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ORIGINAL COMMUNICATION

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Idiopathic spasmodic torticollis is not associated with abnormal kinesthetic perception from neck proprioceptive and vestibular afferences

Abstract Proceeding from recent evidence for a sensory involvement in the pathophysiology of idiopathic spasmodic torticollis (ST), we asked whether the abnormal head posture of these patients is associated with distortions of their internal spatial reference frames due to abnormal processing of neck proprioceptive and/or vestibular input. Twelve ST patients were instructed to estimate, by adjusting a light pointer in the dark, their head and trunk mid-sagittal directions (as representatives of ego-centric references) and to reproduce a remembered target location in space (space centric reference). They did so before and after horizontal head and trunk rotations, which evoked isolated or combined vestibular and/or neck stimulation. In ST patients, unlike in normal controls, pre-stimulus estimates of the head and trunk mid-sagittal directions (baselines) showed a pronounced across-subjects variability, with essentially normal mean values. Their post-stimulus estimates in all tasks, after correction for the individual baseline errors, were normal with respect to both amplitude and variability, independent of stimulus direction, modality and rotation dynamics. Our findings suggest that ST patients have a rather inaccurate knowledge of their head posture, but can effectively use neck proprioceptive input and vestibular cues when estimating head and trunk displacements in ego-centric and space centric spatial orientation tasks. We propose that an offset of a non-sensory set point signal in the neck proprioceptive loop for head-on-trunk control may be responsible for the pathological head deviation in ST.

Key words neck proprioceptive input · vestibular input · spatial orientation · torticollis · dystonia

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Introduction

Dystonia is characterised by prolonged muscle contractions leading to sustained twisting movements and abnormal postures of the affected body parts. Co-contraction of agonist and antagonist muscles and overflow of activity to inappropriate muscles are salient features of the disorder during voluntary movements. The pathophysiology of primary dystonia is still obscure, but most evidence suggests that it results from a functional disturbance of the basal ganglia, leading to an altered motor cortical excitability [6]. An involvement of the sensory systems has recently become a matter of debate in idiopathic spasmodic torticollis (ST), the most common form of focal dystonia, and in other dystonic syndromes [13].

Based on findings of spontaneous nystagmus and directional preponderance of the vestibulo-ocular reflex (VOR) in a high percentage of ST patients, an imbalance of the vestibular tone, due to a breakdown of central vestibular functions, has been discussed as a mechanism for this disorder as well as a disruption of voluntary interaction with the vestibulo-collic reflex [7, 29]. Also, a

JON 1034

special role for dystonia has been attributed to the proprioceptive input stemming from muscle spindle afferents [11, 15, 30, 32]. The increase of cerebral blood flow in the primary sensorimotor cortex, evoked by muscle vibration of a limb in normal subjects, was found to be subnormal in dystonic patients [32]. This stimulus can induce involuntary spasms resembling dystonic postures [15, 32]. Furthermore, vibration may induce limb movement illusions and, when evoking actual movements, these are abnormally perceived by ST patients (magnitude is underestimated), effects that are independent of treatment with botulinum toxin [11, 30]. The latter finding has been attributed to misinterpretation of kinesthetic information mediated by Ia muscle spindle afferent discharges. Finally, vibration of neck muscles in upright stance leads to a forward body sway deviation, the effect being less in ST patients than in controls [16], possibly indicating a reduced role of neck afferents for spatial orientation and postural control. Noticeably, all these studies reported bilateral abnormalities, a fact which cannot be easily related to the asymmetrical head posture in ST.

Other studies have focused on the supraspinal control of sensorimotor integration. They provided evidence that the "gain" of cortical input-output relationships, as assessed by transcranial magnetic stimulation, is increased in dystonic patients [14, 19], while plastic changes of neuronal populations in the primary sensory cortex are considered by some authors to represent a crucial causative factor of hand dystonia [5, 8]. In a review of a number of electrophysiological and imaging studies, Beradelli et al. [6] formulated a concept on the role of the basal ganglia in dystonia. Overactivity in the direct putamenopallidal pathways is thought to lead to disinhibition of the thalamus and thus to altered (mainly increased) thalamic input to the cortex, with local factors in these loops determining a distributed or a more focal manifestation of the dystonic symptoms. There remains the question, which sensorimotor functions would be affected by these alterations.

Spatially oriented motor behaviour usually requires sensory information from more than one source. For instance, when we update the location of a previously seen visual target in space for the purpose of a gaze shift, we have to resort to the previously acquired information of retinal, eye-in-orbit and head-in-space positions and to compare it with the momentary positions. An abstract formalism to describe the sensory interactions would be to view them as discrete steps of coordinate transformations from a retinal frame of reference via the head into space coordinates [4], which have been shown to involve eye position, vestibular and axial proprioceptive inputs [25]. It is still a matter of debate how the multi-sensory derived internal representations of the external stimuli are used for the control of movements. One suggestion is that they are used as set point signals for the proprioceptive feedback loops that control joint posture [21, 22, 26]. In this view, there are two distinct proprioceptive signals involved in the sensorimotor control, one serving the interaction with the environment, the other stabilising the body segments with respect to each other ("local" control). Could it be that only one of the two signals is affected in ST (and in dystonia in general)? There is evidence that primarily the local proprioceptive signal may be affected in ST patients. Recent experiments, in which eye-head coordination was investigated [18], showed that the head movements performed in the wake of gaze shifts to target locations in space are normal in ST patients, if the contribution of the abnormal head-on-trunk posture is taken into account in the data analysis.

There may be a perceptual correlate for this notion of an erroneous head-to-trunk signal. ST patients, when asked to rotate a target line in the frontal plane until it was perceived as parallel to the longitudinal axis of their heads, failed to do so, unlike normals. Instead, they set the line to upright, on average, i. e. parallel to the mid-sagittal plane of their trunks [2]. Similarly, in a previous study in which we tested the subjective visual straight ahead (VSA) after rotations of the head and trunk, ST patients referenced it to their trunks, unlike normal subjects who use a head-centric frame of reference [3]. One could conclude that these findings reveal a direct correlate for an erroneous proprioceptive head-on-trunk signal. However, the finding in patients was independent of the direction of the torticollis and of the rotational stimulus. Furthermore, it is not specific for ST patients; also vestibular loss patients tend to adopt a trunk-centric strategy when performing the VSA task [17]. We therefore considered an alternative explanation and attributed the finding to a strategy, by which ST patients avoid an adapted and therefore unreliable neck-on-trunk signal. Finally, it remained open in the psychophysical studies whether and to what extent the proprioceptive signal, which is used in combination with a vestibular signal for the interaction with the environment, might be affected in ST patients.

