

## REDUCTION OF VISUO-SPATIAL NEGLECT WITH VESTIBULAR GALVANIC STIMULATION

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**ABSTRACT.** The purpose of the present investigation was to determine the effect of galvanic vestibular stimulation on visuo-spatial neglect without inducing nystagmus and associated discomfort. Fourteen patients with right-hemisphere stroke with neglect were assessed with two visuo-motor tasks ("Line crossing" and "Star cancellation") on three occasions. Seven of the subjects received galvanic vestibular stimulation during the second condition (Experiment 1), whereas the other seven received stimulation during the third assessment (Experiment 2). Between-group comparisons of stimulation effects were performed by analyzing change on visuo-spatial neglect from the first to the second condition in the two experimental groups. A significantly larger effect was demonstrated on the "Line crossing" task in Experiment 1. This finding suggests a stimulation effect beyond practice/spontaneous recovery, and may provide new possibilities in rehabilitation research because the stimulation can be given without discomfort.

*Key words:* neuropsychology; rehabilitation; stroke; electric stimulation.

### INTRODUCTION

The neglect syndrome is comprised of a dysfunction in "reporting, responding or orienting" to stimuli contralateral to the brain lesion and can be manifested in a number of modalities including deficits in tactile perception and deviations in body orientation (11). Neglect is more frequent and severe following right hemisphere injury and is not attributed to motor and sensory defects (11). It is influenced by the attentional load of the situation and becomes more apparent in more complex and in less familiar tasks (18).

Visuo-spatial neglect is a common manifestation of the neglect syndrome and entails failure to notice and explore visual stimuli in the visual field opposite the side of the lesion. This dysfunction is displayed in tasks

such as free-hand drawing, figure copying and target cancellation (8).

Neglect is a significant predictor of poor outcome following stroke (7). Although resistant to treatment, a temporary reduction of neglect has been found during various types of stimulation such as optokinetic stimulation (17), mechanical vibration of the neck muscles (14), and transcutaneous electrical stimulation (21, 22). A number of studies have demonstrated a temporary decrease of visuo-spatial neglect during vestibular stimulation (3, 19, 23).

Vestibular alteration has been induced in right-brain injured patients by irrigation of the left external ear canal with cold water or right-ear canal with warm water (19, 23), both generating nystagmus and a leftward deviation of the eyes. The effects of caloric stimulation on a number of dysfunctions associated with neglect have also been investigated. These studies have demonstrated temporary improvement of anosognosia for left hemiplegia (3) tactile hemianesthesia (23), and even transient disappearance of somatoparaphrenic delusion, or denial of a limb belonging to oneself (1).

Whereas electrical stimulation has been used to modify proprioceptive/somatosensory input in patients with neglect (21), the effect on neglect by electrical modulation of the vestibular system has not been investigated. As caloric stimulation is both unpleasant and inconvenient, it does not lend itself to repeated use outside the experimental laboratory. Neither does it allow analysis of vestibular-mediated effects on orientation separately from nystagmus-related gaze alterations of median direction. Thus, inducing vestibular alteration without nystagmus and under comfortable conditions would permit new opportunities for repeated exposure and assessment of potential treatment effects while also providing further understanding of the mechanisms involved in modulating visuo-spatial neglect.

In the present study, we sought to investigate the effects of galvanic stimulation to the vestibular nerves on visuo-spatial neglect in patients with right-hemisphere

infarcts. The aim was to assess whether a temporary reduction in visuo-spatial neglect, as determined by performance on standard visuo-motor neglect measures, could be obtained from vestibular galvanic stimulation while maintaining a current level at a magnitude where nystagmus and associated discomfort could be avoided.

## METHODS

### Subjects

Fourteen consecutively admitted stroke patients with right-hemisphere lesion and left-sided visual neglect ranging in age from 56 to 94 years (median age 75) participated in the study.

