SENSORY AND RESPONSE INTERFERENCE BY IPSILESIONAL STIMULI IN TACTILE EXTINCTION

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Abstract

Extinction is thought to be due to a pathologically limited attentional capacity in which multiple stimuli cannot be processed simultaneously to conscious awareness. Patients with tactile extinction are aware of being touched on a contralesional limb, but seem unaware of similar contralesional touch if touched simultaneously on their ipsilesional limb. The ipsilesional stimulus interferes and competes with the processing of the contralesional stimulus. Most theorists assume that the ipsilesional stimulus affects the sensory processing of the contralesional stimulus, although the precise functional level at which this interference occurs is not clear. We report a series of experiments using signal detection analyses to investigate tactile extinction in one patient (DC). These analyses revealed that ipsilesional stimuli, in addition to interfering with processing of contralateral sensations, also interfere with verbal reports of those sensations. This influence on responses suggests that interference in tactile extinction can occur at a post-perceptual level, further 'downstream' than previously thought.

Key words: attention, intention, neglect, signal detection theory

Introduction

Patients with extinction do not report stimuli located in space contralateral to their damaged hemisphere when the stimuli are presented simultaneously with ipsilesional stimuli (Heilman, Watson and Valenstein, 1993). Extinction to double simultaneous stimulation cannot be attributed solely to a primary sensory deficit since these patients are aware of contralateral stimuli presented individually. Older theories of extinction emphasized the role of abnormal sensory processing of contralesional input (Bender and Furlow, 1945; Birch, Belmont and Karp, 1967). More recent theories emphasize attentional deficits (Di Pellegrino and De Renzi, 1995; Mattingley, Driver, Beschin et al., 1997).

The general idea in attentional theories of extinction is that multiple stimuli compete for attention and awareness (Di Pellegrino, Basso and Frassinetti, 1998; Ito, Tanabe, Ikejiri et al., 1989). Since these patients have a pathologically limited attentional capacity and an attentional bias towards ipsilesional space (Di Pellegrino et al., 1998; Heilman et al., 1993), they are more likely to attend to and become aware of ipsilesional stimuli at the expense of contralesional ones.

Ipsilesional stimuli are thought to interfere or compete with contralesional sensory-perceptual processing. In this paper, we will not consider subtle differences between interference and competition. Both kinds of mechanisms will be referred to as "interference". The specific point at which interference occurs along the sensory-perceptual continuum and its anatomic substrate is unclear. Heilman and coworkers proposed that interference occurs by a gating mechanism at the thalamus (Heilman et al., 1993). The nucleus reticularis (NR) GABAergic efferents are thought to inhibit thalamic somatosensory relay nuclei like the ventralis posterolateralis. Parietal association cortices inhibit the ipsilateral NR and possibly activate the contralateral NR, thus facilitating the transmission of sensory information to the ipsilateral cortex and gating out sensory input to the contralateral cortex. Damage to the parietal cortex would thus diminish inhibition of the NR, and produce greater inhibition of contralateral stimuli. With bilateral stimuli, the undamaged association cortex would increase contralesional NR activity, further inhibiting sensory relays. The net result of brain damage to the right parietal cortex would be inhibition of contralesional stimuli during presentation of bilateral stimuli (extinction).

While thalamic gating may explain extinction in some patients, it does not account for the lack of contralesional tactile awareness in all patients. Recently, Beversdorf, Anderson, Auerbach et al. (1999), using fMRI, reported that when a patient was unaware of being touched contralesionally (in a simultaneously stimulated condition), activation of the somatosensory cortex was similar to activation when the subject was touched only contralesionally. These results suggest that interference in this patient could not have occurred at the thalamic nuclei and must have occurred inter-hemispherically. Kinsbourne (1970) proposed that each cerebral hemisphere directs attention into contralateral space and inhibits the other. Thus, right brain damage, as seen typically in patients with extinction, would leave an unfettered left hemisphere directing attention to right hemispace. The undamaged left hemisphere continues to inhibit the right hemisphere, while the right hemisphere is unable to inhibit the left hemisphere's vector to the right. Attention would then be oriented to the right, and stimuli on the left would not be attended to during bilateral presentation. Observations in callosotomy patients (Reuter-Lorenz, Nozawa, Gazzaniga et al., 1995) and in normal subjects using transcranial magnetic stimulation (Seyal, Ro and Rafal, 1995) support the notion of interhemipsheric inhibition via the corpus callosum.