The present study was undertaken to assess the presumed two proprioceptive signals separately for comparison. To this end we assessed in psychophysical experiments ST patients' estimates of perceived head and trunk mid-sagittal planes (the distinction between the two is determined primarily by neck proprioceptive input) and of target locations in space before and after head and trunk rotations (a task which involves a vestibular-proprioceptive interaction). Since there is literature suggesting that dynamic rather than static aspects of proprioception may be disturbed in ST patients [11, 28, 30], we varied the dynamics of the rotational stimuli.

Patients and methods

Subjects

Twelve ST patients (Ps; age, 43.8 ± 10.7 years) and 12 normal subjects (Ns; 39.4 ± 10.7 years) gave their informed consent to the study, which was approved by the ethics committee of the Freiburg University Clinics. All patients were under treatment with botulinum toxin. They were tested after a minimum interval of 3 months following the last injection of the toxin in the neck muscles. Head turn in the horizontal plane, head tilt in the frontal plane and anteroposterior deviations in the sagittal plane of the body were measured separately by means of a large protractor when sitting at rest (details have been described in a previous paper [3]). The dystonia was quantified using the scale proposed by Tsui et al. [33] excluding shoulder elevation: values were assigned as 0 for absent, 1 for head deviation < 15°, 2 for head deviation 15–30° and 3 for > 30°. Only patients with predominant head turn (deviation in the horizontal plane of the body) participated (mean disease duration 6.1 ± 3.4 years; mean severity score, 3.4 ± 1.0). Patients with prominent head jerks and/or tremor were excluded. Patients' clinical details are given in Table 1. None of the patients was taking CNS-active medication.

Apparatus and stimuli

Subjects were seated on a position-controlled Barany chair in the centre of a cylindrical screen of 1 m radius. Their heads were stabilized by means of a dental bite-board attached to a head holder. During measurements, care was taken to perfectly align the head with respect to the trunk in Ns. Patients' head position, which could vary over time in the wake of their ST, was also fixed, but in a deviation that corresponded to the minimal head turn without producing discomfort (the degree of the remaining abnormal head turn of each patient during testing was recorded; it amounted to 5°, on average, in the direction of the torticollis). This correction was necessitated by mechanical limitations of the head rotation device. The head holder was affixed to the chair, but could be rotated by a servo motor independently from the chair in the horizontal plane (dynamics of chair and head rotation devices were matched to each other under computer control). A light spot, subtending 0.2° of visual angle, could be projected at eye level onto the screen and moved horizontally by means of a mirror galvanometer. The axes of the galvanometer, the turning chair, and the head gear were co-linear.

Table 1 Clinical details of 12 patients with idiopathic spasmodic torticollis. Positive values of head turn signify deviation (in degrees) of the chin to the right. Severity score after [33].

Patient	Age (years)	Disease duration (years)	Head turn at rest	Severity score
1	51	7	–25	3
2	48	16	–15	3
3	51	4	35	4
4	60	6	22	5
5	61	4	–10	2
6	34	4	–35	5
7	24	5	–8	3
8	36	6	–30	4
9	21	3	–10	2
10	44	6	5	3
11	37	7	15	3
12	35	5	25	4

Whole-body rotation (turning the chair alone) was used to generate the vestibular stimulus (VEST). Isolated neck stimulation (NECK) was obtained by rotating both the head gear and the turning chair about the same angle, but counter to each other, so that the head remained stationary in space (the direction of the neck proprioceptive stimulus was defined here by the direction of the trunk displacement relative to the head; see Figs. 2–4, insets). Rotation of only the head gear, resulting in head rotation on the stationary trunk, was used to produce a vestibular-neck stimulus combination (VEST + NECK). The rotation trajectories showed a 'raised-cosine' velocity profile [17]. Angular displacement was kept constant at 16°, while stimulus duration was varied (10, 5, and 1.25 s; measured peak angular velocity amounted to 4, 8, and 28°/s, respectively). These stimuli were designed to contain the following dominant frequencies: 0.1, 0.2 and 0.8 Hz (in order to be able to relate the present findings to the known dynamic characteristics of the vestibular and neck systems, which usually are given for the frequency domain). Notably in earlier work from our laboratory [24] we have shown that subjects' head torque arising during the rotational stimuli does not correlate with their self-motion estimates, which makes it very unlikely that tactile information from the head gear via the dental bite boards influenced the results to a considerable degree.

The mirror galvanometer received two inputs. One input was generated by a computer and stepped the light spot 10° to either side (probe stimulus) and the other stemmed from a joystick, which was handled by the subjects during the psychophysical procedure. The performance of the subjects during the experimental tasks was continuously checked by means of an infrared video camera.

Instructions and experimental procedure

Trials consisted of three parts (see Fig. 1): (a) *Baseline.* After turning off the room lights, a probe stimulus sequence was dispensed consisting of three steps of the light spot in either direction (inter-step interval 2.5 s; step direction changed after each second step). The subject had to bring the light spot into a position given by the task (see below). (b) *Stimulus.* A rotational test stimulus (VEST and/or NECK) was applied in complete darkness. (c) *Response.* Two seconds after stimulus end a second, identical probe sequence was presented to see how the rotational stimulus had affected the perception (see below). Thereafter head and trunk were returned to their starting positions in the dark and the subject was given a short break with the room lights turned on.

The test runs for each of the three tasks listed below consisted of 18 such trials (3 stimulus durations × 2 directions × 3 different test stimuli) in random order and lasted 30–40 minutes. Rest periods of several minutes were allowed after 3–4 trials. The subjects were instructed to relax their neck muscles as much as possible and not to resist, or to help actively the imposed head rotations.