The patients were divided into two treatment-order experiments. The first seven patients participated in Experiment 1 (median age: 77, Interquartile range: 12) and the other seven patients were included in Experiment 2 (median age: 74, Interquartile range: 23). Whereas the majority of the patients had cortical and combined cortical-subcortical lesions on CT, four patients (two from each experiment group: patients 1, 3, 11, and 14) showed only evidence of subcortical lesions on CT. All but two patients were diagnosed with infarctions. One patient had a hemorrhage (patient 14) and no CT was conducted on patient 13 because of old age and limited facilities (a CT was recommended in the event of deterioration but as the patient demonstrated good recovery, no CT was conducted). Demographic data are presented in Tables Ia and Ib. All patients were right-handed. The median duration of illness at the time of the first assessment was 5.5 days (Interquartile range: 5). A fixed time for the first

Table Ia. Demographic data, number of days between onset of illness and first assessment (Nostim1), stimulation (stim) level in mA, and total number of targets (t) and asymmetry percentages (%) on the "Line crossing" and "Star cancellation" tests: Experiment 1 (Nostim1—Stim—Nostim2)

| Patient No. | Days of illness | Age/Gender | Stim. level mA |      | Nostim1 |    | Stim. |    | Nostim2 |    |
|-------------|-----------------|------------|----------------|------|---------|----|-------|----|---------|----|
|             |                 |            |                |      | t       | %  | t     | %  | t       | %  |
| 1           | 3               | 80/F       | 1.25           | Line | 9       | 0  | 19    | 5  | 11      | 0  |
|             |                 |            |                | Star | —       | —  | —     | —  | —       | —  |
| 2           | 11              | 61/F       | 0.90           | Line | 32      | 44 | 36    | 50 | 36      | 50 |
|             |                 |            |                | Star | 24      | 4  | 30    | 33 | 29      | 31 |
| 3           | 3               | 78/F       | 1.10           | Line | 23      | 26 | 36    | 50 | 36      | 50 |
|             |                 |            |                | Star | 19      | 0  | 30    | 10 | 45      | 47 |
| 4           | 4               | 78/M       | 0.80           | Line | 11      | 0  | 31    | 42 | 32      | 50 |
|             |                 |            |                | Star | 8       | 0  | 21    | 0  | 30      | 27 |
| 5           | 7               | 77/F       | 0.70           | Line | 35      | 49 | 36    | 50 | 34      | 47 |
|             |                 |            |                | Star | 42      | 48 | 45    | 44 | 39      | 46 |
| 6           | 7               | 75/F       | 1.50           | Line | 35      | 49 | 36    | 50 | 36      | 50 |
|             |                 |            |                | Star | 47      | 45 | 51    | 47 | 40      | 33 |
| 7           | 2               | 66/M       | 1.70           | Line | 9       | 0  | 36    | 50 | 36      | 50 |
|             |                 |            |                | Star | 14      | 0  | 36    | 31 | 52      | 48 |

Table Ib. Demographic data, number of days between onset of illness and first assessment (Nostim1), stimulation (stim) level in mA, and total number of targets (t) and asymmetry percentages (%) on the "Line crossing" and "Star cancellation" tests: Experiment 2 (Nostim1—Nostim2—Stim)