Wherever the anatomic substrate of interference, to date theories of extinction have focussed on interference of sensory or perceptual processing of contralesional stimuli. The uncertainty has been largely about whether the interference occurs at early or late levels of sensory-perceptual processing. Recently, there has been growing interest in the complex ways in which output variables interact with awareness in neglect and related disorders (Chatterjee, 1998). Limb (Tegnér and Levander, 1991; Watson, Valensein and Heilman, 1978), eye (Bisiach, Tegnér, Làdavas et al., 1995), or even verbal output (Bisiach, Ricci, Lualdi et al., 1998; Smania, Martini, Prior et al., 1996) can affect awareness of contralesional stimuli. However, to our knowledge, the possibility that ipsilesional stimuli in extinction interfere with responses related to contralesional stimuli has not been explored.

Signal detection theory (SDT) offers a framework with which to examine these issues. SDT assumes that background noise factors into perceptual discrimination tasks (Green and Swets, 1966). If a signal is easily discriminated from background noise, decisions are made easily. The parameter d prime (d') in SDT is a measure of how easily a signal is discriminated perceptually from noise. The larger the d', the greater the "perceptual distance" between the signal and noise. When the distribution of the signal and noise overlap, subjects choose a response criterion for reporting the presence of the signal. If their criterion is conservative, they are unlikely to mistake the noise for signal but are likely to mistake some proportion of the signal for the background noise. On the other hand, if they choose a liberal criterion, they are likely to detect the signal frequently but are also likely to have "false alarms", mistaking some proportion of the background noise for the relevant signal. The parameter c in SDT quantifies this response criterion. Higher c values reflect more conservative criteria.

In this report, we introduce the use of SDT to investigate extinction. We address two general questions. First, since SDT assumes that there is always some background noise affecting the system, we investigated whether the nature of this noise (hereafter referred to as the non-salient stimulus) affects contralesional awareness. Second, we wished to learn if ipsilesional stimuli interfere with the response criteria chosen for contralesional stimuli. Interference at a perceptual level affecting the ability to discriminate contralesional stimuli would be reflected in changes in d'. However, interference at a response level affecting the likelihood of verbally reporting contralesional stimuli would be reflected in changes in c.

General Experimental Methods

Patient Description

DC was a 67 year old right-handed woman with a stroke in the posterior division of the right middle cerebral artery. Her speech was fluent and mildly dysarthric. Repetition and comprehension were normal. She initially demonstrated neglect on line bisection and cancellation tasks and contralesional extinction to simultaneous visual, auditory, and tactile stimulation. She did not have a visual field defect. She had intact pinprick, proprioception, vibration, and minimal left distal weakness. Her magnetic resonance imaging scan showed her stroke involved cortical and subcortical structures of the posterior insula, superior temporal gyrus (Area 22), the angular gyrus (Area 39), and supramarginal gyrus (Area 40). Areas 7 and 19 and primary motor cortex were mostly spared. Her neglect, as indicated by her performance on the Behavioural Inattention Test (Wilson, Cockburn and Halligan, 1987), mostly resolved (line crossing 36/36, letter cancellation 39/40, star cancellation 50/54, figure and shape copy 3/4, line bisection 9/9, and representational drawing 3/3). Visual, auditory, and tactile extinction remained. She also had extinction of weight perception, a phenomenon reported in detail elsewhere (Chatterjee and Thompson, 1998).

Stimuli and Procedures

The stimuli for all the experiments consisted of flat textured surfaces (3 cm $\times$ 15 cm) that were covered with two different grades of sandpaper: very rough (50 grit D weight paper) and very smooth (1500 grit B weight paper). DC kept her hands resting on a table a comfortable distance apart (33 cm). Two cm of the stimuli were applied to the index fingers past the distal interphalangeal joint either on the palmer surface when her hands were supinated or on the dorsal surface when her hands were pronated. The stimuli were presented to both hands at the same time by attaching both stimuli probes to a stick. Moving this stick allowed both stimuli to be moved simultaneously at the same rate in a proximal to distal direction. The trials were randomized across conditions within each experiment.