Subjects were asked to perform three tasks according to the following instructions:

(A) "... set the spot in the *head-midsagittal* direction and, when it is stepped to one or the other side, restore its location as fast as possible. After the application of the rotational stimulus, recentre the spot with respect to the middle of your head" ('*head task*').

(B) "... set the spot in the *trunk-midsagittal* direction, and when it is stepped to one or the other side, restore its location as fast as possible. After application of the rotational stimulus, recentre the spot with respect to the middle of your trunk" ('*trunk task*').

(C) "... set the spot in the straight ahead direction and, when it is stepped to one or the other side, restore its location as fast as possible. Remember its *location in space*. After application of the rotational stimulus, restore its former location in space" ('*space task*').

The tasks were performed in a latin square order.

Prior to these experiments, an 'objective' baseline value was obtained, by asking each subject to indicate under visual control (i. e., in the illuminated laboratory) the mid-sagittal of the trunk; after appropriate adjustments of the chair, this value was taken as the 'objective' trunk mid-sagittal (0°).

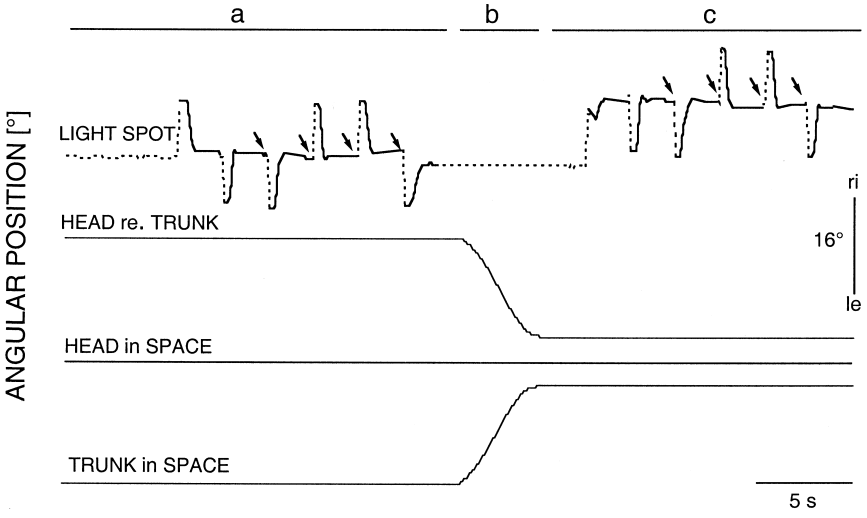

Fig. 1 Experimental paradigm (task: indication of trunk mid-sagittal). (**a**) Baseline (head and trunk aligned). Patient views a light spot (trace 'light spot'; bold curve, spot visible; dashed, spot extinguished), adjusting the spot to the trunk mid-sagittal plane by means of a joystick. He does so six times following a computer generated step of the spot to either side. Arrows indicate spot position values collected for analysis. (**b**) Stimulus (NECK; dominant frequency, 0.2 Hz). In complete darkness patient's trunk is rotated in space 16° to the right (up) and his head relative to the trunk at the same time and by the same amount to the left (down), such that his head remains stationary in space. (**c**) Response. Upon reappearance of the spot, the patient again brings it into the direction of his trunk mid-sagittal (six times).

Data acquisition and analysis

Position readings of the two galvanometer inputs, of the galvanometer output, of chair and head holder potentiometers and of the on-off signal of the light beam were sampled at 100 Hz and stored in a laboratory computer for off-line analysis. The last 20 data points that preceded each step displacement of the light spot were marked with an interactive computer program (Fig. 1, arrows) and were stored as displacement values in relation to the primary (chair and head gear) position. Equal numbers of rightward and leftward steps were analysed [17]. The mean of the 2nd to 5th response (i. e., responses to two steps in either direction) for the baseline and for the response after the vestibular and/or neck stimuli were calculated. The stimulus response was related to the baseline (difference between the two mean values). *Indication variability* was defined as the standard deviation across the second to fifth responses in the step sequences of each subject and its mean value is taken in the following as a measure of the sensorimotor matching performance. *Inter-trial variability* of the baseline was defined as the standard deviation across the corresponding 18 mean values of the baseline indication of each subject with each instruction and its mean value is taken as an accuracy measure for subjects' internal notion of their head or trunk mid-sagittals and VSA, respectively (compare [25]).

Statistical analysis

Significance of findings was tested by analysis of variance unless stated otherwise. The analysis was performed twice, once without normalizing the patients' data with respect to the horizontal direction of their torticollis and a second time after performing such a normalization (i. e., after reversing appropriately the responses of the five patients with rightward torticollis). The statistical results were essentially the same and their presentation in the following refers to the normalized data, as if all of our patients had a leftward torticollis.

Results

At the outset of the measurements we minimized patients' abnormal head turns without causing them discomfort. Their heads were brought from the 'spontaneous' eccentricity in the head-free (unrestrained) condition of $-22 \pm 13°$ to a mean value of $-5 \pm 5°$ (positive/negative values, to the right/left) in the experimental condition, during which their heads were fixed by means of the bite-board (see Methods). Normals always started the trials with the head aligned with the trunk mid-sagittal.

Head task

Normal subjects' judgements of their heads' mid-sagittal direction at trial onset ('baseline' in the primary body position prior to the rotational stimuli) varied between $-2.1°$ and $2.0°$ (across-subjects mean $\pm$ SD, $0.7 \pm 1.2°$). Patients' baseline values (taken with a $-5°$ head-on-trunk offset; see Methods) showed a similar mean value, but a large scatter, varying between -6.5 and $11.4°$ ($-1.0 \pm 5.8°$; note large *across-subjects baseline variability* of $\pm 5.8°$ in patients versus $\pm 1.2°$ in normals; see end of Results section). Noticeably, the patients' judgments were unrelated to both their abnormal head turns at rest and to the head-on-trunk offset at trial onset (Pearson correlation, rho = 0.46 with $p = 0.1$ and rho = 0.52 with $p = 0.1$, respectively). These baseline values served in the following, on an individual basis, as a reference for the subjects' judgments after the stimuli.