| Patient No. | Days of illness | Age/gender | Stim. level mA |      | Nostim1 |    | Nostim2 |    | Stim |    |
|-------------|-----------------|------------|----------------|------|---------|----|---------|----|------|----|
|             |                 |            |                |      | t       | %  | t       | %  | t    | %  |
| 8           | 2               | 84/M       | 1.20           | Line | 35      | 49 | 35      | 49 | 36   | 50 |
|             |                 |            |                | Star | 47      | 45 | 48      | 44 | 54   | 50 |
| 9           | 6               | 56/M       | 1.20           | Line | 34      | 47 | 35      | 49 | 36   | 50 |
|             |                 |            |                | Star | 41      | 44 | 45      | 44 | 45   | 49 |
| 10          | 6               | 71/F       | 0.80           | Line | 36      | 50 | 36      | 50 | 36   | 50 |
|             |                 |            |                | Star | 36      | 28 | 42      | 37 | 42   | 41 |
| 11          | 4               | 75/M       | 1.20           | Line | 33      | 45 | 18      | 0  | 36   | 50 |
|             |                 |            |                | Star | 17      | 0  | 31      | 29 | 49   | 45 |
| 12          | 5               | 74/F       | 1.20           | Line | 18      | 0  | 24      | 29 | 27   | 41 |
|             |                 |            |                | Star | 12      | 0  | 11      | 0  | 30   | 27 |
| 13          | 13              | 94/F       | 1.10           | Line | 8       | 0  | 4       | 0  | 11   | 0  |
|             |                 |            |                | Star | —       | —  | —       | —  | —    | —  |
| 14          | 19              | 61/M       | 1.10           | Line | 36      | 50 | 36      | 50 | 36   | 50 |
|             |                 |            |                | Star | 48      | 46 | 50      | 48 | 51   | 47 |

assessment was not used as time of inclusion depended on the general health of the patient as well as on practical considerations. Patients had to be ambulatory and able to maintain an adequate level of alertness and motivation throughout the evaluation.

Hemianopsia was determined with Donders' test during regular clinical assessment at the time of hospitalization. Hemianopsia was present in 10 patients and suspected in one patient (9). No hemianopsia could be detected in patients 4 and 10 and one patient could not be adequately tested owing to the extent of neglect (patient 12). Global cognitive functioning was assessed with the Mini Mental Status Exam (MMSE) (5).

#### Assessment of visuo-spatial neglect

Two visuo-motor tasks were used for assessment of neglect: "Line crossing" and "Star cancellation" from the Behavioral Inattention Test (25).

**Line crossing:** On this task, the subjects were presented with a sheet of paper containing 40 lines in seven columns. Following a demonstration in which the examiner crossed out four lines in the center column, the subject was requested to cross out all 36 remaining lines on the page. The currently accepted cut-off value is 34 as available norms show scores between 35 and 36 (25).

**Star cancellation:** On this task, the subject was presented with a page containing 56 small stars mixed up with a number of larger stars and words written in capital letters. Subjects were instructed to cross out all the small stars following a demonstration by the examiner in which two centrally located small stars were crossed out. The maximum score is 54. The currently accepted cut-off value has been set at 51 as available normative data show performances that range between 52 and 54 (25).

Criteria for visuo-spatial neglect included scoring at, or below, the cut-off level on either or both tasks while also demonstrating an asymmetry of omissions in the contralesional half of the sheet on the defective task/s. An asymmetry score in percent was computed by dividing the number of detections on the left side with the total number of targets (6). A score below 30% indicates an asymmetry with fewer detections on the left side, whereas a score above 50% suggests a performance bias towards the right. Inclusion in the present study required a score at, or below, 48% on at least one of the tasks, and no test performance above 52%. These criteria are similar to those used by Halligan and co-workers (10). Number of targets and asymmetry scores were both calculated to determine performance on the "Line crossing" and the "Star cancellation" tasks.

Test sheets were attached with adhesive tape on a table in front of, and symmetrical to, the subject's midline. The investigator was seated directly opposite the subject. In accordance with the published test instructions (25), no time limit was imposed, although the time used by the subjects for completing the tests was assessed. Timing started when the subject was told to begin the test and terminated when the subject said he was finished or placed down the pen. During this time, the investigator was silent. Subjects were free to move their head and eyes during testing. All subjects had normal or corrected-to-normal vision.

