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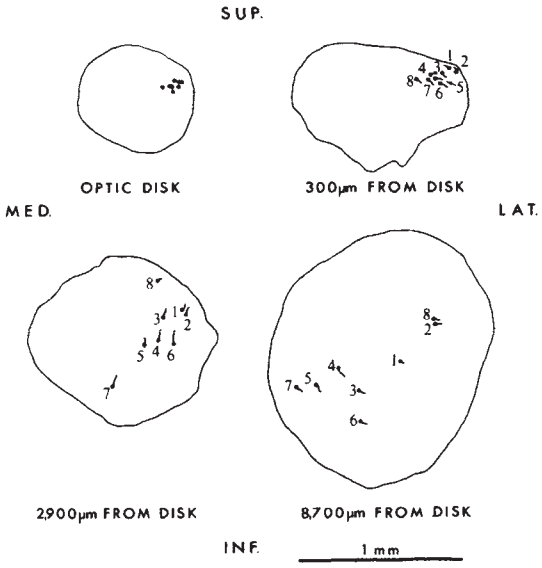

Fig. 3 Position of the eight HRP-labelled fibres at four stages in the optic pathway; their relative thickness has been exaggerated to make them visible. The optic chiasm begins 12,000 μm from the optic disk.

It is apparent that beyond the first few millimetres no strict retinotopy is present in the cat optic nerve although some crude topography may be preserved; axons of adjacent retinal ganglion cells do not generally travel side by side in the nerve. It might be argued that fibres from these adjacent cells are merely being reassorted in the nerve according to cell type, but we think this is unlikely, especially as in this particular experiment all eight labelled cells happened to be of the same cell type. The fibre pattern in the optic nerve is clearly not based on a system of simple retinal coordinates, although we do not conclude that the fibres are arranged haphazardly. They may be organised in some complicated fashion which is not yet clear. It is interesting, in this regard, that once the fibres diverge quickly in the initial portion of the nerve, they tend to maintain a more constant disposition, hinting that the scatter is somehow controlled.

In the light of our findings, it seems unlikely that the physical arrangement of fibres in the optic nerve and tract could alone account for the retinotopy present in the lateral geniculate body. Conceivably, however, retinotopic order is present as fibres first reach their targets, and their relative positions then shift during subsequent development. The critical information is lacking, namely, the temporal and spatial order of the nerve fibres on arrival at the lateral geniculate body in the embryo. It would further be interesting to know how the fibres of the optic nerve are organised and parcelled into their connective tissue fascicles. Finally, it is perplexing that fibres in the mammalian optic nerve should be scattered, in view of the evidence favouring retinotopic order in the optic nerves of fish and amphibia. One wonders if the non-retinotopic arrangement of fibres in the mammalian optic nerve may be of functional significance.

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Information processing of visual stimuli in an 'extinguished' field

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Lesions of the right parieto-occipital cortex in man produce a variety of behavioural disturbances which interfere with the detection of, and orientation to external stimuli[1]. One striking example is extinction to double simultaneous stimulation (DSS), in which presentation of a single stimulus in any area of the visual field results in its accurate description, but lateralised simultaneous presentation of two stimuli, one in each field, results in the verbal description of only the stimulus in the right visual field (RVF)[2]. While extinction to DSS can also be demonstrated in other (non-visual) sensory modalites[3], and is occasionally seen following left-hemisphere lesions[4] our concern here is with visual extinction to DSS following right parieto-occipital lesions whose precise nature is poorly understood although variety of theories have been proposed to account for it[5–7]. One of the critical, yet unexplored questions about extinction concerns the fate of the extinguished stimulus. The following observations demonstrate that although the extinguished stimulus often goes completely unnoticed by the patient, the patients are able to utilise the extinguished stimulus in an interfield comparison task. Accurate same/different judgments between the visual fields could be made in situations in which the patients did not know the identity of, and at times even denied the presence of, the left field stimulus.

The subjects were four right-handed female patients ranging in age from 56 to 70 years who were selected for study by routine neurologic examination. Although all patients had full visual field capacity when tested by a standard perimetry mapping with a single 1-cm, white object, each patient extinguished LVF stimuli on DSS, and left-sided touch stimuli under double simultaneous tactile stimulation. Each patient was alert and oriented and without language disturbance. Patients were tested on the third hospital day, before therapeutic manoeuvres (two cases). Patient no. 3 received steroids over the 36 hours before testing. Patient no. 4 had a persistent defect that remained unchanged during the weeks following surgery. Angiographic analysis and/or computerised tomography[8] revealed that all four patients had tumours in the right parietal lobe. (Cerebral angiography is a standard neuroradiologic procedure in which contrast material is injected into each discrete arterial system of the brain. This procedure aids the neurologist in diagnosis and the neurosurgeon in treatment. Computerised tomography is a brain imaging technique.) Neuropathologic analysis of tissue biopsies confirmed the clinical diagnosis of tumour in all patients.

