

Facilitatory effect of neglect rehabilitation on the recovery of left hemiplegic stroke patients: a cross-over study

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Introduction

Recent evidence [32] indicates that primary neurological impairment may be aggravated by the contralateral part of attentional disorders. This is characterized by space, such as unilateral neglect. This is characterized by the patient's failure to orientate, respond to or report stimuli appearing on the side contralateral to the cerebral lesion [28]. (While often associated with primary sensory deficits, neglect is a central independent disorder as demonstrated by neglect patients with no field defects and

the functional recovery of the two neglect groups was time-locked to the period of the specific training for neglect. At the time of admission, the two neglect groups performed at the same level; after 2 months of rehabilitation, the group with neglect training showed higher functional recovery than the group with only general cognitive intervention. When the latter group received neglect training, there was no longer any difference between the two neglect groups. This pattern was present for both of the functional scales used but not for the neurological scale. Motor and functional recovery of stroke patients with neglect seems to be significantly improved by the simultaneous presence of a treatment specifically focused on neglect.

Key words Hemiplegic · Rehabilitation · Functional recovery · Neglect

by hemianopic patients without neglect [28].) Since neglect is considerably more frequent among patients with right hemispheric lesions, it is not surprising that the incidence of these disorders is asymmetrically distributed in acute strokes. Contrary to the commonly held belief that there is no asymmetry in the incidence of functional impairments in left and right stroke patients [1], recent studies suggest reconsidering the role of the side of the lesion in the outcome and in recovery from stroke. Thus, in a large unselected population of brain-damaged patients, both sensory and motor impairments are more frequent in right-sided than left-sided lesions [29]. The authors sug-

gest that the presence of neglect may be responsible for the more severe left-sided symptomatology.

The recovery of sensory and motor deficits following unilateral hemispheric lesions also shows considerable asymmetry, with a slower and more incomplete functional improvement following right-sided lesions [19]. Compared with patients with left stroke, longer length of stay in a rehabilitation centre [13, 14], greater assistance in daily living [7, 9, 20], and less improvement of motor deficits [7] are typical manifestations of the more severe and long-lasting impairments in unilateral right hemispheric strokes. Although for methodological reasons it may be difficult to compare longitudinal studies, the smaller amount of improvement in motor recovery observed in right-sided lesions has often been associated with neglect, asomatognosia and visuospatial disorders [11, 18, 19, 21].

The effectiveness of cognitive rehabilitation of neurological disease has been recently reviewed [27]: in spite of frequent methodological weaknesses, some studies have documented the positive effects of specific cognitive training on the reduction of neglect [3, 8, 10, 26, 35, 36]. Therefore, because of the described symptomatological association, it seemed important to test systematically whether training specifically developed to improve neglect might facilitate the neurological and functional outcome produced by standard physiotherapeutic techniques.

Subjects and methods

Fifty-nine right-handed, right brain-damaged stroke patients participated in the study. All patients had suffered a single stroke from 2 to 6 months before. The experimental group did not include patients over 78 years of age, with multiple lesions, neoplastic or haemorrhagic aetiology, or with other chronic CNS pathologies (Parkinson's disease, dementia, multiple sclerosis, polynuropathy). Patients were selected and assigned to the different experimental groups so as to reduce all possible sources of bias; they were selected from those patients consecutively admitted over almost 3 years to a single large ward (100 beds). Bed numbers were assigned by the Hospital Administration on the basis of reservation priority. This number (either odd or even) was used to assign blindly the patients to one of the experimental groups (see below). The ward physicians, including the researchers, did not intervene at this point.

All patients were given a neglect screening battery (37), see below) as part of a standard clinical evaluation. This was carried out by a neuropsychologist who did not participate in the research and was not informed of the specific goals of the study; the screening was immediate or delayed treatment. Therefore, assignment to either immediate or delayed treatment was independent from screening results. In turn, group assignment could not influence testing during screening for neglect since the neuropsychologist did not know that the number of the bed was being used to separate patients into different experimental groups.

Based on the results of this screening, 23 patients (9 males and 14 females) were included in the neglect group (N+), and 36 (15 males and 21 females) in the non-neglect group (N-). Patients with odd numbers ($n = 12$) received the training for neglect immediately (N+), and patients having even numbers ($n = 11$) after 2 months (delayed training; N+D). Informed consent was obtained from all patients.