#### Vestibular stimulation

Vestibular disturbance was produced by bipolar binaural galvanic stimulation to the vestibular nerves, induced by two

50 × 35 mm large carbon-rubber electrodes (CEFAR AB, Lund, Sweden) placed on the mastoids (2). During galvanic stimulation, the electrodes over the mastoids were of opposite polarity. With the intention of producing a vestibular disturbance in the lateral plane with a deviation to the left (neglected) side, negative charge was placed at the right mastoid and positive charge at the left mastoid.

A specially designed generator (24) delivered galvanic stimuli at various current levels specifically adjusted for each patient. Each patient was initially given a 5–10-second trial with a current of 1.5 mA. The current was adjusted down to a level where it was not experienced by the individual patient. This threshold level differed between patients with a range of 0.7 mA to 1.7 mA (median: 1.15). During the experimental, stimulation condition the subject completed the "Line crossing" and "Star cancellation" tasks while simultaneously receiving vestibular stimulation at the individually determined current. No current was given between tasks. Stimulation was started when the patient was told to begin the test and terminated when the patient said he was finished or put down the pen.

#### Experiment 1

Seven stroke patients with visuo-spatial neglect (patients 1–7) participated in a no stimulation–stimulation–no stimulation experimental design. Subjects were first assessed, using the two neglect measures, without stimulation (Nostim1). Subjects were assessed with the same measures the following day while receiving stimulation (Stim). Testing and adjustment of current level was performed just prior to the Stim condition on the second day. The third day, patients were assessed once more without receiving stimulation (Nostim2).

#### Experiment 2

In order to allow between-group comparisons for assessing stimulation effects beyond natural recovery, seven additional stroke patients (patients 8–14) were included in a design where stimulation was provided at the third and last assessment. Stroke patients who fulfilled the described criteria for visuo-spatial neglect were included in the study. As in the previous experiment, baseline neglect measures were obtained without stimulation (Nostim1). Subjects were assessed without stimulation (Nostim2) again the following day. The third testing, with stimulation (Stim), was also conducted the second day 15–30 minutes after Nostim2.

No feedback or encouragement regarding test performance was provided. Prior to the stimulation condition, subjects in both experiments were informed that they would receive electrical stimulation at a current magnitude level "not higher than a small battery" while doing some tasks. Informed consent was obtained after the nature of the procedure had been fully explained. Attempts were made to assess each patient during a time of the day when the level of alertness was optimal. Once a patient was included, efforts were made to conduct the second and third conditions at the same time of the day.

#### Statistical analyses

The performances of the subjects in the two experimental designs were analyzed separately. The Friedman analyses of variance were conducted on each variable. Significant *p*-values were further analyzed with pairwise comparisons using the Wilcoxon matched-pairs signed-ranks tests. Two-tailed tests

Table IIa. Performance results on the MMSE, total number of targets crossed and asymmetry scores in percent on the "Line crossing" and "Star cancellation" tests, time spent on completing "Line crossing" and "Star cancellation" Median and interquartile range (IQR): Experiment 1 (Nostim1—Stim—Nostim2)

|                  | N | Nostim1<br>Median (IQR) | Stim<br>Median (IQR) | Nostim2<br>Median (IQR) |      |
|------------------|---|-------------------------|----------------------|-------------------------|------|
| MMSE             | 7 | 24 (11)                 | 22 (11)              | 25 (12)                 | n.s. |
| Line targets     | 7 | 23 (26)                 | 36 (5)               | 36 (4)                  | *    |
| Line asymmetry % | 7 | 26 (48)                 | 50 (8)               | 50 (3)                  | *    |
| Line time (sec.) | 7 | 60 (45)                 | 60 (46)              | 50 (28)                 | n.s. |
| Star targets     | 6 | 22 (31)                 | 33 (19)              | 40 (17)                 | n.s. |
| Star asymmetry % | 6 | 2 (45)                  | 32 (38)              | 39 (17)                 | n.s. |
| Star time (sec.) | 6 | 136 (116)               | 135 (80)             | 137 (135)               | n.s. |

\*  $p < 0.05$  in one or more pairwise comparisons. |—| and |—| indicate significant pairwise comparisons.