Normals centred the light spot after the vestibular stimulus (VEST, whole body rotation to the right, + 16°, and left, −16°) almost perfectly in the direction of their head mid-sagittal, i. e. their responses were veridical in that they fell close to the ideal values of + 16° and −16°. They did so similarly across the three frequencies tested and for the two directions of rotation (Fig. 2, VEST, hatched areas). Similarly, the responses for NECK (head rotation under the stationary head) and for VEST + NECK (head rotation on stationary trunk) were approximately veridical, apart from a small illusory shift

of the subjective head mid-sagittal upon NECK at low frequency in the direction of the relative head-to-trunk displacement (2.8 ± 5.3° at 0.1 Hz).

Patients' responses, after correction for the individual baseline errors, closely resemble those of normals (Fig. 2; full and dashed lines connecting means). They were statistically not different from normals' responses when treated by a 3 X 3 X 2 X 2 factorial ANOVA with Stimulus Condition (VEST, NECK and VEST + NECK), Duration (10, 5 and 1.25 s) and Direction of stimulus (left versus right) as the within-subject repeated measures factors and Group (Ps versus Ns) as the Between groups factor. Thus, patients' judgments of their head mid-sagittal were independent of the direction of the torticollis and were not affected by their head-on-trunk offsets that prevailed during recordings.

Note that the *across-subjects responses variability* in patients shown in Fig. 2 (SE bars) is similar to that of normals. This also applied to the *indication variability* of the baseline (Ns: ± 0.8°, Ps: ± 1.1°) and the responses (Ns: ± 1.1°, Ps: ± 1.4°), as well as to the *inter-trial variability* of the baseline values (Ns: ± 2.1°, Ps: ± 2.0°; tested by factorial ANOVA as above). Thus, baseline-corrected variability of the responses to the rotational stimuli was essentially normal in patients, unlike the variability of the baseline itself across subjects (see above).

Trunk task

Normal subjects' baseline values for the trunk mid-sagittal (0.8 ± 2.2°) were very similar to the baseline values in the head task. Also the patients' baseline values were like those before (0.6 ± 5.5°). As before, there was no correlation with head turn at rest or offset during testing in the patients. Statistically, their baseline values closely resembled those of normals (note, however, that *across-subjects baseline variability* is again considerably larger in patients than in normals, ± 5.5° vs. ± 2.2°). *Inter-trial variability of the baseline* was comparable between normals and patients (± 2.2° vs. ± 2.0°, on average), as was the *indication variability* of the baselines (± 0.7° vs. ± 0.9°) and the responses (± 1.1° vs. ± 1.3°).

The responses for the indication of the trunk mid-sagittal plane are given in Fig. 3. Both groups estimated correctly their trunk mid-sagittal, i. e. their responses corresponded approximately to the 16° trunk excursion after VEST and NECK at all frequencies tested and fell close to 0°, on average, when the trunk remained stationary and only the head was rotated (VEST + NECK). Statistical analysis of these responses with ANOVA (same as for the head task) did not reveal any differences between normals and patients.

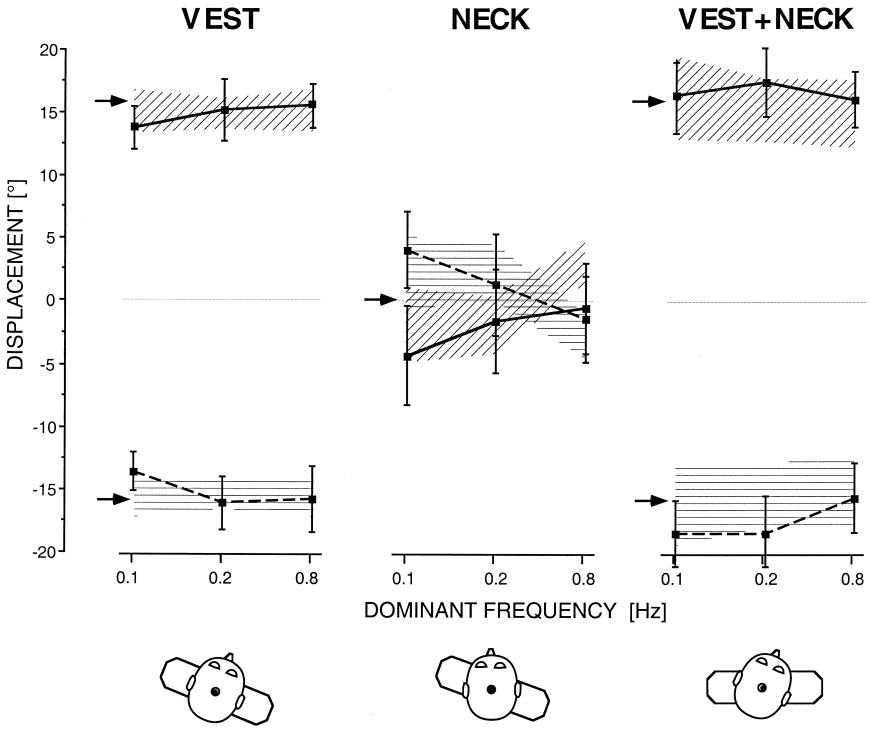

Fig. 2 Estimation curves for head mid-sagittal ('head task'). Responses of normal subjects (shaded areas, means ± 1 SE; averaged for left and right rotations, since there was no statistical difference for the two directions) and the patient group (means connected by solid and dashed lines for rightward and leftward rotations, respectively; error bars represent ± 1SE) following vestibular, neck, and combined stimulations (VEST, NECK, VEST + NECK) relative to baseline values. Horizontal arrows indicate where ideal (veridical) values would fall for the head-midsagittal. Pictograms (subject from above) represent the position of body segments after rightward rotational stimuli. Note close correspondence between the curves of patients and normal subjects.