Mean age was 61.5 years (SD 13.22) in the N- group, 68.0 (SD 7.19) in N+ and 70.0 (SD 5.46) in N+D ($F(2, 56) = 2.32$, n.s.); average time from onset of disease was 47.11 days (SD 31.65) in N-, 64.33 days (SD 40.51) in N+, and 63.36 days (SD 37.25) in N+D ($F(2, 56) = 1.48$, n.s.).

Instruments

Functional and neurological scales

Both functional disabilities and neurological impairments were assessed by means of three widely used scales:

Rivermead Mobility Index. This scale (derived from the Rivermead Motor Assessment) [4] detects the ability of a patient to perform 15 common daily movements: turning over in bed, lying to sitting, sitting balance, sitting to standing, standing unsupported, transfer, walking inside, stairs, walking outside (even ground), walking inside with no aid, picking up something from the floor, walking outside on uneven ground, bathing, up and down four steps, running. A score of 1 is given for each correct response and 0 for each wrong one. Thus, the scale ranges from a score of 0 (totally unable) to 15. The scale proved to be valid and reliable for evaluating mobility after stroke and head injury [4], and it has been recently used in a randomized crossover trial in stroke rehabilitation [34].

Barthel Index. Activities of daily living status were monitored using the Barthel Index [22], a ten-item scale that measures the functional abilities of patients, such as eating, dressing, grooming, walking, and bowel and bladder functions. This scale gives a score between 0 and 100. The top score implies functional independence, not necessarily normality. It is widely used with stroke patients [33] and has proven to be of functional prognostic value in previous stroke outcome studies [16, 17].

Canadian Neurological Scale. We used the revised version [6] of the scale [5] to measure the severity of the stroke. The eight-item scale measures level of consciousness, orientation, speech, facial weakness, and motor function, for a maximum score of 11.5 in non-comatose patients. A separate section is used for patients with comprehension deficits. It has undergone extensive validation and reliability tests [6].

Evaluation of hemi-spatial neglect

All patients were administered a battery for hemi-spatial neglect [37]. This included the Letter Cancellation Test [10], the Barrage Test [2], the Wundt-Jastrow Area Illusion Test [23] and the Sentence Reading Test [25].

In the first two tests, the number of items (either lines or letters) correctly crossed is measured. In order to express the degree of

This test uses a version of this well-known optical illusion modified to favour the detection of spatial asymmetries. Two fans of the same shape and surface are presented, however, due to the spatial arrangement of the display one of the two figures appears longer (over 99% of judgements in control subjects). Forty stimuli are given with ten different sizes, ranging from 5.7° to 57° of visual angle in ten equally spaced steps. Each stimulus size is presented in four different ways: fans pointing either to the left or to the right, with convexity oriented upward or downward. For each stimulus the patient is requested to say or to indicate by pointing whether the top or the bottom fan was longer. The responses are classified as "expected" (in agreement with the known illusory effect) or "unexpected" (in the direction opposite to the illusion). For more details see [23].

asymmetrical performance the following laterality coefficient was used:

$$L_c = \frac{L - R}{L + R}$$

where "e" is the number of errors and "c" the number of correct responses; "L" indicates the left and "R" the right part of the page (observer's view). Larger positive values indicate more severe neglect.

In the Wundt-Jastrow Area Illusion Test, the number of responses consistent with the direction of the optical illusion when the two fans appear oriented either to the left or to the right is recorded (possible score: 0-20 in each case). Previous research has shown that neglect patients display fewer expected responses when the two fans point to the left, while they perform normally when the two fans appear oriented to the right [23]. Consequently, only the number of expected responses when the fans were oriented to the left was the dependent measure used in the analysis. In the Sentence Reading Test, the score was the number of sentences (0-6) read without omissions. Two patients (one in the N+ and one in the N+D group) were illiterate; therefore, they were not given the Reading Test.

Cut-off scores for the presence of neglect were available for all tests. All neglect patients failed in at least three tests.

Neuroanatomical examinations

Site and volume of the lesion in mm³ were based on MRI (0.2 T, Hitachi Esa-Tompa 4000 MR Unit), performed before the beginning of the study and during the in-rehabilitation stay. All examinations performed in the acute phase have been repeated.

Treatments

Physical rehabilitation

Immediately after admission all patients started the physical rehabilitation treatment, based on Bobath's therapeutic exercises. It has been shown that this approach produces functional improvements comparable with a variety of other therapeutic approaches [12]. All patients received the treatment 6 days a week (two 1-h sessions daily).