Statistical Analysis

Chi square analyses were used to test for differences in proportions of stimuli detection across relevant conditions. Signal detection analyses were also used in experiments 1, 2, 4, and 5. This analysis was conducted as follows. In each case, the rough tactile texture was considered the signal to be reported by the patient. We were interested in her ability to discriminate this signal from the background noise (which varied across experiments) on her left hand. For each experimental condition, two d' (discriminability) and c (response criterion) parameters were calculated and compared (MacMillan and Creelman, 1991). d' and c were calculated for her ability to detect the signal (rough touch) on the left when the signal was also presented to the right hand. Similarly, d' and c was calculated for her ability to detect the signal (rough touch) on the left when only noise was presented to the right hand. Thus, we examined the patient's ability to discriminate signal from noise on her contralateral hand and how this discriminability was affected by stimuli (signal or noise) on her ipsilateral hand. We used a correction factor in calculating these parameters as suggested when extreme values are found in some conditions (Snodgrass and Corwin, 1988).

Experiment 1. Tactile Extinction

We first wanted to establish that DC had tactile extinction.

Procedure

DC sat at a table with her hands in front of her 33 cm apart and pronated so that her palms and fingers rested comfortably touching the table. She was touched with the rough probe on the left or right hand, on both hands simultaneously, or was not touched on either hand. She was asked to report where she was touched with the probe.

Results

DC was always correct (100/100) when she was not touched with the probe. She was also accurate (99/100) when only touched on the right. When touched

TABLE I

DC's Performance in Experiment 1: bilateral rough stimulation (**), passive smooth stimulation (stimulation from the table surface) on the left and rough on the right (_), rough on the left and passive smooth stimulation on the right (*_), and passive smooth stimulation on both hands (_ _)*

Stimuli \ Response	**	_*	*_	_ _	Total
**	36	64	0	0	100
_*	1	99	0	0	100
*_	0	0	87	13	100
_ _	0	0	0	100	100

only on the left, she was quite accurate (87/100). However, with simultaneous bilateral stimulation, she was accurate only 36/100 times (see Table I). DC was more likely to detect the rough stimulation on the left when presented unilaterally than when presented bilaterally and therefore demonstrated left sided extinction: χ^2 (1) = 52.79, $p < 0.001$.

For her ability to detect the rough texture on the left when touched on the right, she had the following parameters: d' = 1.835 and c = 1.273. For her ability to detect the rough texture on the left when she was not touched on the right, she had the following SDT parameters: d' = 3.684 and c = 0.734. The d' values were significantly different (cimulative z score = 2.988, $p < 0.01$), and the c values showed a trend toward significance (cumulative z score = 1.74, $p = 0.08$).

Comments

DC exhibited tactile extinction. She was less likely to report the rough tactile touch on the left when touched simultaneously on the right than when not touched on the right. SDT analyses revealed that she was better able to discriminate the rough touch from non-touch on the left when she was not touched on the right. Being touched on the right interfered with her sensory-perceptual processing on the left. When she could more easily discriminate sensations on the left, she had a trend toward using a more liberal response criterion (a lower c value).

Experiment 2. Tactile Extinction (b)

In Experiment 1, DC did not detect touch on the left unilaterally 13% of the time. We wondered if simply having her palms and fingers touch the table surface, albeit passively, increased the background noise and interfered with her processing of left-sided stimuli. To test this hypothesis, the experiment was repeated but with DC placing her hands palms up so that the dorsum of her hand rested comfortably on the table. Her fingers curled upwards so that her fingers past the proximal interphalangeal joint were not in contact with the table. The same protocol was followed as before with the experimenter applying rough stimulation on the left, on the right, on neither hand, or on both hands.

Results

DC was always correct when she was not touched (100/100), when she was touched only on the right (100/100), and when she was touched only on the left (100/100). By contrast, when touched simultaneously, she only detected touch on the left 1/100 times (see Table II). DC was significantly better at detecting rough touch on the left when touched unilaterally than when touched bilaterally: χ^2 (1) = 196.04, $p < 0.001$. For her ability to detect the rough texture on the left, when she was not touched on the right, she had the following SDT parameters: d' = 5.152 and c = 0.

