

## LASTING AMELIORATION OF SPATIAL NEGLECT BY TREATMENT WITH NECK MUSCLE VIBRATION EVEN WITHOUT CONCURRENT TRAINING

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**Objective:** It has been shown recently that neck muscle vibration in combination with an exploration training leads to lasting amelioration of spatial neglect. The present study evaluated whether vibration of the left posterior neck muscles alone has the potential to induce lasting reduction in spatial neglect.

**Design:** A multiple baseline design was used to control for spontaneous recovery or uncontrolled change caused by external events.

**Patients:** Six patients with spatial neglect following right hemisphere stroke.

**Methods:** Daily vibration treatment of the left posterior neck muscles for 20 minutes on 10 consecutive days. During vibration, patients did not perform any specific activities.

**Results:** We observed significant amelioration of spatial neglect after terminating the vibration therapy. The improvement was found to be stable at follow-up testing about 1.4 years later.

**Conclusion:** Vibration of the left posterior neck muscles is a useful, non-invasive tool supplementing the established methods of spatial neglect treatment. It does not necessarily require the patient's co-operation, which is an important advantage especially in the early phases of rehabilitation.

**Key words:** spatial neglect, neck muscle vibration, rehabilitation, brain damage, human.

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### INTRODUCTION

Spatial neglect is a frequent sequel of right-hemisphere lesions. The exploratory behaviour of these patients is shifted toward the right side, leading to neglect of stimuli situated on the left (1, 2). Spatial neglect has an important impact on post-stroke recovery and functional outcome. At discharge from the rehabilitation unit, these patients show lower Barthel index scores, despite having received more therapy than patients with no spatial neglect but with comparable stroke pathology and motor severity (3). Spatial neglect is also associated with lower performance on measures of sensory-motor abilities, as well as

on measures of activities of daily life (4, 5). For a high proportion of patients the disorder becomes chronic. In patients with spatial neglect, 20–40% still show the disorder 6 months or more post-stroke (e.g. 6, 7). For these reasons, efficient strategies for the treatment of the neglect syndrome are required.

The majority of current neuropsychological training programs aim to train search strategies subserving visual exploration of the surroundings. Compensation for the deficit is obtained by an increase in gaze shifts to the contralateral side (8–10). A recent model of the mechanisms leading to spatial neglect assumes the central transformation of afferent sensory information (from the retina, neck muscle spindles, vestibular organs) into non-retinal spatial reference systems to be disturbed (11, 12). In line with this assumption, asymmetric vestibular stimulation (13, 14), optokinetic stimulation (15) and neck muscle vibration (16) were found to be powerful tools to evoke transient remission of neglect symptoms. Moreover, Rossetti et al. (17) observed considerable improvements in patients with spatial neglect in clinical neglect tests after visuo-motor adaptation to a rightward prismatic shift of the visual field.

However, the critical question about the use of such techniques for rehabilitation is whether or not these types of stimulation induce lasting as well as transient recovery of spatial neglect. Lasting amelioration has been reported recently using prism adaptation (18). Likewise, substantial recovery outlasting the duration of the application has been demonstrated for neck muscle vibration (19, 20). Ferber et al. (19) observed a considerable reduction in neglect symptoms in a single patient, who suffered from a right-hemisphere temporo-parietal lesion, after 20 minutes of daily vibration on 5 consecutive days. The improvement was found to be stable even after treatment off-set. Schindler et al. (20) evaluated the long-term efficacy of combined vibration and exploration treatment with that of visual exploration training alone in a group of 20 patients with spatial neglect. In the combination treatment, the patients performed the same visual exploration training while the contralesional neck muscles were vibrated. The authors observed a specific and lasting reduction in neglect symptoms with neck muscle vibration, which was superior to that achieved by visual exploration training alone. The reduction in the visual modality transferred to the tactile modality with a concomitant improvement in activities of daily living. At follow-up testing 2 months after discharge, the improvements were found to be unchanged.

The study of Schindler et al. (20) applied neck muscle vibration in combination with visual exploration training. The

goal of the present study was to investigate whether the lasting amelioration seen with neck muscle vibration depends on a combination treatment with visual exploration training or whether it is also possible to achieve lasting improvement in neglect symptoms by applying neck muscle vibration alone.