Specific training for neglect

The patients with neglect received specific treatment, which has been described in detail elsewhere [26]. It consists of five 1-h sessions per week. Four different procedures were used:

1. Visual scanning: patients were required to detect digits appearing in sequence on a large screen (2 x 3 m) in several different positions. At the beginning the digits were presented in a linear sequence from right to left; the patient, after a warning signal and a request by the therapist, had to identify the stimuli (manipulators), read them aloud and press a button as quickly as possible. As the patient's scanning abilities improved, less predictable sequences were used and facilitations were progressively reduced.
2. Reading and copying: newspaper headlines and handwritten sentences were presented to the patient, who read and copied them. The words and sentences were of different degrees of linguistic and/or perceptual complexity (i.e. word frequency, length of sentences, size of written material, etc.).
3. Copying of line drawings on a dot matrix: in this procedure line drawings of solid lines connecting dots were presented on the left side; the patient was required to copy them on a matrix on his/her right side. The number of dots (from 4 to 20) and lines was progressively increased.

4. Description of scene: black and white pictures were shown to the patient, who had to describe them in detail. Increasing difficulty consisted in a greater number of elements to be described in the scene.

Verbal and visual warning signals were provided in the early stages of treatment and were progressively reduced when the patient's exploration ability improved.

General cognitive intervention

To test the specificity of the effect of the treatment for neglect, this was alternated with an intervention aimed at providing broad cognitive stimulation. A volunteer interacted with patients using magazines, playing cards, puzzles, etc. This intervention took place 3 days a week, in 1-h daily sessions.

In order to reduce sources of variability, all patients were treated by the same four physical therapists, by one cognitive therapist for neglect rehabilitation and by one volunteer for the general cognitive intervention.

Procedure

The three scales were administered three times by the same physician who was unaware of the aims of the study. The first evaluation (T1) took place upon admission. All patients with and without neglect began physical therapy immediately. The physical therapists were not informed of the patients' assignment to a treatment. The N+D subgroup began the specific cognitive treatment for neglect immediately, while the N+D group received the general cognitive intervention. At the end of the first 8 weeks, all patients underwent a second assessment (T2). After this evaluation, the two types of training were reversed. Thus, N+D patients started the general purpose cognitive intervention, and N+ patients started the training for neglect. Both programmes lasted for 8 consecutive weeks. At the end of this second period, all three groups underwent the third assessment (T3).

Results

Functional disability and motor impairment

Three ANOVAs with "group" (N+D, N+D) as independent measure and "time of testing" (T1, T2, T3) as repeated measure were performed on the three neurological and functional scales. Whenever significant, main effects or interactions were further analysed using Duncan's a posteriori test. These computations have been frequently used to analyse the data of functional scales such as the ones adopted in this study (see [24] for a statistical discussion). However, since all these scales are ordinal measures the results were also backed up by the use of non-parametric statistics to control further for the change over time between the different groups.

A separate one-way ANOVA with "time of testing" as repeated measure was performed on the N- subgroup.

Rivernhead Mobility Index

The ANOVA showed a main effect for "time of testing" [$F(2, 42) = 55.13; P < 0.001$]; the interaction Group x Time

of testing [$F(2, 42) = 3.28; P < 0.05$] was significant. Figure 1 shows the mean values for the two groups according to the time of testing.

Duncan's test showed that the two neglect groups were not significantly different at T1 and at T3; the difference was significant at T2 ($P < 0.01$). Using Mann-Whitney's test, the differences were again not significant at T1 and T3 ($U = 53.5$ and $U = 49.5$, respectively), but they were significant at T2 ($U = 34; P < 0.05$).

The performance of N- patients improved significantly during testing [$F(2, 70) = 92.92; P < 0.001$]. These results are presented in Fig. 1 for comparison with the N+ patients. It should be noted that this subgroup was less impaired in all three observations compared with the neglect patients.