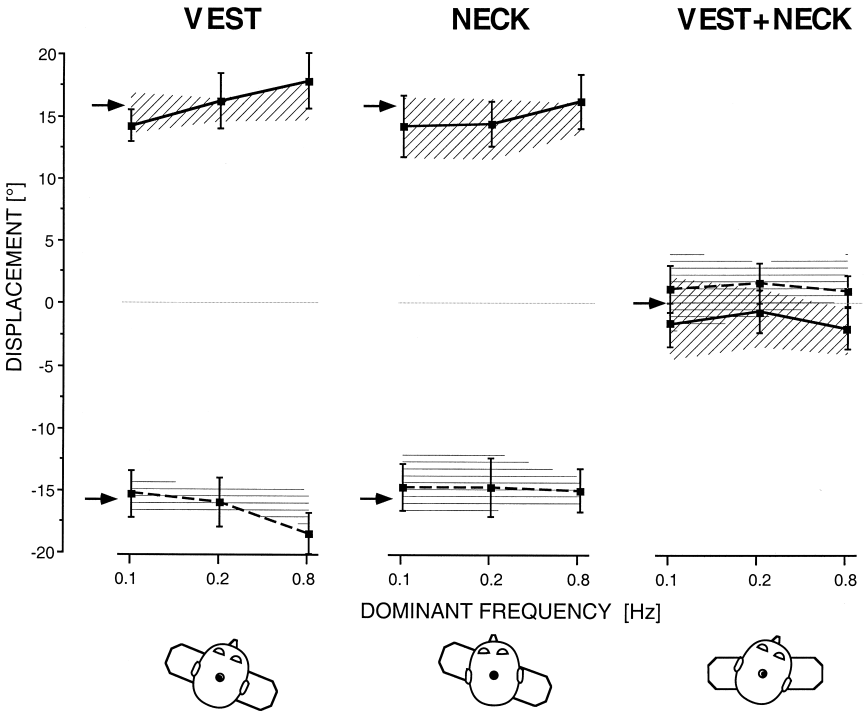

Fig. 3 Estimation curves for trunk mid-sagittal ('trunk task'). Presentation as in Fig. 2. Horizontal arrows indicate where ideal (veridical) values would fall for the trunk-midsagittal.

Space task

The subjective visual straight ahead (VSA) direction, which served as baseline for the space task, averaged 0.2 ± 2.2° for normals and –0.3° ± 4.6° for patients, thus resembling the baseline values in the previous tasks. As before, the values for patients were unrelated to the head turn at rest and the head-on-trunk offset during testing (Pearson rho = 0.23 with p = 0.5, and rho = 0.48 with p = 0.1, respectively). Note that the *across-subjects baseline variability* is again larger in patients than in normals (± 4.6° vs. ± 1.2°).

The responses to the rotational stimuli are shown in Fig. 4. Following the VEST + NECK stimulus, updating of the location of the light spot was almost ideal, after correction for the individual baseline errors for all three frequencies in both groups (arrows indicate veridical responses: 0° in all three stimulus conditions). Close-to-ideal updating also applied to VEST and to NECK at 0.8 Hz. When lowering stimulus frequency of both VEST and NECK, the responses showed a progressively increasing error in the direction of trunk excursion (± 16°). The error for VEST amounted at 0.1 Hz to 8.2 ± 6.0° for normals and to 8.8 ± 6.6° for patients (means ± SD across the two rotation directions). The corresponding mean errors for NECK were slightly higher (normals: 12.0 ± 6.7°; patients: 11.6 ± 7.9°). Statistical analysis with ANOVA (same as above) showed that there is no significant difference between the two groups. Note that the frequency dependent error of the vestibular and neck contingent updating of object localization in space, which reflects the high-pass characteristics of the corresponding self-motion perception, and its elimination with VEST + NECK during head rotation on stationary trunk closely corresponds to previous findings from this laboratory [17, 23, 25, 27].

Normals' and patients' *indication variability* of their baseline (± 0.8° and ± 1.0°) and responses (± 1.0° and ± 1.3°, respectively) resembled each other and were similar to those obtained in the head and trunk tasks. The same applied to baseline *inter-trial variability* (± 2.3° and ± 2.4°). In contrast, *across-subjects response variability*, though similar in the two groups, was larger in the 'space task' than in the 'head task' and the 'trunk task' (compare SE bars in Fig. 4 to those in Figs. 2 and 3).

When comparing with ANOVA the baseline values of subject groups across the three tasks (3 X 2 factorial ANOVA, with Task as the within-subject repeated measures factor and Group as the between groups factor) we found no significant differences or interactions (i. e., the mean values were close to zero in both groups with all three tasks). However, *across-subjects baseline variability* was higher in patients than in normals with all three tasks when tested with the Fisher test for variance ratio ($p < 0.02$ for all tasks). Furthermore, a comparison between baseline values in the three tasks revealed that they were highly correlated with each other in patients ($p < 0.0001$ with all three possible pairs), unlike in normals.

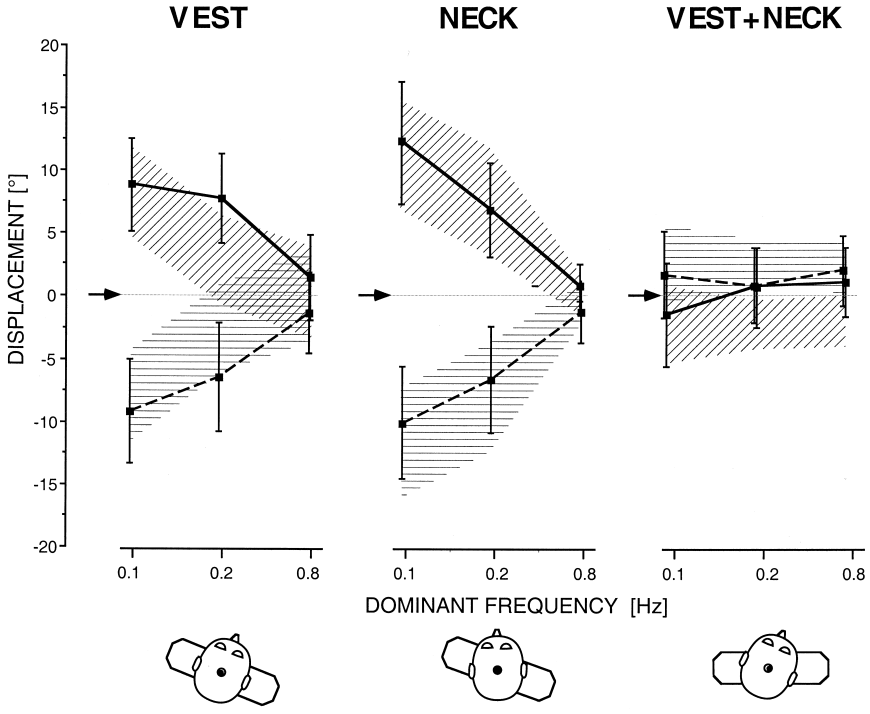

Fig. 4 Estimation curves for normal subjects' and patients' reproduction of visual target location in space following VEST, NECK, and VEST + NECK ('space task'). Horizontal arrows indicate where ideal values would fall for a veridical reproduction (0°). Otherwise presentation as in Fig. 2.

