Adaptive changes of saccadic eye–head coordination resulting from altered head posture in torticollis spasmodicus

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Summary
We asked whether and how the abnormal head posture in torticollis patients affects saccadic gaze shifts and impairs the associated head movements. We wanted to learn to what extent observed changes directly result from the disease or reflect compensatory mechanisms, secondary to the altered head posture. We compared the results of patients with those of normal subjects. When patients viewed a centric target, their heads were a priori deviated in the direction of the torticollis, with orbital eye position showing a compensatory offset in the opposite direction. These abnormal eye and head positions were re-established when patients returned from an eccentric gaze position by means of a centripetal gaze shift, independently of its direction and magnitude, unlike in normal subjects who always centred eyes and head. In normal subjects the share of the head in the total gaze shift amounted to about 70%, whereas in patients it contributed only 30%, necessitating correspondingly larger orbital eye displacements and eccentricities.

Moreover, patients’ head movements were asymmetric; they were larger when gaze was shifted into, or returned from the hemifield contralateral to the torticollis direction compared with gaze shifts in the ipsilateral hemifield. The eyes displayed a reversed asymmetry. Patients showed a significant increase in gaze latency and head versus eye delay as well as in the number of corrective saccades. However, head velocity was normal in four out of seven patients. Moreover, all patients made normal eye saccades (peak velocity, duration, gaze error), except for the increase in latency, which also occurred when gaze was shifted without head movements. Thus, patients’ saccadic eye–head coordination showed abnormalities which mainly concerned the involved head movements. We suggest that the observed changes do not reflect a direct involvement of the disease upon the gaze shift mechanism, but can be interpreted as adaptive changes that compensate for the altered head posture. We formalized this view in the form of a dynamic model.

Keywords: spasmodic torticollis; eye–head coordination; saccadic; head posture

Abbreviations: LED = light emitting diode; SC = superior colliculus; TC = idiopathic spasmodic torticollis; VOR = vestibulo-ocular reflex

Introduction
Idiopathic spasmodic torticollis (TC) is the most common form of adult onset focal dystonia. It is defined as involuntary turning and twisting of the neck caused by abnormal muscle contraction (Fahn et al., 1987). A wide variety of abnormal head and neck postures may be assumed, the most common component being rotatory with the chin deviating towards the shoulder on one side (see Dauer et al., 1998). The aetiology of TC is still unknown (Nutt et al., 1988; Fahn, 1988; for review, see Dauer et al., 1998). So far, genetic abnormalities have been found in only a small proportion of patients with adult onset (Leube et al., 1997). Only exceptionally does one find a cervical dystonia of the TC type secondary to tumours, cysts or lesions of the brainstem, cervical spine, cerebellum and IVth, VIIIth and IXth cranial nerves (Kiwak et al., 1983; Suchowersky et al., 1988; Cammarota et al., 1995, Dauer et al., 1998).

Considerable efforts have been focused on the function of sensory systems in TC. For instance, a remarkable increase in dystonia was reported during muscle vibration by Kaji and colleagues (Kaji et al., 1995b). Since the effect was attenuated by pharmaceutical blocking of the muscle spindle afferents, the authors suspected that abnormalities of this
input represent an aetiologically important factor for TC. Furthermore, vestibular abnormalities in terms of an asymmetrical caloric and rotational nystagmus in the dark have been reported for TC patients (contralateral preponderance relative to the TC direction; Bronstein and Rudge, 1986), as well as an asymmetrical vestibulo-ocular reflex (VOR) which fails to become symmetric after botulinum toxin injections (Stell et al., 1989). However, it appears that these vestibular abnormalities are found in only a few patients, and if present, tend to occur mainly if the disease has already a long history (Colebatch et al., 1995). Furthermore, the notion of relevant abnormalities in vestibular and neck proprioceptive input in TC patients was not supported by recent work from Anastasopoulos and colleagues. Their patients’ estimates of visual straight-ahead direction and of head and trunk mid-sagittal directions as well as the updating of a given location in space following vestibular and neck stimulation were symmetric (Anastasopoulos et al., 1998).