Table 1 Single visual field naming

Patient no.	Visual field: Left	Visual field: Right
1	1.00 (15)	1.00 (12)
2	0.94 (16)	0.89 (9)
3	0.86 (14)	1.00 (15)
4	0.91 (33)	0.88 (33)

The proportion of trials that were correctly named by each patient in each visual field is shown. Numbers in parentheses represent total number of trials presented to each visual field. Performance differences between the visual fields were not significant ($t(3) = 1.12$, $P < 0.4$). Variation in total number of trials presented to each patient is described in the text.

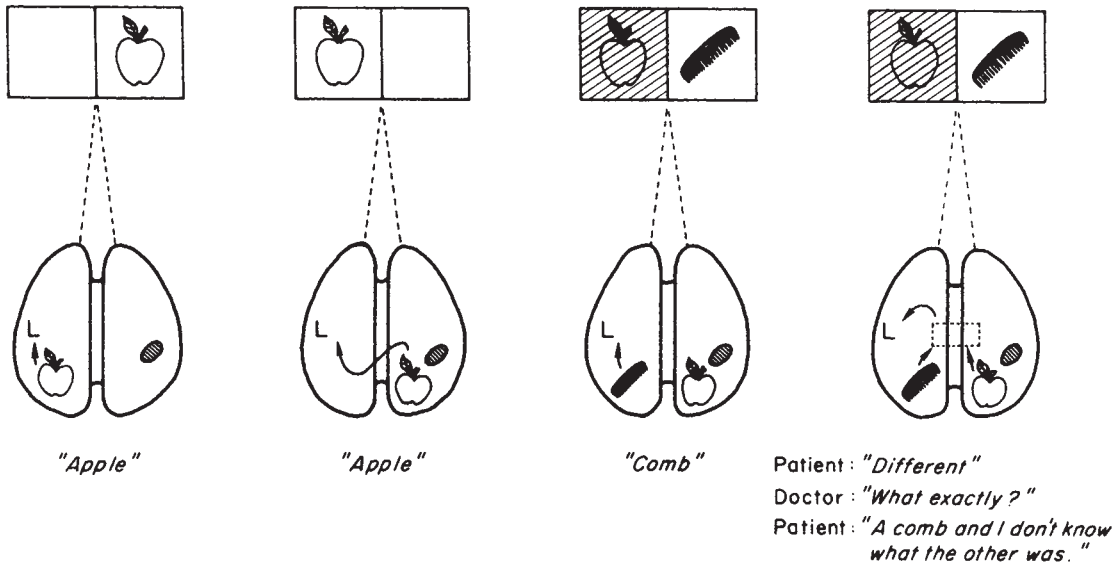

Fig. 1 This composite picture represents each of the experimental paradigms. The two pictures on the left describe the typical left and right single visual field naming trials. The two pictures on the right describe a typical response during the simultaneous bilateral visual field trials, in the 'same/different' paradigm.

In the test conditions, all tasks involved the lateralised presentation of visual stimuli in a manner previously reported[9]. All experiments were carried out in a room in which it was not possible to control the level of background lighting completely. The room was generally as dim as possible, but allowed the experimenter to record the results. The subject was seated 1 m from an opaque screen and instructed to fixate on a dot in the centre of the screen. By means of a standard slide projector fitted with an electronic shutter, stimuli were presented 3° to the right and/or left of fixation for 150 ms. The stimuli were positive photographic slides of three- or four-letter words or simple line-drawn pictures that were rear-projected onto a screen which the subject faced. A representative series of word stimuli subtended 2° of horizontal visual angle and 5° of vertical visual angle. Because of the line-drawn nature of the picture and word stimuli, measurements of luminosity varied less than 0.5% on all bilateral simultaneously projected trials irrespective of similarity or difference. Due to restraints regarding the medical care of these patients, testing sessions were 30 min in duration, and the variability in the number of trials among the patients reflects this primary factor.

Each patient was seated in front of the screen and after fixation on the centre point, the words or pictures were presented randomly to either the left or right visual field. All patients named the stimuli with high accuracy when singly presented to either visual field (see Table 1).