Table IIb. Performance results on the MMSE, total number of targets crossed and asymmetry scores in percent on the "Line crossing" and "Star cancellation" tests, time spent on completing "Line crossing" and "Star cancellation" Median and interquartile range (IQR): Experiment 2 (Nostim1—Nostim2—Stim)

|                     | N | Nostim1<br>Median (IQR) | Nostim2<br>Median (IQR) | Stim<br>Median (IQR) |      |
|---------------------|---|-------------------------|-------------------------|----------------------|------|
| MMSE                | 7 | 21 (17)                 | 23 (18)                 | —                    | n.s. |
| Line targets        | 7 | 34 (18)                 | 35 (18)                 | 36 (9)               | n.s. |
| Line asymmetry %    | 7 | 47 (50)                 | 49 (50)                 | 50 (9)               | n.s. |
| Line time (sec.)    | 7 | 50 (45)                 | 62 (43)                 | 37 (45)              | n.s. |
| Star targets        | 6 | 39 (32)                 | 44 (23)                 | 47 (13)              | *    |
| Star asymmetry %    | 6 | 36 (45)                 | 40 (24)                 | 46 (12)              | *    |
| Star time (seconds) | 6 | 134 (85)                | 149 (69)                | 141 (74)             | n.s. |

\*  $p < 0.05$  in one or more pairwise comparisons. |—| and |—| indicate significant pairwise comparisons.

were used in all applicable analyses. Comparisons between the two groups in order to assess any effect of treatment beyond spontaneous recovery/practice effects were conducted using Mann-Whitney U tests on the difference scores between the first assessment and the second assessment. Mann-Whitney U was also used to determine any differences between the two experiment groups. In addition, degree of improvement in subjects with earlier vs later inclusion in the study was determined with Mann-Whitney U tests.

## RESULTS

### Experiment 1

MMSE scores obtained just prior to the three conditions (Nostim1—Stim—Nostim2) did not differ significantly. Individual performances on the "Line crossing" and "Star cancellation" tasks from Experiment 1 are pre-

sented in Table Ia. Table IIa demonstrates target and asymmetry performances in median values and interquartile ranges. As demonstrated in Table IIa, there were no significant differences in time spent (in seconds) on the neglect tests between the three conditions.

A significant difference between conditions was found when assessing "Line crossing" target performance with the Friedman analysis of variance ( $\chi^2 = 8$ ,  $p < 0.01$ ). Patients demonstrated a significant improvement from Nostim1 to Stim ( $Z = 2.36$ ,  $p < 0.02$ ) with all seven patients scoring higher during the Stim condition. There was no significant difference between the Stim condition and the Nostim2 condition on day three. However, the improvement from Nostim1 on the first day of assessment and Nostim2 on the third day of assessment was significant ( $Z = 2.11$ ,  $p < 0.04$ ) as six subjects scored

higher at Nostim2. When assessing "Line crossing" asymmetry scores a significant result was also demonstrated ( $\chi^2 = 6.92$ ,  $p < 0.03$ ). Follow-up analyses on asymmetry scores showed a significant improvement from Nostim1 to Stim ( $Z = 2.36$ ,  $p < 0.02$ ). Other comparisons were non-significant.

Six subjects were able to complete the "Star cancellation" task (subject 1 was unable fully to follow the instructions). Friedman analyses of variance on targets and asymmetry scores from the "Star cancellation" task did not produce significant  $p$ -values. However, it is noteworthy that all six subjects completing this test showed improved target performance from the Nostim1 condition to the Stim condition the following day. Half of these subjects demonstrated further improvement and half showed a decline at Nostim2 on the third day of testing.