Other work has been undertaken to analyse the head posture and movement of TC patients. The studies of Zangemeister and co-workers (Zangemeister et al., 1982; also Stark et al., 1988) focused primarily on fast voluntary, so called ‘time-optimal’ head movements (in order to reduce variability of subjects’ responses). From the dynamic effects (time functions of position, velocity and acceleration) observed for head movements with and against the deviation of static position, the authors concluded that most of the observed effects are not directly related to a disturbance of the central motor command, but rather represent secondary effects from asymmetric muscle activation. Abnormalities of gaze reorientation in TC patients have been suspected for a long time. One of the older, but outstanding, attempts to relate the functional deficit in torticollis to central mechanisms stems from Hassler and Dieckmann who postulated a bilateral central system for versinal orienting movements (’Wendesubstrat’) (Hassler and Dieckmann, 1970). Based on experimental animal work and clinical findings, these authors postulated that a unilateral lesion in the putamen disinhibits certain neurones in the pallidum, yielding an asymmetry between the two sides and leading to an imbalance of neck muscle tone and thus to a head deviation. However, the versinal movements elicited in their experimental work consisted of gaze deviations, whereas in TC the eyes are not deviating together with the head in a compulsory way. From a retrospective point of view, their theory actually fits better to the syndrome of oculogyric crisis, a pathological entity of abnormal eye–head deviations related to disturbances in basal ganglia and midbrain (Sacks and Kohl, 1970; Leigh et al., 1987; Breggin, 1993). In fact, it has been shown that saccadic eye movements (random, predictive remembered, and self-paced) in TC patients are normal, a finding which suggests that the oculomotor parts of the corticostriatal loops are not primarily impaired, unlike in Parkinson’s disease and Huntington’s disease (Stell et al., 1990).

A considerable number of details about gaze reorientation by means of combined eye and head movements have come to be known since the time of Hassler’s work. Saccadic gaze re-orientations with amplitudes larger than 10° are usually accompanied by head movements. The intervention of the head requires a precise coordination with the eyes in order to ensure that gaze displacement, the sum of eye-in-orbit and head-in-space displacement, equals the desired reorientation (for an overview, see Bizzi et al., 1976; Lauritis and Robinson, 1986). Two ‘automated’ mechanisms have been implied in this coordination. A vestibulosaccadic reflex would adjust the amplitude of an ongoing eye-in-head saccade to account for the contribution of the accompanying head movement (Lauritis and Robinson, 1986), whereas the VOR, after being silenced during the eye saccade, would stabilize gaze in space after the eye saccade if the head movement is still continuing (as is the case in almost every gaze shift involving a head movement). Little is known, so far, as to the neural substrates of eye–head coordination during goal-directed gaze shifts and, in particular, the question where and how the amount of head contribution is ‘decided’. Undoubtedly, a key structure for orienting visuomotor behaviour is the superior colliculus (SC). Recent results from microstimulation experiments and thorough analyses of single unit discharges (Freedman and Sparks, 1997b; Freedman et al., 1996) suggest that at the level of this structure, it is still the amount of desired gaze displacement (tantamount to target displacement during goal-oriented behaviour) which is being coded for. Therefore, the dissociation into motor signals determining the eye-in-orbit saccade and the head-on-trunk rotation must occur downstream of the SC. The results of behavioural experiments indicate that the process underlying this dissociation takes into account the initial orbital eye position; indeed, for gaze displacements of given magnitude, head contribution increases as initial eye position approaches the limits of ocular motility on the side toward which the gaze shift is directed and the delay of the head movement upon the eye saccade decreases (Becker and Jürgens, 1992; Freedman and Sparks, 1997a). Functionally, these dependencies on orbital position lower the risk for the eyes of ‘running into a stop’ during gaze shifts and reduce static eye eccentricity during fixation of the new target.

With respect to reorienting head movements as part of a gaze shift, little is known so far for TC patients. A recent study compared the kinematics of head movements contributing to gaze shifts towards visual targets in the frontal plane in normal subjects and TC patients in terms of Donders’ law (which defines a strategy that reduces the three mechanical degrees of freedom of head rotation to two physiological degrees) (Medendorp et al., 1999). As a result of this law, head rotation vectors are confined to a (slightly curved) surface in normal subjects. Interestingly, rotation vectors were confined to such a surface in TC patients. However, these surfaces were less stereotyped and offset in comparison to those of normal subjects, indicating a less strict obedience to Donders’ law and a considerable torsional component.
The Medendorp study did not consider the coordination between eyes and head though, ignoring such aspects as the relative contributions of head and eyes to a gaze displacement, their dynamics, and their temporal relationships. Because orbital eye position modulates the pattern of eye–head coordination (c.f. above), it can be predicted that at least the relative contributions to total gaze displacement of the head and the eyes will differ between normal subjects and TC patients. In fact, with respect to a visual space centred on the trunk axis, mean orbital eye position is displaced contralaterally relative to TC pulling direction in patients.