For her ability to detect the rough touch on the left, when she was also touched on the right, she had the following SDT parameters: d' = 0.386 and c =

TABLE II

DC's Performance in Experiment 2: bilateral rough stimulation (**), no stimulation on the left and rough on the right (_), rough on the left and no stimulation on the right (*_), and no stimulation on both hands (_ _)*

Stimuli \ Response	**	_*	*_	_ _	Total
**	1	99	0	0	100
_*	0	100	0	0	100
*_	0	0	100	0	100
_ _	0	0	0	100	100

2.383. The *d'* values were significantly different (cumulative z score = 5.27, $p < 0.0001$) as were the *c* values (cumulative z score = 5.26, $p < 0.0001$).

Comments

Having DC's hands facing upwards changed her level of extinction. This observation was consistent with our hypothesis that the passive tactile stimulation from the table in the previous condition had some interference effects. In the absence of this passive stimulation, her extinction was more extreme. She made no errors with unilateral rough stimulation on the left, unlike the large numbers of errors she made in the previous experiments. Also, her performance with bilateral stimulation fell (from 36/100 correct in Experiment 1 to 1/100 correct in this experiment). Her ability to discriminate the signal from the noise also improved (as reflected in an increase in the *d'*) when she was not touched on the right. Again, her increased ability to perceptually discriminate the signal from noise on the left was associated with a more liberal criterion in reporting when she was touched contralesionally.

Experiment 3. Sensory Discrimination

The previous two experiments suggested that non-salient stimuli (the background stimuli from the fingers touching the table surface) can affect the responses to salient stimuli. To further explore effects of non-salient stimulation on the detection of contralateral salient stimulation, we planned experiments in which DC would have to detect the same rough probe as in the previous experiments, but in which the non-salient stimulus would be a smooth texture probe. The results of such an experiment would only be relevant if DC could easily discriminate rough from smooth stimulation on either side. Therefore, we first assessed DC's ability to discriminate rough from smooth touch. DC was touched with a rough or smooth probe on the dorsal surface of either her left or right index finger. Her hands rested comfortably in a pronated position with the palms and fingers of her hands resting comfortably on the table. She was not touched on both hands simultaneously in this experiment. There were 200 trials with 50 in each condition.

Results

DC was correct on 197/200 trials (98.5%). The three mistakes were on the left (stating no stimulation when she was touched on the left with the rough probe).

Comments

These results established that DC could distinguish between the rough and smooth probes accurately. She did not have a sensory discrimination deficit that would confound interpretation of subsequent results.

Experiment 4. Tactile Textural Discrimination

From Experiments 1 and 2 we established that even minimal stimuli such as the passive somatosensory sensation from fingers touching the table interfered with the processing of contralateral tactile sensations. To further explore the effects of non-salient stimuli, two probes were used bilaterally in every trial. The first probe was textured roughly and the second was textured smoothly. DC sat with her hands pronated such that her palms and fingers touched the table as in the first experiment. The stimuli were applied to the dorsal aspect of her index fingers. DC was asked to report where she felt the rough stimulation as in the first two experiments. There were 100 trials with rough stimulation on the left and smooth on the right, 100 with rough on the right and smooth on the left, 100 with no rough, both fingers had smooth stimulation, and 100 with bilateral rough stimulation.

Results

DC responded accurately (100/100) when she was not touched with the rough probe on either finger. When touched with the rough probe on the right, she was accurate 87/100 times. Her thirteen errors were thinking that she was also touched on the left with the rough probe. When touched with the rough probe on the left, she was accurate only 22/100 times. She always erred in thinking that she was not touched with a rough probe on the left. Surprisingly, when touched with a rough probe on both fingers, she was accurate 64/100 (see Table III). She was significantly worse at detecting the contralateral rough stimulation in the unilateral than bilateral stimulation condition: χ^2 (1) = 34.29, $p < 0.001$.