### Experiment 2

Analysis of MMSE scores from the experiment with condition order Nostim1—Nostim2—Stim produced no significant differences between scores at Nostim1 and performances the following day (prior to Nostim2 and Stim conditions). Individual performances on the "Line crossing" and "Star cancellation" tasks are demonstrated in Table Ib. Performance results of targets and asymmetry scores in median values and interquartile ranges are presented in Table IIb. There were no significant differences between the three conditions with regard to time spent (in seconds) for completing the "Line crossing" and "Star cancellation" tests.

Friedman analysis of variance did not result in significant  $p$ -values on the "Line crossing" target performance or asymmetry scores. It is worth noting that two subjects had already reached ceiling performances during the first condition.

Six subjects completed the "Star cancellation" task. One patient (subject 13) was unable to follow the instructions. Using Friedman analyses of variance, significant results were obtained on the "Star cancellation" targets ( $\chi^2 = 8.3$ ,  $p < 0.02$ ) and asymmetry scores ( $\chi^2 = 7.7$ ,  $p < 0.03$ ). All six subjects demonstrated superior target performance ( $Z = 2.2$ ,  $p < 0.03$ ) and less asymmetry ( $Z = 2.2$ ,  $p < 0.03$ ) during Stim than during Nostim1. There was also a significant difference with regard to asymmetry scores between Stim and Nostim2, with significantly less asymmetry during the Stim condition ( $Z = 2$ ,  $p < 0.05$ ). Remaining pairwise com-

parisons on "Star cancellation" targets and asymmetry scores did not reach significance at the 0.05 level.

### Comparisons and analyses of both experimental groups

Comparisons between the two experimental groups did not result in any significant differences in (i) age; (ii) MMSE scores at Nostim1; (iii) number of days from onset of illness to start of experiment; (iv) stimulation level in mA; (v) asymmetry scores from "Line crossing" and "Star cancellation" at Nostim1 and asymmetry sum scores from all three conditions; (vi) target performances from "Line crossing" and "Star cancellation" at Nostim1 and overall sum target performances from all three conditions. Visual analysis of the results from the two patients with no hemianopsia suggests no apparent pattern of performance or response to stimulation.

The impact of treatment vs spontaneous recovery/practice was assessed by comparing difference scores from the first and the second conditions in the two experimental groups. By using a Mann-Whitney U test on "Line crossing" difference targets, a significantly larger effect was demonstrated between Nostim1 and Stim from Experiment 1 (Median = -10, Interquartile range = 19) than between Nostim1 and Nostim2 from Experiment 2 (Median = 0, Interquartile range = 5,  $Z = 2.64$ ,  $p < 0.01$ ). Similarly, when analyzing the difference asymmetry scores from the "Line crossing" test, a greater effect was again found between Nostim1 and Nostim2 from Experiment 1 (median = -6, Interquartile range = 41) than between Nostim1 and Nostim2 from Experiment 2 (median = 0, Interquartile range = 2,  $Z = 2.26$ ,  $p < 0.03$ ). No significant results were obtained when conducting the same calculations on the "Star cancellation" test.

Comparisons of subjects included earlier vs later after onset of illness were calculated. All subjects were divided by the median day of first assessment, resulting in a group of subjects with their first testing completed by day five or earlier vs subjects included on day six or later. Data from the earlier vs the later inclusion group are presented in median values and interquartile ranges in Table III. As demonstrated in Table III, subjects receiving earlier vs later treatment/assessment did not differ for age or global cognitive functioning as measured with the MMSE. The two groups did not differ at the first assessment with regard to target performances on the "Line crossing" task, whereas performances on "Line crossing" asymmetry scores ( $Z = 2.04$ ,  $p < 0.05$ ), "Star cancellation" asymmetry scores ( $Z =$