In the present report, we examined whether and how gaze shifts, and the associated head movements especially, are changed in TC patients. Given such changes, we wanted to assess whether they are direct consequences of the disease or only secondary, compensatory changes helping the patients to cope with their altered head posture. Our results suggest that most of the differences between TC patients and normal subjects are adaptive consequences of the patients’ abnormal head posture, whereas the head movements contributing to reorienting gaze shifts appear to be unimpaired in many TC patients. This suggestion will be illustrated in the form of a descriptive model of eye–head coordination in patients.

Methods

Patients and controls

Seven patients with spasmodic torticollis and seven age-matched normal subjects gave their informed consent to the study, which was approved by the ethics committees of Freiburg and Ulm universities and conformed to the Declaration of Helsinki. The magnitude of the patients’ neck dystonia was assessed while they were sitting at rest. Head deviation about the vertical axis at the time of investigation was quantified as absent (0); mild (grade 1 < 15°); moderate (grade 2 15–30°); or extreme (grade 3 >30°; compare severity scale of Tsui et al., 1986). Patients with prominent laterocollis, retrocollis, anterocollis or head jerks were excluded. Only one patient had a mild laterocollis. Patients were aged 51, 48, 60, 34, 24, 44 and 52 years, had disease durations of 7, 16, 6, 4, 5, 7 and 11 years and severity scores of −2.5, −1.4, 0.8, −2.2, −0.5, −1 and −2.1, respectively (six had leftward, one rightward TC). All patients had been treated for TC by regular Clostridium botulinum toxin injections in the neck muscles for >2 years. In order to minimize possible short-term effects of botulinum toxin on muscle afferent inflow, the experiments were performed after a minimum interval of 3 months following the last injection. None of the patients or normal subjects took any drugs at the time of measurements.

Apparatus and stimuli

Subjects were seated on a chair in a dark room and viewed a perimeter (radius 1.8 m) centred on their axis of head rotation and equipped with a row of red light-emitting diodes (LEDs) at eye level. LEDs were spaced at 5° intervals over a range of 120° (from 60° left to 60° right of the subject’s sagittal trunk axis). The LEDs served as saccade targets and were switched on in a pseudo-random order by a computer program, one at a time. There were two experimental conditions.

(i) Head-free condition. Target displacements ranged from 10 to 120°; subjects were instructed to ‘accurately fixate the light spot and follow it as rapidly as possible when it jumps’. We wanted subjects to use their natural pattern of eye–head coordination. Therefore, in order to avoid the impression that head movements were compulsory, it was mentioned in the instruction that they were free to move their heads if they liked.

(ii) Head-fixed condition. Target displacements ranged from 5 to 60°; subjects were again instructed to track the light spot as accurately and as rapidly as possible, but were told in addition to ‘keep the head stationary’; there was no mechanical head restraint or support in this condition, but head position was measured to monitor compliance with the instruction.

The sequence of target steps in conditions (i) and (ii) consisted predominantly, but not exclusively, of purely centrifugal, centripetal or symmetrical (from one side to the other) steps. Each condition comprised 180 steps. The target position achieved during the nth step always served as the fixation position prior to the (n + 1)th step. Correspondingly, the head position assumed at the conclusion of the nth response was generally the same as the initial head position at the onset of the (n + 1)th response.

Data acquisition and analysis

Subjects wore a lightweight plastic helmet which was coupled via a torsionally rigid, but otherwise flexible metal hose to a potentiometer (for more details, see Maurer et al., 1998). Eye movements (in orbit) were recorded by conventional electro-oculography (DC coupled EOG; bitemporal Ag–AgCl electrodes). This technique was chosen because of its wide linear range. Both the potentiometer and the EOG signals were filtered by a 4th order Butterworth filter with 25 Hz corner frequency. This low corner frequency, which was necessary to remove neck EMG signals, causes temporal distortions and a reduction of the apparent eye and head velocities. However, as both signals (eye and head) are affected in a similar way and as the same filtering was used with all subjects, these distortions in no way compromised our comparisons between normal subjects and patients.

Eye, head and gaze position as well as corresponding velocity readings (obtained by electronic differentiation) and a code of target displacement were written out on a strip-chart recorder for on-line inspection, and were sampled (at 400 Hz) and stored by a laboratory computer. In addition, a measure of gaze position, obtained by electronically adding
the head-in-space and eye-in-orbit signals, was displayed on the strip chart recorder. To calibrate the eye and gaze signals, subjects were instructed to fixate at the centre LED while slowly rotating their heads to either side by \(-30\degree\) at a frequency of \(<0.25\) Hz. At such a low frequency, the patients’ smooth pursuit system can stabilize gaze in space very effectively so that their eye movements faithfully reflect head rotation. Therefore, the EOG signal was adjusted so as to match the potentiometer signal recording head movement.

