres, while the left side is attended only by the right hemisphere (damage to which leaves the left side of space devoid of adequate attentional resources) [Heilman and Van Der Abell, 1980]. Several findings support such an asymmetry of visual attention mechanisms in the brain [Corbetta et al., 1993; Mangun et al., 1994]. Recently, findings from an MMN study have suggested that this asymmetry holds for attention to auditory space as well [Deouell et al., 1998a]. Scalp current densities revealed that while bilateral temporal generators of the MMN were more strongly activated by contralateral compared with ipsilateral deviants, a frontal generator was asymmetrically activated across the hemispheres. This frontal activity was elicited bilaterally by right-side deviants, but mainly over the right hemisphere by left-side deviants, reminiscent of the distribution of visual attention mechanisms. It is possible that this anterior generator is related to the attention switch provoked by the deviant event [Giard et al., 1990].

Conclusions and Future Perspectives

The processing stage at which the breakdown occurs in patients suffering from neglect is an open question of a fundamental nature. Answering this question might be important not only from a theoretical point of view, but also for planning rational rehabilitation treatments. Data based on performance measures mainly implicated rather

late stages of information processing, involving attention mechanisms, consciousness and action, although one influential account, the representational theory [Bisiach and Berti, 1987], cannot be clearly defined in terms of early or late processing stages. In contrast, the main burden of electrophysiological evidence cited in this review points to the existence of deficits rather early in the stream of processing of stimuli appearing on the contralesional side of neglect patients. Thus, by opening a window into underlying physiological processes, ERP studies contribute to the understanding of this elusive phenomenon. Moreover, a few of the ERP findings might suggest possible links between deficits in the early stimulus registration and higher-order deficits usually ascribed to neglect. For example, the reduced MMN elicited by contralesional stimuli may indicate a failure of an incoming stimulus (deviant) to trigger, in a bottom-up manner, an attention shift towards it. Therefore, the attentional problem observed in the patients' performance might be linked to an early dysfunction of detecting potentially important stimuli. Consequently, the failure of allocating attention to the contralesional stimulus, probably reflected in the reduced N_d , may further hamper the stimulus processing.

The special vulnerability of the processing of spatial location, suggested both by the auditory MMN findings [Deouell et al., 2000] and by the steady-state VEP findings [Spinelli et al., 1996], may be linked to the suggested breakdown of spatial representation [Bisiach and Berti, 1987]. Whether this breakdown is responsible for the failure to register spatial locations or vice versa is not clear, however. Moreover, the difficulty in registering the stimulus location may preclude its conscious perception, as external events (real or imagined) that do not occupy a point in time or space may not be perceivable for our cognitive system.

The ERP studies cited in this review are scanty, yet they clearly show the potential contribution of electrophysiological investigations to the understanding of ne-

glect, as well as other neuropsychological phenomena. For example, ERPs can be used to map the distribution of attention over space in neglect, using, for example the augmentation of the P_1/N_1 components by attention [Mangun et al., 1993], or the N_d [Eimer, 1994; Schröger, 1994], as an index. Another interesting direction is to find ERP correlates of the implicit processing of neglected stimuli, reported in a few studies [Berti and Rizzolatti, 1992; Marshall and Halligan, 1988; McGlinchey-Beroth et al., 1993; Volpe et al., 1979]. For example, the modulation of the N_{400} [Bentin et al., 1985] may be used as an index of semantic processing of neglected words (in audition and in vision), and N_{170} [Bentin et al., 1996] may be used to index the perception of faces presented in the neglected field. ERPs, especially ones like the MMN, which can be elicited without requiring the subjects' or patients' response, may potentially be used for the diagnosis and monitoring of recovery under different treatment programs. In addition, the specifics of electrophysiological activity in neglect patients may reflect the variability of neglect manifestations. As has previously been pointed out [Marshall et al., 1993], 'neglect' is probably only a heading for a variety of yet unspecified cognitive deficits, which are characterized by a lateralized spatial bias. Accordingly, damage to several brain regions may cause neglect. Hopefully, the convergence of information from electrophysiology and other methodologies will augment our understanding of this variability and will help us develop more specific, and thus more effective, rehabilitation strategies.

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