RIVERNHEAD MOBILITY INDEX

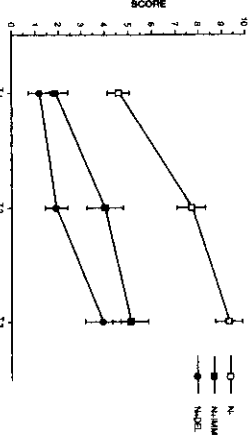


Fig. 1 Performance on the Rivernhead Mobility Index for the three groups of patients according to time of testing

BARTHEL INDEX

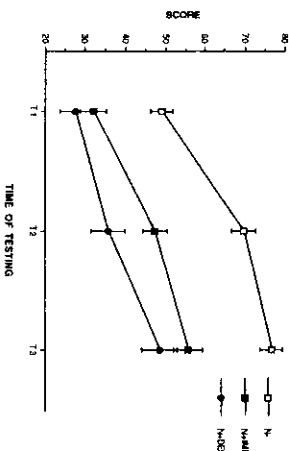


Fig. 2 Performance on the Barthel Index for the three groups of patients according to time of testing

Barthel's Index

The analysis showed a significant "time of testing" [$F(2, 42) = 79.02; P < 0.001$] effect; the interaction was also significant [$F(2, 42) = 3.40; P < 0.05$]. The overall pattern was very similar to that of the previous analysis (see Fig. 2).

Duncan's test showed that the two neglect groups were not significantly different at T1 and T3; the difference was significant at T2 ($P < 0.05$). These results were confirmed using Mann-Whitney's test: no difference was observed at T1 and T3 ($U = 55$ and $U = 47$, respectively) and the two groups were significantly different at T2 ($U = 35; P < 0.05$).

The N- group improved steadily during the test period [$F(2, 70) = 138.02; P < 0.001$; see Fig. 2].

Canadian Neurological Scale

The main effect of the "time of testing" factor was significant [$F(2, 42) = 32.43; P < 0.001$]. For the group as a whole, improvement was observed between T1 ($\alpha = 5.67$) and T2 ($\alpha = 6.15; P < 0.01$) and between T2 and T3 ($\alpha = 6.59; P < 0.01$). The interaction Group x Time of testing was not significant [$F(2, 42) = 0.99; n.s.$], indicating that improvement was similar in the two groups.

The N- group improved steadily during the test period [$F(2, 70) = 58.74; P < 0.001$].

Neglect

Performances of N- patients on hemi-neglect tests were nearly flawless in all tests; thus, they were excluded from the subsequent analysis.

Four separate ANOVAs, one for each measure of neglect, were performed on the two neglect groups similar to those described above. The respective means for these analyses are presented in Table 1.

As for the Letter Cancellation Test, the ANOVA showed a main effect for "time of testing" [$F(2, 42) = 33.95; P < 0.001$]; the interaction Group x Time of testing [$F(2, 42) = 6.45; P < 0.005$] was significant. Duncan's test showed that the two neglect groups were non significantly different at T1 and T3; the difference was significant at T2 ($P < 0.01$), with the N+D group performing less well than the N+ group.

This general pattern was replicated in the ANOVAs on the other neglect tests with minor differences. In particular, the time of testing factor was always significant (at least $P < 0.001$). In the Barrage test, the pattern of improvement was similar; however, the interaction Group x Time of testing fell short of significance [$F(2, 42) = 2.48; P = 0.09$]. As for the Wundt-Jastrow Area Illusion Test, the ANOVA showed the interaction Group x Time of testing [$F(2, 42) = 5.25; P < 0.01$]. Duncan's test showed that the two neglect groups were significantly different at T2

Table 1 Mean values and standard deviations for the four tests of neglect in the two subgroups of N+ patients in the three testing evaluations. In the first two tests, values are laterality coefficients (larger values indicate more severe neglect); in the Wynd-Jastrow Area Illusion Test, the number of expected responses for left pointing to the left is presented. In the Sentence Reading Test, the number of correct responses is reported (in these last two tests greater values indicate better performance)

	Letter cancellation		Barrage Test		Wynd-Jastrow Area Illusion		Sentence Reading	
	N+1	N+D	N+1	N+D	N+1	N+D	N+1	N+D
T1	0.94 ±0.57	1.06 ±0.59	0.44 ±0.53	0.73 ±0.49	6.67 ±6.65	8.73 ±6.42	2.45 ±2.7	2 ±2.62
T2	0.21 ±0.43	0.91 ±0.74	0.06 ±0.2	0.49 ±0.61	16.25 ±4.2	12.36 ±7.19	5.64 ±0.92	1.6 ±2.5
T3	0.19 ±0.38	0.49 ±0.87	0.12 ±0.33	0.13 ±0.37	16.33 ±3.26	16 ±5.23	5.55 ±0.69	5.5 ±1.27

($P < 0.01$) but not at T1 and T3. In the Sentence Reading Test, unlike all the other cases, a main effect of the group factor was present [$F(1, 19) = 5.89; P < 0.05$]: the N+1 group had a better mean performance (4.55) than the N+D group (3.03). The interaction Group \times Time of testing [$F(2, 38) = 9.31; P < 0.001$] was significant. Duncan's test showed that the two neglect groups were not significantly different at T1 and T3; the difference was significant at T2 ($P < 0.001$).