Details of the analysis procedure have been reported elsewhere (Maurer et al., 1998). Briefly, an interactive computer program searched in the aftermath of a target step each of the three data tracks eye, head and gaze, for the occurrence of eye-in-head saccades, head movements and gaze saccades, respectively. Search results were displayed and could be corrected manually. For each movement detected in any of these tracks, the program generated a parameter table noting the position and velocity of eye, head and gaze during the following five sample instants: (i) 40 ms before start of movement; (ii) start of movement; (iii) time of peak velocity; (iv) end of movement; and (v) 40 ms after end of movement. The complete description of a subject’s gaze response generally required several such tables, depending on the number of separate saccadic events that made up the response (e.g. main saccade and corrective saccades). These tables were then processed using custom tailored FORTRAN programs and commercial spreadsheet programmes. To establish the relationship between any two parameters (e.g. reaction time versus target displacement, peak velocity versus amplitude, etc.), we calculated the median values of the dependent (y-) parameter for each given value of the independent (x-) parameter in all subjects and averaged them across subjects. If the x-parameter had distributed values (e.g. amplitude of gaze saccade) it was divided into bins of 5° (condition ii, head fixed; maximum target displacement, 60°) or 10° (condition i, head free; maximum displacement, 120°) and the median values of the x- and y-parameters contained in each bin were determined. The data were then plotted giving straight line graphs. From these plots the ordinate values corresponding to a set of equally spaced abscissa values (either \(\pm 5\degree\), \(\pm 10\degree\), \(\pm 15\degree\) . . . or \(\pm 10\degree\), \(\pm 20\degree\), \(\pm 30\degree\) . . . ) were read (procedure equivalent to a linear interpolation) and averaged across subjects.

Results

Head-free gaze saccades of normal subjects reach their targets by a combined action of eye and head. Typically, the first event is an eye saccade which brings gaze already close to the target. While this saccade is on its way, a slower head movement starts which clearly outlasts the eye saccade. After the saccade, this continuing head movement is offset by a compensatory back-rotation of the eyes in the orbit so that gaze remains stable in space. Depending on the initial accuracy, one or more corrective eye saccades will follow, which may still be ‘embedded’ in the ongoing head movement. This behaviour, which has been repeatedly described in previous work (Gresty, 1974; Uemura et al., 1980; Lauritis and Robinson, 1986), was found in all of our normal subjects and patients; in particular, patients’ gaze always reached the target. As an example, Fig. 1A and C shows original recordings of a head-free gaze reorientation of a normal subject in response to a 80° target displacement (position traces in part A, velocity in part C).

Gaze reorientation reactions of patients, although basically similar to those of normal subjects, show a number of deviant details. For example, as illustrated in Fig. 1B and D, the amount of head movement may depend on the direction of the saccade, with head displacement towards the side of torticollis being smaller than in the opposite direction. In addition, patients’ head movements typically exhibit longer delays with respect to the primary eye saccade than is observed in normal subjects, frequently beginning only after the eye saccade ended (see example in Fig. 1B, left part). Further, head position during periods of fixation between successive gaze reorientations was not as stable as in normal subjects. In the patient of Fig. 1B and D the head was found to drift slowly in the pulling direction of the torticollis between reorientation reactions (see heavy dashed line connecting H curves of the left and right halves of Fig. 1B). The same pattern was observed in a second patient, whereas the head tended to drift against the torticollis direction in two others and in three patients there was no drift.

Parts E–H of Fig. 1 show a reconstruction of the gaze shifts in parts A–D using the calibrated samples of position and velocity stored in the aforementioned parameter table. A comparison between parts A–D and E–H demonstrates that these tables provide good descriptions of the essential features of a subject’s response.

We now focus mainly on the head-free condition, with results of the head-fixed condition being mentioned as far as they complement the characterization of patients’ performance.

**Head position and displacement during gaze fixation**

Figure 2A shows a comparison of the final head eccentricity as a function of gaze eccentricity at the end of a gaze reorientation reaction in normal subjects (hatched areas, \(\pm 95\%\) confidence intervals) and in patients (individual curves). Patients displayed a smaller slope of head versus gaze position, reflecting a correspondingly smaller head contribution to gaze displacement (see also below). Moreover there was a clear offset towards the torticollis direction (plotted in negative direction). For example, when fixating at 0° following centripetal gaze shifts, patients’ heads were turned by 9.7 \(\pm 6.9\degree\) (mean \(\pm\) standard deviation) into the torticollis direction (trunk is taken as reference).