The next series of tachistoscopic test trials was preceded by a group of illustrative trials where words or pictures were, simultaneously, bilaterally projected to the right and left of the fixation point. The patients were shown several such examples under prolonged exposure conditions (5–10 s) so they could identify both stimuli. They were then told that on each subsequent trial there would be two stimuli, one on each side on fixation, and that their task was simply to judge whether the two stimuli were the 'same' or 'different'. In addition to representing quite different items on the 'different' trials, the simultaneously flashed picture stimuli bore no semantic relationships to one another (for example, bicycle and comb). The words flashed on the 'different' trials were three or four letters in length, semantically unrelated, and spelled differently, with, at most, only a single similar letter (HOT and WON for example). On these bilateral DSS trials all patients performed both the same and different comparison with high accuracy (see Table 2).

After verbally reporting in the same/different test situation, the patients were then asked to respond again and name the stimuli. On the trials in which the stimuli were identical, naming of the item in the LVF was an easily accomplished deduction from naming the RVF stimulus. On the same response trials that were correct, there were no LVF naming errors. On the trials in which the stimuli were different, the LVF stimulus could not be deduced from the RVF stimulus. Patients nos. 1 and 2 could not name the left visual field stimuli, although they had performed accurately on the same/different judgments. In fact, during bilateral simultaneous projection, these two patients could not name any of the left visual field stimuli (Table 3), and asserted further that the task was 'silly', since there was no stimulus in the LVF with which to compare the RVF stimulus. Patients nos. 3 and 4 performed as accurately as the previous two on the same/different judgments, but were able to name some of the left visual field stimuli on the critical different trials (Table 3). Although these latter two patients were more often aware of the presence and nature of the LVF stimuli than the first two patients, all patients' accuracy on 'same/different' judgments was statistically greater than their accuracy at naming the LVF stimulus ($t(3) = 3.53$, $P < 0.05$).

These experimental observations focused on the residual cognitive abilities of four patients with right parietal lesions. Manipulation of exposure duration below 250 ms, the use of single digits, and the use of nonsense pictures and nonsense syllables did not alter the pattern of results. The patients uniformly made accurate judgments when comparing information simultaneously presented to both visual fields, in spite of their inability to verbally characterise with a similar level of accuracy the left visual field information. These data bear relation to the results of studies showing that under certain test conditions normal subjects can be influenced by information they frequently are unable to identify[10–13].

Our patients responded to information presented to the extinction field in two ways. In some instances, especially with patients 3 and 4, they felt that something had appeared in the LVF, but they were unable to characterise it. In other instances, as with patients 1 and 2, they were completely unaware that anything had been presented in the LVF. Yet, it is clear that some features of the extinguished stimuli were attended to and

Table 2 Same/different judgment with double simultaneous visual field presentation

Patient no.	Same/different judgments	'Different' trials correct	'Same' trials correct
1	1.00 (17)	1.00 (7)	1.00 (10)
2	0.88 (26)	0.88 (16)	0.90 (10)
3	0.95 (39)	0.96 (25)	0.93 (14)
4	0.90 (68)	0.89 (35)	0.91 (33)

Proportion of same/different judgments that were correct is shown. Correct proportions for trials judged as 'same' and 'different' are separately indicated. Numbers in parentheses represent total number of trials. Each patient compared the bilaterally projected stimuli with high accuracy, and errors occurred with equal frequency on the same and different trials.

Table 3 LVF naming after same/different judgments on double simultaneous visual field presentation trials

Patient no.	Same/different judgments	LVF naming in 'different' trials
1	1.00 (17)	0.00 (7)
2	0.88 (26)	0.00 (16)
3	0.95 (39)	0.48 (25)
4	0.90 (68)	0.23 (35)

The proportion of correct same/different judgments and proportion of different trials in which LVF stimulus was correctly named are shown. Numbers in parentheses represent total number of trials. The accuracy of the same/different judgments was significantly greater than the accuracy of LVF naming ($t(3) = 3.53$, $P < 0.05$).

perceived, for the 'same/different' judgments were accurately made on the basis of these stimuli. It thus becomes difficult to assert that the so-called extinguished stimulus is extinguished at all. Rather, this disturbance seems to involve a selective breakdown in a mechanism through which information which is attended to and perceived reaches some level of neuronal processing which allows for verbal description, if not conscious awareness (see Fig. 1).

Parietal lobe extinction thus offers the possibility of observing, under appropriate test conditions, a breakdown in the flow of information between conscious and non-conscious mental systems. The stimulus comparison task in our study appears to have been carried out at a post-perceptual, pre-verbal level, with only the resultant comparison entering consciousness. Extension of this paradigm may provide a mechanism for studying non-conscious information processing in man.