Discussion

The point of departure of the present study was the current debate whether sensory input, or its central processing, is impaired in ST patients as a pathophysiological factor determining the abnormal head posture, with the focus of interest on neck proprioception. Previous findings concerning the role of neck proprioception for torticollis are controversial. We conceived the possibility that this may be due to the fact that there are at least two different neck proprioceptive signals, which have not been so far selectively assessed in ST patients. We addressed this issue, following the hypothesis that sensorimotor control of head movement involves two different proprioceptive signals, one that is used in vestibular-proprioceptive interactions for the referencing of action and perception to the external world (space) and the other for the local control of inter-segmental joints, here the neck [21, 26]. In particular, we proceeded from previous work that indicates that psychophysical methods allow us to differentiate between the two signals [17, 23, 25, 27] and tried to identify one of them as being responsible for the dysfunction.

A simplified scheme is presented in Fig. 5 to explain in brief the concept of the two proprioceptive signals (for details, see [25]). In the figure we assume a 'local control' mechanism of neck muscle activity by means of a proprioceptive negative feedback loop (I), which stabilizes the head on the trunk in a given position. The currently desired position or position change is determined, by supra-segmental signals among others, which are fed into the loop as set point signals. One of these signals stems from the vestibular system and is used for controlling the head in space, e. g. when gaze is stabilized in space during locomotion or rotation of the trunk

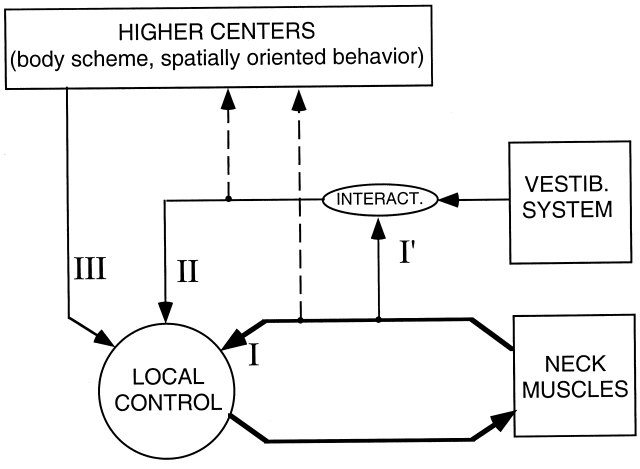

Fig. 5 Schematic representation of the information flow to the hypothesized local control mechanism of the head-on-trunk stabilization. (**I**) Local proprioceptive negative feedback loop. (**I'**) Proprioceptive signal, which interacts with vestibular signals and contributes to the elaboration of a set point signal (**II**), which upgrades the local loop from trunk to space coordinates. Both proprioceptive signals can be assessed separately by psychophysical methods (dashed arrows); they indicated a normal signal processing in I and II upon the rotational stimuli in our ST patients. Higher centres provide set point signals (**III**) related to posture and movement on the basis of multiple sources (e. g. voluntary control). We assume that III contains an erroneous static set point signal in ST patients.

(torso). For the head-in-space control it is necessary to know the current trunk-to-head position because the trunk represents the platform for the head. The information is derived from a second proprioceptive signal (I´), which can be distinguished from the former because of its slightly different transfer characteristics. The vestibular signal interacts with this proprioceptive signal before it is fed as a set point signal into the local control loop (II). As indicated by the dashed arrows, these afferent signals are in addition transferred to 'higher centres' and can be assessed in psychophysical experiments and in spatial orientation tasks as used in the present experiments (see above). Other set point signals appear to stem from the higher centres, for voluntary action and other purposes (III).

We would expect from this concept that a disturbance of information flow through the proprioceptive feedback in loop I should lead to changes in the adjustment of the light spot to the head and the trunk mid-sagittal planes following the rotational stimuli, while a disturbance of information flow through the vestibular-proprioceptive interaction loop II should lead to errors in the spatial re-localization task.

In the following we refer to this scheme when discussing the findings. In the scheme, the outflow of the local control to the neck muscle shows a considerable bias in patients, leading to the abnormal head-on-trunk posture (spontaneous pathological head deviation, –22°, on average, adjusted to –5° during testing). This motor bias may initially lead to an asymmetrical proprioceptive inflow, which tends to adapt at the level of the receptors and afferents over time. However, adaptation starts within several seconds, as evident in brainstem relay neurons carrying neck proprioceptive information [20]. There appears to be, in addition, a central, high-level mechanism, which further reduces such biases in afferent inflow, so that perception and posture control are no longer asymmetric after prolonged head deviation [12]. This would explain why the baseline values of our patients' estimates of head mid-sagittal were close to zero despite the head turn. Interestingly, ST patients show a strong shift towards the trunk mid-sagittal when estimating the VSA and the vertical head mid-sagittal plane [2, 3], as mentioned and interpreted before in the Introduction. In these tasks, as in the present head task, the adaptive mechanism may have led the patients to experience their heads as having a normal orientation with respect to the trunk as the ground-based ego-centric reference.

Concerning the static condition, patients' estimates may therefore not yield an exact measure of the proprioceptive inflow. Yet, we hold that signal transmission in the proprioceptive pathway is essentially correct, as witnessed by the patients' normal responses following the slow, intermediate, and fast rotational stimuli. This applied to both proprioceptive loops in the scheme (to all three experimental tasks) and, noticeably, to both accuracy and variability of the responses when the individual bias was taken into account.