## METHODS

### Subjects and baseline measurements

Twenty consecutive patients (median age 74 years, range 51–89) admitted to a rehabilitation unit (Fachkliniken Hohenurach, Bad Urach) over a period of 1.5 years were investigated. Spatial neglect was diagnosed when the patients fulfilled the criteria in at least 2 of the following 4 neglect tests: the “Letter cancellation test” (21), the “Bells test” (22), the “Baking tray task” (23) and a copying task. For details of test analysis and criteria used for the diagnosis of neglect, see reference 24. The median time post-stroke at testing was 29.5 days (range 10–159 days).

All 20 patients underwent repeated neglect testing up to 5 times within a period of about 14 days after admission. The tests were administered by the neuropsychologists working at the rehabilitation unit, while data analysis was performed by the authors. Patients were excluded from the study when their test performance did not show stable neglect but rather spontaneous improvement, i.e. a trend of increasing test performance over the 5 baseline measurements.

Ten patients with spatial neglect were excluded from the subsequent experiment because of spontaneous improvement during the period of baseline measurement. The remaining 10 patients exhibited stable neglect across these 5 examinations. Two of these patients refused to take part in the subsequent experiment and 2 patients were transferred to another hospital for medical reasons before the experimental protocol could be completed. Thus, 6 patients participated in the present study. The patients and their relatives were informed about the technical procedure related to the daily application of neck muscle vibration. They gave their informed consent to participate in the study, which was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Table I gives an overview of the demographic and clinical parameters of these patients.

The first examination of the 6 neglect patients took place at a median of 54.5 days (range 19–159 days) after the stroke. They stayed in the rehabilitation unit for a median time of 52 days (range 49–63 days). During the whole period they received the conventional therapy program

provided by the unit, comprising standard physiotherapy, occupational therapy and neuropsychological training.

### Experimental protocol

We used a single case, multiple baseline design (25). In terms of group comparisons across time series, the multiple baseline design constitutes an incomplete study design. Nevertheless, the multiple baseline design resembles the most naturally arising study design in clinical practice. It has the advantage that each sequential single case spans a differing length of baseline due to individual complexities and clinical conveniences. This feature controls for the amount of baseline assessment (training) and spontaneous recovery. Furthermore, different lengths of baseline reduce the possibility of a correlation between the phase change and external events (25–27).

Severity of neglect was monitored using the “Bells test” (22) and the “Letter cancellation test” (21). The first 5 times of testing were part of the baseline measurements (see above) preceding the vibration interval. (For medical reasons, patient 3 was assessed only 4 times with the Bells test and the Letter cancellation task during the baseline period.) In the 6 patients participating in the study, the baseline was obtained over a median period of 17 days (range 14–24 days). After termination of the vibration interval, 3 further test sessions were carried out within a median period of 11 days (range 10–14 days). An additional follow-up examination, at a median of 410.5 days (range 112–866 days) after vibration, completed data acquisition. It is important to note, that the 6 patients had already received the conventional therapy program provided by the rehabilitation unit for a median duration of 26.5 days (range 21–32 days) before neck muscle vibration started.

### Vibration treatment

On 10 subsequent working days, each patient underwent daily transcutaneous mechanical vibration for 20 minutes on the left posterior neck muscles in a normally lightened room. During stimulation, the patients did not perform any specific activities besides a conversation with the investigator. Conversation was directed towards unspecific topics, such as the daily activities of the patient in the rehabilitation unit or the patient’s biography.

In order to find the optimal position of the vibrator on the left posterior neck muscles, each patient was asked to fixate straight ahead on a red light-emitting diode (LED) in a completely darkened room. The LED was located just in front of the sagittal body midline at a distance of 2 metres. The experimental, handheld vibrator (V 200 Series, Ling Dynamic Systems LTD, Royston, UK) was positioned on the left posterior neck muscles. The tip of the experimental vibrator was 1.5 cm

Table I. Demographic and clinical data for the participating neglect patients with ischaemic infarct. All patients were right-handed