Her ability to discriminate the rough probe from the smooth on the left when she was touched with the rough on the right had the following SDT parameters: $d' = 1.463$ and $c = 0.377$. Her ability to discriminate the rough probe from the smooth probe on the left when she was touched with the smooth on the right had the following parameters: $d' = 1.814$ and $c = 1.669$. The c values differed significantly (cumulative z score = 4.75, $p < 0.0001$), but the d' values did not (cumulative z score = 0.644, $p > 0.05$).

Comments

This experiment confirmed and extended our finding that ipsilesional non-salient stimuli interfere with processing of contralesional salient stimuli.

TABLE III

DC's Performance in Experiment 4: bilateral rough stimulation (**), active smooth stimulation (smooth probe) on the left and rough on the right (_), rough on the left and active smooth stimulation on the right (*_), and active smooth stimulation on both hands (_ _)*

Stimuli \ Response	**	_*	*_	_ _	Total
**	64	36	0	0	100
_*	13	87	0	0	100
*_	0	0	22	78	100
_ _	0	0	0	100	100

Paradoxically, DC was more accurate with bilateral stimulation (bilateral rough) than unilateral stimulation (rough on the left), a result directly opposite to that expected with extinction patients. Signal detection analysis provided insight into the reasons for this paradoxical finding and the functional locus of interference in this paradigm. DC's ability to discriminate rough from smooth on the left was not affected by whether she was touched with the rough or smooth probe on the right. Instead, the criterion at which she reported the rough stimulus on the left changed. When she was touched with the smooth stimulus on the right, she was more conservative in reporting the rough on the left than when she was touched with the rough probe on the right. Consequently, she was more likely to report the rough on the left when touched with the rough probe bilaterally than when touched with the rough probe only on the left.

Experiment 5. Replication

Since the results from Experiment 1 were paradoxical, we wished to replicate the results. If our results were stable, then again DC would be better able to detect the contralateral rough probe when presented with rough probes bilaterally than when presented with a rough probe on the left and a smooth probe on the right. Such a paradoxical finding would again be accounted for by a shift in her response criterion. We tested DC again using the identical procedure as in the previous experiment.

Results

DC was correct on 100/100 trials when not touched on either hand with the rough probe. She was accurate 99/100 times when only touched on the right with the rough probe. She was accurate only 8/100 times when touched with the rough probe on the left and the smooth probe on the right. Finally, she was accurate 23/100 times when touched with the rough probe bilaterally (see Table IV). Once again, she was more likely to report the contralesional rough touch when she was touched with rough stimuli bilaterally than when only touched contralesionally, χ^2 (1) = 7.48, $p < 0.01$.

SDT analyses revealed the following: d' = 1.461 and c = 1.460 when comparing bilateral rough versus smooth on the left and rough on the right, and d' = 1.197 and c = 1.978 when comparing rough on the left and smooth on the

TABLE IV

DC's Performance in Experiment 4: bilateral rough stimulation (**), active smooth stimulation (smooth probe) on the left and rough on the right (_), rough on the left and active smooth stimulation on the right (*_), and active smooth stimulation on both hands (_ _)*

Stimuli \ Response	**	_*	*_	_ _	Total
**	23	77	0	0	100
_*	1	99	0	0	100
*_	0	0	8	92	100
_ _	0	0	0	100	100

right versus smooth on the left and smooth on the right. The two d' values were not significantly different (cumulative z score = 0.42, $p > 0.05$) while the c values were (cumulative z score = 1.655, $p = 0.05$, one-tailed).

Comments

Despite a decrement in DC's overall performance, the paradoxical pattern of performance observed in Experiment 4 remained: DC was less likely to report the rough texture on the left when presented unilaterally than when presented bilaterally. Further, the ratio between the number of correct trials on the bilateral rough condition to the number of correct trials on the rough on the left condition was exactly 2.9 in both experiments: 64/22 = 2.9 (Experiment 4) and 23/8 = 2.9 (Experiment 5). The results confirmed results of the previous experiment to suggest that smooth stimulation on the right caused DC to be more conservative in reporting rough on the left. Importantly, her ability to perceptually discriminate the signal from noise contralesionally was not affected by whether the ipsilesional stimulus was itself the signal (rough texture) or noise (smooth texture).