A striking finding was, however, that the baseline showed considerable individual variations across the patients (abnormal across-subjects baseline variability; in contrast, all other variability measures were normal in patients). This finding suggests that Ps had less accurate knowledge of their static head-on-trunk position than normals. We consider this to represent the consequence of the aforementioned peripheral and central adaptation process. Spontaneous fluctuations of torticollis may be an additional factor, since the adaptation would then have to change continuously.

Because of these findings and considerations we deem it unlikely that the proprioceptive inflow is responsible for the bias in motor outflow. Rather, we assume that the misaligned motor outflow may stem from higher centres (cf Introduction), which feed a faulty static set point signal into the local loop (loop III in the scheme of Fig. 5). This notion is still speculative, but receives support from the observation that in patients, in whom the so-called 'geste antagoniste' ameliorates torticollis, the effect can stem from cutaneous input of either side of the face and may occur even before the finger touches the skin [34].

Our notion of a normal signal processing in the neck proprioceptive (and vestibular) pathways and of a faulty static set point signal is furthermore supported by the aforementioned findings of essentially normal head movement parameters of ST patients during visual gaze shifts when their abnormal head posture is taken into account in the data analysis [18].

A possible objection against our notion is that in a closed negative feedback control system as described in our scheme, the internal error signal may be small as compared with the motor effect (depending on open loop gain of the system), so that it may not be detected in the psychophysical data. Furthermore, the simple scheme does not consider the coupling and balance between the agonist and antagonist parts of the motor system, for which a neuroanatomically and physiologically more realistic model would be required. We would agree that the concept presented in the scheme is still preliminary, but like to refer to more sophisticated dynamic models of head movement control for ST patients and normals and of vestibular-proprioceptive interaction for spatial orientation in our previous work [18, 25], which would be in line with the view presented here.

Another objection could be that there might exist basic, qualitative differences between the central sensory processing leading to action and from that leading to perception. However, there is no convincing evidence so far for this assumption. It is true that dissociations between action and perception may occur in certain situations, but they can be explained in a different way. For

instance, human self-motion perception during slow rotational stimuli may considerably differ from the simultaneously occurring oculomotor reponses (in the form of the vestibulo-ocular reflex, VOR), but this difference can be explained by a relatively high detection threshold, which is required as an add-on for perception, unlike for action. When using clearly supra-threshold stimuli, as in our experiments, the threshold plays no major role and subthreshold errors and biases can be detected (see [25, 27]).

A methodological difficulty in our experiments was given by the mechanics of the head gear which limited the passive head excursions and led us to fixate the patients' heads and to adjust them to the minimal tolerated deviation. One may ask to what extent the fixation, the reduced deviation and the use of passive rotational stimuli may have affected the results. We cannot give a final answer, but would like to point out that (i) head fixation did not abolish the pathological neck contraction (see torque measurements in [3]), (ii) we expect that the effect of changing the head offset in patients has hardly any lasting effect on the estimates; in control experiments of a previous study we observed that such an offset, in normal subjects at least, leads to an only transient offset of the VSA, which soon tends to return to the initial value, starting within the first minute after head excursion [3], and (iii) it is not conceivable, how the reduction of the head offset and the passive stimulation would have eliminated from the patients' estimates a presumed 'faulty' signal in the afferent input, responsible for the torticollis.

Finally, because our Ps were all treated with botulinum toxin, it may be argued that our results could be biased by this treatment, since the toxin is supposed to affect muscle spindle afferent discharges [9, 10, 31]. We attempted to account for this possibility, by always testing the patients about 3 months after the last injection. This precaution would, of course, not account for possible long-term effects of the toxin, which are presently unknown. However, since the patients' responses to head-on-trunk rotation were normal in all tasks, we assume that the neck signal they used in these tasks had a gain of unity.

Last, but not least, it would be interesting to relate our notion of an essentially normal proprioceptive inflow and sensorimotor processing during movements to other findings in the literature on ST or dystonia in general. For instance, it has recently been shown that dystonic patients underestimate muscle vibration induced flexion at the elbow when indicating the perceived movement by a mirror movement with the other arm [11, 30]. A possibly analogous finding is that postural reactions upon neck muscle vibration are abnormally small in ST patients [16]. It is generally difficult to interpret the effects evoked by artificial stimulation, such as muscle vibration or electrical nerve stimulation, since the CNS mechanisms activated clearly differ from those during natural stimulation. However, a simple and straightforward explanation for these effects could be an abnormally fast adaptation to changes in proprioceptive inflow in the presumed high level centres during the rather long lasting vibration stimuli, a hypothesis that remains to be investigated. A possibly related phenomenon is that ST patients, when slowly rotated in vertical planes through the earth vertical, indicate perceived body verticality clearly earlier than normals, i. e. at a wider angle from true vertical [1]. Assuming that the aforementioned stimuli were lasting into the static range, we would have no difficulty to subsume them under our concept of a selective disturbance of a static set point signal in the local proprioceptive control loop.

In *conclusion*, we show that ST patients make adequate use of vestibular and neck proprioceptive information in ego-centric and spatio-centric indication tasks (after data correction for individual static offsets that are not related to the direction and amount of torticollis). These findings may help to narrow the search among the various subsystems in sensorimotor integration that might be impaired in, and possibly cause spasmodic torticollis, in that they suggest a normal signal transmission in the proprioceptive afferent pathways used for the kinematic head-on-trunk and head-in-space control. They prompted us, together with earlier evidence (mainly related findings for patients' head movement control in eye-head coordination during visual gaze shifts) to postulate an erroneous static set point signal for head posture in the local neck proprioceptive control loop. The presumed error is thought to stem from higher brain centres involving the basal ganglia and to result from a more general and wide spread disturbance, which may manifest itself focally in the form of torticollis. This assumption has to be validated by means of further experimental evidence.