Overall, these results indicate the effectiveness of the specific training for neglect and closely confirm previous results with the same procedure [26].

Lesion size

Lesion size was compared in the three groups. An ANOVA with "group" as independent measure did not show a group difference [$F < 1$, n.s.]: the mean volumes were 168.7 mm³ (SD = 510.8) for the N-, 91.9 mm³ (SD = 67.8) for the N+1 and 132.7 mm³ (SD = 95.9) for the N+D. The very large variability of the N- subsample was due to the presence of one exceptional outlier in this group.

Discussion

In the patients without spatial neglect, all scales showed a relatively constant improvement in patients' motor and functional capacities following 2 and 4 months of treatment. The immediate N+ group improved and diverged from the delayed N+ group at T2 after receiving the specific training for neglect; the delayed group improved comparably only after receiving the same specific treatment. Thus, this training was not only successful in producing an improvement in the patients' capacity to attend to and perform actions in the contralateral hemisphere, but also fostered a significant improvement in their functional adaptation. It must be noted, however, that the functional

prognosis of N+ patients, even if treated, was worse than that of N- patients. Thus, the final values of the Barthel Index and the Rivermead Mobility Index indicated comparatively poor independence in daily living activities, mobility and ambulation.

It is also important to observe that the effect of the training for neglect was present in the case of the two scales assessing functional independence but not in the case of the Canadian Neurological Scale. This second scale measures a number of neurological functions with the general aim of assessing stroke severity. This pattern of findings points to the selectivity of the attentional training in modifying patients' behaviour.

From a clinical point of view, it is interesting to note that the effect of the training for neglect was observed both in the immediate and delayed paradigm. The cumulative effect of the two cognitive treatments brings the patients to a similar functional level, regardless of the order of administration.

Interpretations of this pattern other than the specific effect of the training for neglect should be considered. From a methodological standpoint, there was a specific attempt to control for the possibility of bias in group assignment or in the effect of this on testing. Even though the procedure of assigning the patients to experimental groups based on their odd-even bed number is not customary and should not be viewed as strictly random, it proved easy and reliable in keeping information separate between researchers on the one hand and neuropsychological clinicians and therapists on the other. Overall, it appears extremely unlikely that failures in this procedure may have artefactually produced the pattern of results obtained.

A different interpretation may be that the results are due to the mere inclusion of a treatment in addition to physiotherapy. For several reasons this possibility also seems unlikely. First, in very general terms, it is now well established that neglect is rather stable after the 1st month after stroke (e.g. [37]); consequently, no significant change is expected unless a specific treatment is carried out. Second, an attempt was made in the present study to

compare the specific treatment for neglect with a general cognitive intervention. The effects of this procedure were found to be negligible; thus, for example, the N+D group did not improve after this intervention in either neglect or functional scales. However, it is of note that this procedure could be performed for fewer hours than the neglect training (3 vs 5 h per week). This limitation was due to the choice of having a single volunteer treat all patients rather than having different individuals seeing different patients. Therefore, the possibility that differences in the intensity of stimulation may have contributed towards shaping the results cannot entirely be excluded. Finally, a different study [3] comparing the "general cognitive" treatment with the specific treatment for neglect again did not show any significant change in performance after 2 months of intervention, while the specific treatment was highly significant in a simple randomized design. If non-specific training does not produce any change in the neglect disorder, it is unlikely that it can have positive effects on motor behaviour.

In the present study, specific versus non-specific treatments were compared to avoid an interpretation of greater improvement because of more attention being given to one group of patients. However, in the future it would be interesting to compare the functional outcome of neglect patients not receiving any cognitive treatment at all with the two groups studied here.

The nature of the association between improvement in neglect and functional recovery may be interpreted in several ways. Denes et al. [7] interpreted the smaller improvement in right versus left hemispheric lesions as connected either to an emotionally less appropriate comprehension of the deficits or to greater anosognosia, which is particularly frequent in patients with neglect. Recently, it has been found that patients with neglect and anosognosia have a consistently worse prognosis of motor recovery than comparable neglect patients without anosognosia or non-neglect patients [15]. The reduction of neglect and its

associated disorders would produce beneficial effects by improving the patients' emotional involvement and general awareness of the whole rehabilitative effort.