Sex/Age (years)	Lesion location	Days since onset at first testing	Visual field defect	Paresis* of contralateral side	Somatosensory deficit of contralateral side (touch)	Barthel Index	Bells test†	Letter cancellation‡	Baking tray task§	Copying task¶
F/74	T,P,I	40	Hemianopia	Arm 3.5 Leg 3.5	Yes	35	Left 0 Right 5	Left 0 Right 22	Left 3 Right 13	Left – Right –
M/77	T,BG	70	Hemianopia	Arm 0 Leg 0.5	Yes	5	Left 0 Right 4	Left 2 Right 10	Left 5 Right 11	Left – Right –
F/71	FL,T,P,BG,Th,I	19	No	Arm 0 Leg 0	Yes	5	Left 0 Right 1	Left 0 Right 3	Left 3 Right 13	Left – Right –
F/54	FL,T,P,BG,I	159	Hemianopia	Arm 2.5 Leg 2.5	Yes	25	Left 2 Right 14	Left 1 Right 21	Left 2 Right 14	Left – Right +
F/76	FL,P	69	No	Arm 0.5 Leg 3.5	Yes	5	Left 0 Right 5	Left 0 Right 21	Left 0 Right 16	Left – Right +
M/58	FL,T,P,BG,I	21	No	Arm 0 Leg 3	No	15	Left 1 Right 10	Left 0 Right 10	Left 7 Right 9	Left – Right +

T = temporal lobe; P = parietal lobe; I = Insula; BG = basal ganglia; FL = frontal lobe; Th = thalamus. All lesions were demonstrated by magnetic resonance imaging or computed tomography. \* Paresis of the contralateral arm and leg was scored with the usual clinical ordinal scale, where 0 = no trace of movement and 5 = normal movement. † Number of correct targets on each half of the test sheet,  $n_{\max} = 15$ . The 5 targets of the central column were not regarded. ‡ Number of correct target letters on each half of the test sheet,  $n_{\max} = 30$  on either side. § The ideal number of items within each half of the test sheet is 8. ¶ Multi-object scene consisted of 4 elements (a fence, a car, a house and a tree) 2 in each half of a DIN A4 sheet of paper: – = omission of at least 1 whole object; + = copying without omissions.

wide and oscillated with an amplitude of 0.4 mm and a frequency of 80 Hz. The position of the vibrator was varied on the neck muscles until the patient consistently reported an illusory horizontal movement of the stationary LED to the right. This location was marked by means of a water-resistant pencil. When the patient reported no reliable illusory movement of the LED, the starting position under the left occiput was marked. This was done in 3 of the 6 patients (numbers 1, 2 and 3). Subsequently, the room light was turned on and the first 20-minute vibration interval started.

RESULTS

We averaged the performance of the patients across the baseline period as well as across the post-treatment phase and computed separate analyses of variance (repeated measures design) for the “Bells test” and for the “Letter cancellation test” over the 3 measurement periods (baseline, post-treatment, follow-up). We found a significant difference between the 3 periods in the “Bells test” ( $F(2, 10) = 11.82, p = 0.002$ ) and in the “Letter cancellation” task ( $F(2, 10) = 8.35, p = 0.007$ ). For *post hoc* analysis, we calculated paired *t*-tests between baseline and post-treatment period and between the post-treatment period and the follow-up examination using a Bonferoni corrected  $\alpha$ -level. We found a significant improvement between baseline and post-treatment period for the “Letter cancellation” test ( $t = -3.20, p = 0.02$ ), but not for the “Bells test” ( $t = -2.93, p = 0.03$ ). The comparison between the post-treatment period and the follow-up examina-

tion did not reach significance for the “Bells test” ( $t = -2.31, p = 0.07$ ) or for the “Letter cancellation” task ( $t = -2.04, p = 0.10$ ).

Thus, analysis of the group data revealed a significant improvement in spatial neglect in the “Letter cancellation” task, which was stable for a follow-up period of more than 1 year. Although not statistically significant, comparable observations were made for the “Bells test”. The 6 patients showed an average improvement of 25% in the “Letter cancellation” task and of 29% in the “Bells test” after stimulation (post-treatment interval). One patient (number 2) did not profit from the vibration treatment (c.f. Fig. 1). Across the whole experimental period of 37 days, he showed no improvement in neglect symptoms. Since this subject did not report a consistent illusory movement of the LED upon stimulation, a non-optimal location of the vibrator on the left posterior neck muscles might have been selected. However, 2 other patients (numbers 1 and 3) also did not report an illusory movement of the LED, but nevertheless improved by the vibration treatment.