DISCUSSION

Investigations of extinction have focussed traditionally on how salient ipsilesional stimuli interfere with the processing of contralesional stimuli. We raise two questions that have not received much scrutiny. First, what effect, if any, do non-salient ipsilesional stimuli have on processing of contralesional salient stimuli? Second, do ipsilesional stimuli affect the subjects' responses in addition to, or independent of, the effects on sensory processing? To address these questions, we used signal detection theory (SDT) to analyze our findings.

Rough tactile texture was the salient stimulus in all experiments. When the non-salient stimulus was no stimulus at all, DC performed as expected. She almost always detected the contralesional stimuli when presented in isolation and almost never when presented simultaneously with ipsilesional salient stimuli. Her ability to discriminate the rough from no texture on the contralesional side diminished markedly when she was touched ipsilesionally with the rough texture. These observations are consonant with traditional views of extinction.

Salient ipsilesional stimuli interfere with the processing of contralesional stimuli, and her ability to perceptually discriminate the signal from noise on the left was impaired.

When DC's palms faced down so that her fingers were touching the table, some sensory information was presumably being transmitted even when not touched by the examiner. Now the non-salient stimulus, or the background "noise", changed from an absence of touch on her fingers to the passive touch of the table. In this condition, DC's pattern of responses changed somewhat but continued to be typical of patients with extinction. She was better able to detect contralesional salient stimuli when not touched ipsilesionally than when she was also touched with the rough texture ipsilesionally. However, these data suggest that even the passive somatosensory input from her fingers resting on the table influenced her contralesional awareness. SDT analyses of these data were consonant with traditional accounts of extinction. Ipsilesional stimuli affected sensorial processing of contralesional stimuli, as reflected in the diminished d' for her ability to detect the signal from noise on the left. These experiments also showed that the better ability to discriminate left-sided signal from noise was associated with a more liberal response criterion (a lower c value).

When DC was actively touched on both sides with a stimulus probe, she performed in a counterintuitive, paradoxical way: she made more errors when touched with the salient stimulus unilaterally that when touched with the salient stimuli bilaterally. These observations are also at odds with a recent report by Aglioti, Smania, Moro et al. (1998) that patients with tactile extinction are more aware of contralesional stimuli when the double simultaneous stimuli are different then when they are the same. SDT analysis provided insight into DC's paradoxical behavior. Ipsilesional rough and smooth probes interfered with sensory processing of left-sided touch similarly, as reflected in the similar d's. However, the nature of the ipsilesional touch affected her response criterion c. With the smooth probe on the right, DC was more conservative in her judgments of whether she was touched with the salient probe on the left. As a consequence, she was less likely to report being touched on the left when touched with the rough texture unilaterally than when touched with the rough texture bilaterally. The ipsilesional stimuli (rough or smooth textures) had different interference effects with her response criteria and not with her perceptual processing of the contralesional stimuli.

The general implications of these data are that ipsilesional stimuli may interfere with the processing of contralesional stimuli at many levels in patients with tactile extinction. The data imply that at least for some extinction patients, interference occurs at a response level, in this case at the level of verbal output. Ipsilesional non-salient stimuli can compete for resources devoted to the subjects' responses, independent of its effects on resources devoted to contralesional sensory processing. Thus, when DC was touched with the smooth texture on the right, she was biased to reporting that the left texture was also smooth. When she was touched with the rough texture on the right, she was biased to reporting that the left texture was also rough. These biases changed even though her ability to perceptually discriminate the rough from smooth texture on the left was not affected differently by whether she was touched with the rough or smooth texture on the right.

Anatomically, interference at a thalamic level cannot explain all extinction phenomena. Such interference would preferentially affect sensory processing. Even at a cortical level, cross-callosal interference may occur more anteriorly, affecting responses or verbal output, than usually postulated with theories of interference of higher order sensorial processing.

In summary, inter-hemispheric interference may occur at many levels in patients with extinction. Our data show that ipsilesional stimuli interfere with the processing of contralesional stimuli as most theorists assume. However, ipsilesional stimuli can also affect the patient's responses, distinct from its effects on the sensory processing of contralesional stimuli.

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