Table III. Comparisons of patients included earlier (before day 6) vs later (day 6 or later) after onset of illness: Age, results at inclusion (Nostim1) on MMSE, "Line crossing" and "Star cancellation" targets and asymmetry percentages. Improvement from first to third assessment (difference scores) on "Line crossing" and "Star cancellation" targets and asymmetry percentages. Median and interquartile range (IQR)

|                                  | N | Earlier inclusion<br>Median (IQR) | N | Later inclusion<br>Median (IQR) |      |
|----------------------------------|---|-----------------------------------|---|---------------------------------|------|
| Age                              | 7 | 78 (6)                            | 7 | 71 (16)                         | n.s. |
| MMSE-Nostim1                     | 7 | 17 (13)                           | 7 | 24 (7)                          | n.s. |
| Line targets-Nostim1             | 7 | 18 (24)                           | 7 | 35 (4)                          | n.s. |
| Line asymmetry-Nostim1           | 7 | 0 (45)                            | 7 | 49 (6)                          | *    |
| Star targets-Nostim1             | 6 | 16 (15)                           | 6 | 42 (14)                         | *    |
| Star asymmetry-Nostim1           | 6 | 0 (11)                            | 6 | 44 (24)                         | *    |
| Line targets—difference scores   | 7 | -9 (19)                           | 7 | -1 (3)                          | *    |
| Line asymmetry—difference scores | 7 | -24 (49)                          | 7 | 0 (3)                           | *    |
| Star targets—difference scores   | 6 | -24 (18)                          | 6 | -4 (9)                          | **   |
| Star asymmetry—difference scores | 6 | -36 (26)                          | 6 | -3 (21)                         | *    |

\* Indicates  $p < 0.05$  pairwise comparison.

\*\* Indicates  $p < 0.01$  pairwise comparison.

2.41,  $p < 0.02$ ), and "Star cancellation" target performance ( $Z = 2.16$ ,  $p < 0.03$ ) were superior in the late inclusion group at Nostim1.

Improvement of neglect symptomatology in relation to timing of inclusion following onset of illness was also determined. Significant differences between the two groups were obtained when assessing overall improvement by using difference target scores between the first and the third assessment on the "Line crossing" ( $Z = 2.18$ ,  $p < 0.03$ ) and the "Star cancellation" ( $Z = 2.88$ ,  $p < 0.005$ ) tasks. As observed in Table III, subjects included earlier after onset of illness demonstrated greater improvement on both measures than subjects who were tested/treated later. Similar findings were obtained using asymmetry scores from "Line crossing" ( $Z = 2.14$ ,  $p < 0.04$ ) and "Star cancellation" ( $Z = 2.24$ ,  $p < 0.03$ ) as subjects included earlier demonstrated greater improvement on asymmetry scores than subjects who were included later.

## DISCUSSION

The present results support the hypothesis that galvanic stimulation of the vestibular system can, at least temporarily and partially, reduce the evidence of left visuo-spatial neglect. This finding was most notable on the "Line crossing" task. A treatment effect beyond spontaneous recovery was demonstrated on the "Line crossing" task as the difference target- and asymmetry scores between the first and the second assessment in the Experiment 1 group (Nostim1—Stim—Nostim2) was significantly larger than the difference scores between

Nostim1 and Nostim2 in Experiment 2 (Nostim1—Nostim2—Stim).

The findings from the "Star cancellation" task are more equivocal. No significant stimulation effect was obtained in Experiment 1, whereas significantly less asymmetry during stimulation than during no-stimulation conditions was demonstrated in Experiment 2. Using a between-experiment group comparison, a treatment effect beyond practice/spontaneous recovery could not be proven as the "Star-cancellation" difference target- and asymmetry scores between the first and second assessment in the Experiment 1 group did not differ from the difference scores between Nostim1 and Nostim2 in Experiment 2. Consequently, any stimulation effect on "Star cancellation" performance was not sufficient to rule out adequately the contributing effects from training and/or spontaneous recovery.