DISCUSSION

The patients participating in the present study were representative of those with severe spatial neglect. They were not selected for any particular variable except that they showed stable neglect during the period of baseline measurement (see methods chapter). Thus, it is not surprising that our sample was skewed

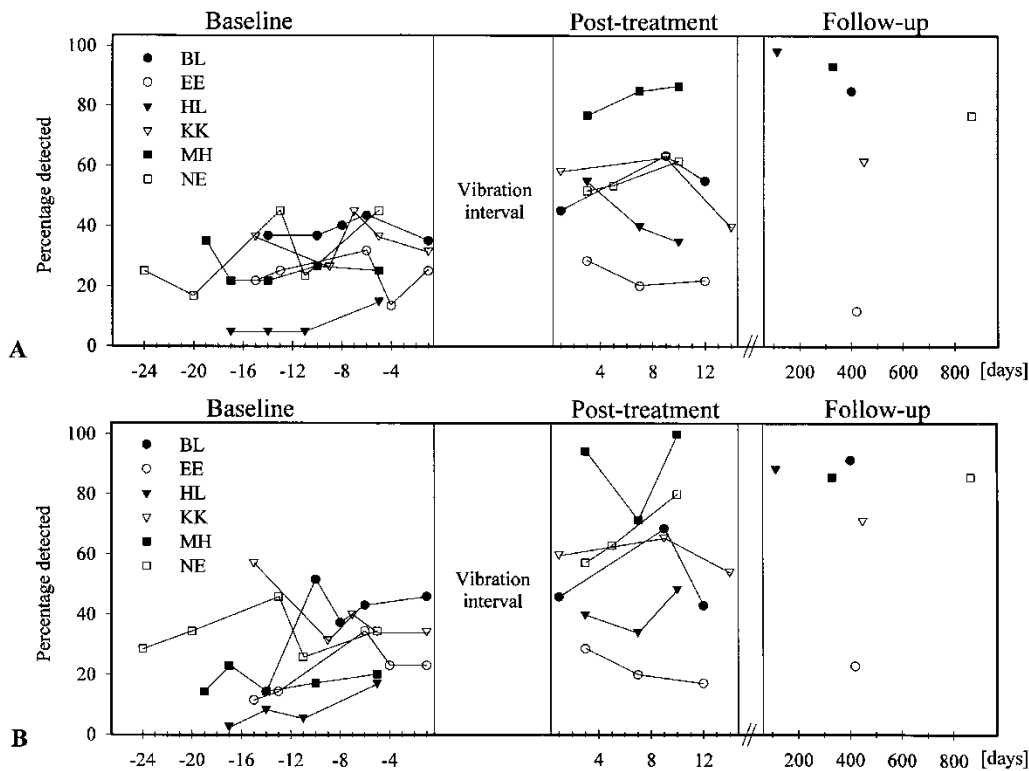


Fig. 1. Percentage of detected targets in (A) the “Letter cancellation” task and (B) the “Bells test”. Each patient is illustrated separately. Patients were examined 5 times during the baseline period and 3 times after the vibration interval. (Patient 3 was the only subject examined only 4 times during the baseline period). The patients had a further re-evaluation on average 1.4 years after the vibration therapy terminated.

towards major strokes and severe neglect since patients with less severe neglect symptoms are more likely to show spontaneous recovery. We found daily application of sole left posterior neck muscle vibration to result in a reasonable amelioration of spatial neglect in clinical standard tests for spatial neglect. The positive treatment effect was observed directly after terminating the vibration period and still was found stable after 1.4 years (on average) when the patients were re-examined. Thus, daily neck muscle vibration is capable of inducing an improvement in neglect symptoms even without concurrent visual exploration training as has successfully been used by Schindler et al. (20).

A possible objection to the efficacy of treating spatial neglect by neck muscle vibration in the present study might be the assumption of a placebo effect. This possibility had been excluded in the study of Schindler et al. (20) who used a crossover design, but could not be controlled in the present investigation using a single case, multiple baseline design (25). Nevertheless, several aspects argue against this assumption. Firstly, we did not perform neglect tests during the vibration interval. The experimenters thus had no knowledge of any improvement or degradation to be fed back to the patients. In addition, before and after the 10 days vibration interval, the patients were not given any feedback regarding their performance in the clinical neglect tests. Moreover, all patients were extensively cared for by the regular staff of the rehabilitation unit. The patients thus received various feedback information on their general recovery process before, during and after the vibration interval due to the conventional therapy program of the rehabilitation unit. The intervention by neck muscle vibration was only one feature of the daily rehabilitation program and thus did not have a prominent status for the patients.