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A central role for denervated tissues in causing nerve sprouting

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One of the oldest known forms of neuronal plasticity is the ability of peripheral nerves to grow and form functional connections after damage to neighbouring axons[1]. Yet the source of the signal which elicits this 'sprouting' remains unknown. In mammalian muscles, paralysis—which gives rise to many of the changes which occur in denervated muscles[2,3]—causes motor nerve terminals to sprout[4–6]. Could the inactive muscle fibres (rather than nerve degeneration products, another likely source[7–9]) be responsible for some of the sprouting found in partial denervation? We confirm in this paper that direct stimulation of a partially denervated muscle inhibits sprouting[10,11] and show that stimulation does so by activating the denervated fibres. Consequently after partial denervation the same signal as that which causes terminal sprouting in a paralysed muscle is able to spread from the denervated muscle fibres to the nerves on the innervated fibres and initate terminal sprouting.

The soleus muscles in young adult mice anaesthetised with chloral hydrate were partially denervated by cutting one or both L_4 rami, or were completely denervated by crushing the soleus nerve close to the muscle. Teflon-coated multi-stranded stainless steel wires were implanted on both sides of the soleus muscle for muscle stimulation, or around the sciatic nerve in the thigh for nerve stimulation, drawn under the skin along the tail and brought to the surface. Only one leg per animal was stimulated.

So that the mouse would not feel pain, it was either spinalised at a low thoracic level or the dorsal roots supplying the stimulated leg were cut. The stimulation pattern was 100-μs square wave pulses of alternating polarity, at 100 Hz for 0.5 s/30 s, or 150 Hz for 0.5 s/10 s (there being no difference in the results obtained). For nerve stimulation the current was set at three times the threshold for ankle extension, delivering 5–20 mA. For direct stimulation currents of 30–40 mA were used. Stimulation was started immediately after the operation. This pattern of stimulation can maintain the acetylcholine sensitivity of a denervated muscle at normal values[3].

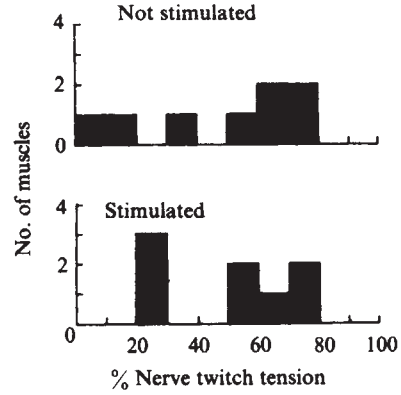

Fig. 1 Histograms of the proportion of the direct twitch tension produced by stimulating the muscle nerve. In eight mice the soleus nerve was crushed close to the muscle on both sides and wires implanted around the left or right muscle. Six to eleven days later both soleus muscles were isolated with their nerves, and the nerve and directly evoked maximal isometric tensions measured. (The crush caused complete absence of nerve-evoked tension in two mice at 2 days.) Two mice were examined at 6 days, five at 7 days and one at 11 days after the nerves were crushed. Clearly, directly stimulating the muscle does not inhibit reinnervation by the crushed nerves. Mean % of direct twitch tension produced by stimulating the nerve = 48% on both sides. This confirms other work[15,16], and demonstrates that direct electrical stimulation of a muscle does not inhibit all nerve growth by some mechanism such as damaging the growing tips of axons.

Dorsal root section central to the dorsal root ganglion does not affect the amounts of sprouting in otherwise normally innervated muscles[9], but spinalisation seems to cause a small increase, presumably due to the muscle inactivity caused by this procedure (unpublished observations).

The soleus muscle and nerve were isolated 6–11 days later and the isometric tensions produced by nerve and muscle stimulation compared. The muscles were then stained in zinc iodide and osmium tetroxide[5,12], a procedure which clearly demonstrates both the myelinated and unmyelinated portions of the nerves. Two types of motor axon sprouting have been described, nodal (unmyelinated outgrowths from nodes of Ranvier), and terminal (similar outgrowths from the unmyelinated nerve terminal itself)[7]. The soleus muscle rarely produces much nodal sprouting[13]. Attempts have been made to subdivide terminal sprouting into two forms pre-terminal and ultra-terminal[14] but we have classified the two together. Histological examination of the muscles for terminal sprouting was conducted 'blind', at least 50 endplates per muscle being examined. An endplate was classified as sprouting if the normal smooth contour was broken up by fine outgrowths[5].

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