The subjects in our study exhibited a trend towards improvement of neglect symptomatology even without receiving stimulation. This is consistent with the natural course of the symptom, as the majority of patients with acute neglect show remission within weeks (12). An improvement within one session, as demonstrated in some patients in Experiment 2, however, is unlikely to happen spontaneously. The likelihood of observable symptoms of neglect generally does increase during repeated use of the same test within one session (4), as performance on cancellation tasks appear to be more influenced by fatigue than practice effects. Thus, an effect from galvanic stimulation may have overridden any fatigue-induced deterioration.

The present investigation included two neglect

measures that differ with regard to degree of sensitivity and specificity. The "Star cancellation" has been found to be a highly sensitive neglect measure (9), whereas "Line crossing" primarily identifies patients with major visuo-spatial neglect. Stimulation-related effects on the "Star cancellation" task were not convincingly proven in our study. One possible explanation may be that the performance on "Star cancellation" is more susceptible to fatigue, motor impersistence/retardation, and comprehension impairments than performance on a more uncomplicated task such as the "Line crossing" test. For a number of subjects in our investigation (most notably subjects 1 and 13), the "Star cancellation" task gave difficulties seemingly unrelated to neglect. Severely impaired patients had difficulties in comprehending and remembering the instructions as well as in maintaining the motor persistence necessary for completing the task. Thus, a number of extraneous factors could have washed out any specific stimulation effects on the "Star cancellation" task. The "Line crossing" test, on the other hand, may lead to false-negative identifications. A ceiling performance is easily reached, and the test is limited in identifying improvement when symptoms of neglect are less severe. This could be observed in the present investigation as significant improvement became more difficult to obtain when a number of patients reached ceiling-, or near ceiling, performances at onset.

The vestibular stimulation in the present study is likely to be associated with a general increase of cortical activation, which has been demonstrated during vestibular stimulation with cold-water calorics (20). A general activation of cortical regions may not only increase the attentional capacity (13) but also stimulate neural processes associated with recovery and plasticity (15). In line with this thinking, it seems at least possible that repeated galvanic vestibular stimulation may improve cognitive functions other than neglect and possibly accelerate the general recovery process.

Whereas a stimulation-induced increase of general activation is expected, we also propose an effect beyond unspecific generalized arousal. The low-level galvanic stimulation used in the present investigation produces an asymmetry of the optokinetic afternystagmus indicating an effect on visual orientation (2) which unspecific alerting stimulation does not (16). Thus, low-level galvanic vestibular stimulation may moderate symptoms of neglect by inducing general arousal as well as specific effects on visual orientation.

Most previous studies with vestibular or cervical

proprioceptive stimulation on neglect subjects have been carried out on chronic patients who may differ from acute patients with a recovery process. We found greater improvement of neglect in patients who were included in the study during the first few days of their illness. Spontaneous recovery was probably a contributing factor as these subjects demonstrated poorer performance at onset. However, it is possible that sensory stimulation may further improve outcome when provided during the early phases of illness.

The present investigation is the first to demonstrate a decrease of neglect during vestibular electrical stimulation. In addition, this study demonstrates a reduction in neglect without a simultaneous induction of nystagmus, a finding not previously observed. The low-level galvanic stimulation in our study is considerably milder than nystagmus-evoking caloric irrigation and hence may affect semicircular and otolith-organ afferents somewhat differently. Our findings introduce new opportunities in rehabilitation research, as repeated stimulation can be provided while avoiding the discomfort associated with nystagmus and the caloric technique. Still, the results from the present investigation should be considered with caution until replication of these findings can be demonstrated. Most importantly, the investigator in the present study was not "blind" to whether the subjects were receiving stimulation or not. Thus, it is important that future research on galvanic vestibular stimulation includes randomized procedures where the investigator is "blind" to whether and when a subject receives stimulation. Investigations including reversal of polarity would also be of interest. Future studies should also aim at determining the spontaneous recovery course of neglect and to what extent this process can be facilitated or permanently improved by sensory stimulation.

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