The asymmetrical behaviour observed in patients with spatial neglect has been hypothesized to rely on disturbed central co-ordinate transformations necessary to obtain non-retinal representations of space (11, 12). In order to generate these non-retinal representations, the central nervous system has to integrate multimodal afferent information. In monkeys, Grueser et al. (28, 29) located an area for integrating vestibular, somatosensory and visual cues in the posterior insula. The authors suggested that this region processes information concerning the movement of the head in space and movement of the head in relation to other parts of the body. The human homologue of this area has been investigated by Brandt et al. (30). In 23 brain-damaged patients with vestibular dysfunction, they found a lesion overlap in the posterior insula. In search for those cortical regions, that integrate the different afferent information to encode non-retinal coordinate systems, Bottini et al. (31) conducted a positron emission tomography (PET) study. They found the insula and the retroinsular cortex amongst other areas to be responsive to both caloric vestibular and neck muscle vibration. Bottini et al. concluded that such convergence may constitute one neural basis for the building up and updating of non-retinal representations of space. Vibration of left posterior neck muscles thus can be regarded as a bottom-up activation of these higher-order transformation processes.

The properties of neck muscle vibration were examined more closely by Karnath et al. (32) in healthy subjects. The authors investigated the interaction between visual information and neck proprioception in the perception of the "subjective straight ahead" as a function of stimulation duration. Without a visual reference, neck muscle vibration led to a disparity between subjective perception and objective position of the body midline. This displacement of the subjective straight ahead was sustained throughout the entire stimulation period of 28 minutes. Moreover, prolonged vibration of the neck muscles led to a continuing disparity even after offset of the vibration. The longer the preceding vibration, the more persistent the illusory deviation of body orientation. Their results thus showed that the deviation of the subjectively perceived body orientation induced by prolonged asymmetric neck vibration does not habituate under stimulation and has effects which endure after the vibration terminates. In this respect, the present clinical study demonstrates that daily vibration of the left posterior neck muscles over a period of 2 weeks may result in lasting recalibration of the egocentric co-ordinate systems in patients with spatial neglect.

The selective activation of these neural processes of spatial co-ordinate transformation for therapeutic purposes has considerable advantages that supplement the conventional treatment approaches. The established methods for treatment of spatial neglect depend on certain cognitive and motivational suppositions on the side of the patient. The patient has to be able to cooperate for a certain time period and needs to be willing to acquire and to use the learned exploration strategies. These capabilities cannot be expected in each patient, especially not in the acute phase after the stroke. Stimulation by neck muscle vibration does not depend on the general cognitive status of the patient and thus seems to be a useful supplement of the conventional rehabilitation techniques.

Another bottom-up approach for the treatment of spatial neglect is based on the observation of considerable improvements in spatial neglect in clinical standard neglect tests following short-term adaptation to prismatic lenses creating a visual shift of 10 degrees to the right (17, 33). After adapting to the visual shift and removal of the prisms, neglect patients showed a significant improvement in performance, which lasted for at least 2 hours. Frassinetti et al. (18) extended these findings. Seven patients with spatial neglect were treated by twice-daily sessions of prismatic adaptation on 10 consecutive working days. The improvements in spatial neglect on a variety of different tasks were shown to be stable for at least 5 weeks after the treatment period. The authors reported an increasing amelioration of spatial neglect as a function of time following the termination of the treatment. Interestingly, this upward trend in recovery following the offset of the treatment was also seen in some patients in the present study.

To summarize, neck muscle vibration significantly improved spatial neglect in the absence of any concurrent exploration training. Amelioration was not only transient but still was present when patients were re-examined more than 1 year after

treatment off-set. Neck muscle vibration has the advantage of being suited for stimulus application anywhere and anytime, even at home after discharge from the hospital. The vibration treatment is tied to less prerequisites concerning the functional status of the neglect patients, which is an important advantage especially in the early phases of rehabilitation. Furthermore, neck muscle vibration is non-invasive, has no side-effects and is technically easy to apply. It thus seems to be a useful tool to supplement the established methods in the rehabilitation of spatial neglect.

Future research has to investigate the transfer of pure vibration treatment to activities of daily life as this has been done for the combination of vibration with exploration training by Schindler et al. (20). Furthermore, it remains to be proved whether a combination of neck muscle vibration with other bottom-up treatment approaches might lead to additive effects. For example, it is known that the stimulation of proprioceptive receptors by muscle vibration augments the after-effect of adaptation to a prismatic shift (34, 35). Therefore, the regular combination of neck muscle vibration with, for example, adaptation to a prismatic shift might result in an even more pronounced improvement in spatial neglect.

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