A second explanation can be found in the nature of the measures used to assess recovery. Any functional measure quantifies the amount of success in performing complex sequences of actions (e.g. dressing, eating, toileting, etc.). A patient with neglect may fail because s/he ignores part of the situation, which has to be faced in the contralateral hemisphere, and/or has a reduced tendency to perform actions in the contralateral space (chopstick use) [30]. The improvement of both of these aspects by cognitive training may favour recovery of all actions, such as those of everyday life, which require attending to and moving in both parts of space.

Third, a number of recent investigations have suggested that neglect is the result of a spatial imbalance between retinotopic and egocentric representations of external space [30]. The hypothesized de-coupling between these two representations produces negative consequences both in interpreting sensory information and in organizing motor responses directed toward the neglected side. Consequently, a reduction of this imbalance, through a specific treatment for neglect, may have positive effects on the organization of motor behaviour in these patients.

It should be noted that these three interpretations are not mutually exclusive; further research is needed to establish which mechanisms are more likely to be predominant in explaining the role of neglect treatment on functional recovery. In any case, from a clinical perspective, it seems clear from the present data that the treatment of hemiplegia benefits significantly from an association of physical and cognitive treatment whenever spatial neglect is present.

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MRI detection of epidural spinal abscesses at noncontiguous sites

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Abstract We report the cases of two patients with the very uncommon clinical finding of two noncontiguous spinal epidural abscesses, which were located in the cervical and lumbar spine. In each case the diagnosis of the second spinal abscess was made by MRI only after the appearance of a new neurological deficit. Decompressive spinal surgery and intravenous antibiotic therapy led to complete recovery in one patient; the other patient was moderately disabled. As epidural spinal abscesses can occur at noncontiguous sites,

Key words Epidural spinal abscess · *Staphylococcus aureus* · Magnetic resonance imaging

weakness of both lower limbs. The deep tendon reflexes in the lower extremities were absent. Erythrocyte sedimentation rate (116 mm/h) and white blood cell count (28,200/mm³) were elevated. The developed septicaemia due to *Staphylococcus aureus* requiring catecholamine therapy and intravenous antibiotics. Because of neck pain, progressive tetraparesis, and bowel and bladder dysfunction she was referred to our department 1 month after admission. Neurological examination at our department showed severe spastic tetraparesis and impaired sensation to pinprick and touch below the level of C6. She had decubital ulcers in the sacral region and on both heels. Sagittal T1-weighted spin-echo MRI of the cervical spine revealed an epidural mass (Fig. 1a). A decompressive surgical procedure at C5-6 was performed. Intraoperative cultures revealed *S. aureus*. Intravenous antibiotic therapy with fluioxacillin, ceftriaxone and meropenazole was initiated. The patient's clinical condition improved during the next few days. However, 5 days after surgery she developed complete paralysis of a lower extremities, and the left biceps muscle deteriorated to a grade 2/5 paresis. MRI of the entire spine showed evidence of a persistent epidural mass with compression of the spinal cord at the C5 level. MRI of the thoracic spine was normal. MRI of the lumbar spine showed an abscess at the level of L3-5 in the dorsal epidural space (Fig. 1b) and abscesses in the paraspinal muscles. Another decompressive and stabilizing surgical procedure was performed at C5/6. In addition, the patient underwent L3-5 laminectomy; again *S. aureus* was isolated from pus. Follow-up MRI of the cervical and thoracic spine 7 weeks after admission re-

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Introduction

The main clinical symptoms and signs of an epidural spinal abscess are spinal pain, tenderness, radiculopathy, paraesthesia, fever, and weakness that can progress to paralysis [12]. The diagnostic method of choice is MRI [2]. Three to six adjacent spinal cord segments are involved in most cases, and a spinal epidural abscess typically has a single epicentre at which spinal cord and nerve root damage may occur [1, 4, 5]. The entire length of the spinal cord may be involved in very rare cases [1, 13]. Here we report on the very unusual finding of spinal epidural abscesses detected by MRI at noncontiguous sites (cervical and lumbar) in two patients.

Case reports

Patient 1

A 61-year-old adipose woman was admitted to her local hospital for progressive lumbar pain lasting 4 weeks. She had a 4-year history of diabetes mellitus. On admission the patient had slight