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References

1. Anastasopoulos D, Bhatia K, Bisdorff A, Bronstein AM, Gresty MA, Marsden CD (1997) Perception of spatial orientation in spasmodic torticollis. Part I: The postural vertical. Mov Disord 12: 561–569
2. Anastasopoulos D, Bhatia K, Bronstein AM, Marsden CD, Gresty MA (1997) Perception of spatial orientation in spasmodic torticollis. Part 2: The visual vertical. Mov Disord 12:709–714
3. Anastasopoulos D, Nasios G, Psilas K, Mergner T, Maurer C, Lücking CH (1998) What is straight ahead to a patient with torticollis? Brain 121:91–101

4. Andersen RA, Snyder LH, Li C-S, Stricane B (1993) Coordinate transformations in the representation of spatial information. Curr Opin Neurobiol 3:171–176
5. Bara-Jimenez W, Catalan MJ, Hallett M, Gerloff C (1998) Abnormal somatosensory homunculus in dystonia of the hand. Ann Neurol 44:828–831
6. Berardelli A, Rothwell JC, Hallett M, Thompson PD, Manfredi M, Marsden CD (1998) The pathophysiology of primary dystonia. Brain 121:1195–1212
7. Bronstein AM, Rudge P (1986) Vestibular involvement in spasmodic torticollis. J Neurol Neurosurg Psychiatry 49: 290–295
8. Byl N, Merzenich M, Jenkins W (1996) A primate genesis model of focal dystonia and repetitive strain injury. Neurology 47:508–520
9. Fillippi GM, Errico P, Santarelli R, Bagolini B, Manni E (1993) Botulinum A toxin effects on rat jaw muscle spindles. Acta Otolaryngol (Stockh) 113: 400–404
10. Giladi N (1997) The mechanism of action of botulinum toxin type A in focal dystonia is most probably through its dual effect on efferent (motor) and afferent pathways at the injected site. J Neurol Sci 152:132–135
11. Grünewald RA, Yoneda Y, Shipman JM, Sagar HJ (1997) Idiopathic focal dystonia: a disorder of muscle spindle afferent processing? Brain 120:2179–2185
12. Gurfinkel VS, Popov KE, Smetanin BN, Shlykov VY (1989) Changes in the direction of vestibulomotor response in the course of adaptation to protracted static head turning in man. Neirofiziologiya 21:210–217
13. Hallett M. Is dystonia a sensory disorder? (1995) Ann Neurol 38:139–140
14. Ikoma K, Samii A, Mercuri B, Wassermann EM, Hallett M (1996) Abnormal cortical motor excitability in dystonia. Neurology 46:1371–1376
15. Kaji R, Rothwell JC, Katayama M, Ikeda T, Kubori T, Kohara N, Mezaki T, Shibasaki H, Kimura J (1995) Tonic vibration reflex and muscle afferent block in writer's cramp. Ann Neurol 38:155–162
16. Lekhel H, Popov K, Anastasopoulos D, Bronstein AM, Gresty MA, Marsden CD (1997) Postural responses to vibration of neck muscles in patients with idiopathic torticollis. Brain 120: 583–591
17. Maurer C, Kimmig H, Trefzer A, Mergner T (1997) Visual object localization through vestibular and neck inputs. I. Localization with respect to space and relative to the head and trunk mid-sagittal planes. J Vest Res 7:119–135
18. Maurer C, Mergner T, Lücking CH, Becker W (2001) Adaptive changes of saccadic eye-head coordination resulting from altered head posture in torticollis spasmodicus. Brain 124:413–426
19. Mavroudakis N, Caroyer JM, Brunko E, Zegers de Beyl D (1995) Abnormal motor evoked responses to transcranial magnetic stimulation in focal dystonia. Neurology 45:1671–1677
20. Mergner T, Anastasopoulos D, Becker W (1982) Neuronal responses to horizontal neck deflection in the group x region of the cat's medullary brainstem. Exp Brain Res 45:196–206
21. Mergner T, Huber W, Becker W. (1997) Vestibular-neck interaction and transformations of sensory coordinates. J Vestib Res 7:119–135
22. Mergner T, Maurer C, Peterka RJ (2002) The vestibular functions: an overview. In: Resin RC, Nuwer MR, Hallett M, Medina C (eds) Adv Clin Neurophysiol (Suppl to Clin Neurophysiol, Vo. 54) pp 511–518
23. Mergner T, Nasios G, Anastasopoulos D (1998) Vestibular memory-contingent saccades involve somatosensory input from the body support. NeuroReport 9:1469–1473
24. Mergner T, Nardi GL, Becker W, Deecke L (1983) The role of canal-neck interaction for the perception of horizontal trunk and head rotation. Exp Brain Res 49:198–208
25. Mergner T, Nasios G, Maurer C, Becker W (2001) Visual object localisation in space. Interaction of retinal eye position, vestibular and neck proprioceptive information. Exp Brain Res 141: 33–51
26. Mergner T, Rosemeier T (1998) Interaction of vestibular, somatosensory and visual signals for posture control and motion perception under terrestrial and microgravity conditions. Brain Res Rev 28:118–135
27. Mergner T, Siebold C, Schweigert G, Becker W (1991) Human perception of horizontal head and trunk rotation in space during vestibular and neck stimulation. Exp Brain Res 85:389–404
28. Moreau MS, Cauquil AS, Costes Salon MC (1999) Static and dynamic balance function in spasmodic torticollis. Mov Disord 14:87–94
29. Münchau A, Corna S, Gresty M, Bathia KP, Palmer JD, Dressler D, Quinn NP, Rothwell JC, Bronstein AM (2001) Vestibulo-collic reflex and vestibulovoluntary interaction in patients with spasmodic torticollis. Brain 124:47–59
30. Rome S, Grünewald RA (1999) Abnormal perception of vibration-induced illusion of movement in dystonia. Neurology 53:1794–1800
31. Rosales RL, Arimura K, Takenaga S, Osame M (1996) Extrafusal and intrafusal muscle effects in experimental botulinum toxin-A injection. Muscle Nerve 19:488–496
32. Tempel LW, Perlmutter JS (1990) Abnormal vibration-induced cerebral bood flow responses in idiopathic dystonia. Brain 113:691–707
33. Tsui JKC, Eisen A, Stoessl AJ, Calne S, Calne BD (1986) Double-blind study of botulinum toxin in spasmodic torticollis. Lancet 2:245–247
34. Wissel J, Müller J, Ebersbach G, Poewe W (1999) Trick maneuvers in cervical dystonia: investigation of movement- and touch-related changes in polymyographic activity. Mov Disord 14: 994–999