On average, the head position at the end of a gaze reaction was not significantly different from the position at the

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Fig. 1 Examples of combined eye and head (= gaze) shifts. Original recordings of head-free gaze saccades evoked by target steps of 80° in a normal subject (A) and in a torticollis (TC) patient with leftward TC (B). C and D show corresponding velocity traces of eye-in-head (E), gaze (G) and head (H). (E–H) Reconstruction of the same saccades from the data generated by the interactive analysis procedure. Crosses mark the sample instants used by the analysis program. Arrows point to corrective saccades. Position/velocity values are positive for rightwards and negative for leftwards.
Fig. 2 Head eccentricity and displacement. (A) Head eccentricity at the end of gaze reorientation reactions as a function of gaze eccentricity. Single curves (± standard errors) represent patients (Ps); data plotted according to gaze eccentricity relative to torticollis pulling direction (negative values, ipsilateral; positive, contralateral). Dotted areas = 95% confidence range of normal subjects (positive: right, negative: left). (B) Head displacement as a function of target displacement in the head-free condition. Single curves = patients (Ps); data plotted according to displacement direction relative to TC pulling (presentation as in A). Note that normal subjects cover more than two-thirds of the target displacement with their heads, whereas in patients this varies between one- and two-thirds.

beginning of the next gaze reorientation reaction occurring \(\sim 2-3 \text{ s}\) later. However, as already mentioned in the context of Fig. 1, between successive reactions, while fixating at the target, individual patients might exhibit slow head position changes either in or against TC direction.

Figure 2B shows a comparison of the average head displacement of normal subjects (hatched areas delimiting ± 95% confidence intervals) and the individual curves of seven torticollis patients with their standard error bars as a function of target displacement (averages across centrifugal, centripetal, and midline crossing target steps). The figure suggests that in normal subjects the head covers 60–70% of the target displacements. For example, 60° gaze shifts were accompanied by head displacements of 35.8 ± 12.0° in normal subjects, whereas patients moved their heads only by 20.5 ± 11.7°, a difference which is statistically highly significant (t test, \(P < 0.0001\)).

In our further description of patients’ head contribution to gaze saccades we shall distinguish between the direction of their head movements and the hemifields (or fields for short) from where these movements originate or in which they terminate; the fields indicate to which side (ipsilateral or contralateral to TC pulling) head position deviates from trunk orientation (and, by the same token, from zero target position) during a movement. Thus, a head movement returning from the side of TC pulling to a centre position is said to have contralateral direction but to be executed within the ipsilateral field. Analogous definitions apply for the eyes; thus, the eye movement field indicates whether before, during or after a saccade the eyes deviate from the primary orbital position to the ipsi- or contralateral side.

When averaged across all gaze shifts tested in the experiment, patients’ head contribution to their gaze saccades was about the same for movements of both ipsilateral and contralateral direction. However, when we restricted our analysis to centrifugal and centripetal saccades (excluding the midline crossing ones) and distinguished gaze shifts performed within the ipsilateral and contralateral hemifields, significant asymmetries of head involvement emerged. This is shown in Fig. 3. First, consider part A which summarizes the characteristics of centrifugal gaze shifts in patients as a function of final gaze position (which is virtually identical to target position): whereas gaze started from 0° (dotted zero line), initial head position was ipsilaterally deviated (average 9.4 ± 7.1°) as depicted by the two bold, almost horizontal curves through the hatched area; the continuous curve shows head position before gaze shifts into the ipsilateral hemifield, the dashed one corresponds to shifts into the contralateral field. The curves delimiting the upper and lower borders of the hatched area give the corresponding final head positions after termination of centrifugal gaze shift. Accordingly, the width of the hatched area below (or above) the curves of initial head position indicates the amplitude of the head movements into the ipsilateral (or contralateral) hemifield. Clearly, during gaze shifts into the ipsilateral field, head movements were smaller than during shifts into the contralateral field. The reverse was true for the final head positions with respect to the trunk; they reached larger
Fig. 3 Head and eye contributions to gaze shift. Head eccentricity (heavy curves) and orbital eye eccentricity (light curves) before and after gaze reorienting reactions as a function of gaze position; data averaged across subjects. (A and C) Centrifugal gaze shifts. Abscissa refers to gaze position after completion of reorientation. Horizontal curves mark head and eye positions before onset of gaze shift, ascending and descending curves positions after shift. (B and D) Centripetal shifts. Abscissa refers to gaze position before start of reorientation. Horizontal curves mark final head and eye positions, ascending and descending curves initial positions. (A and B) Patients; data plotted according to hemi-field. Continuous curves = head and eye positions associated with gaze shifts into (A), or returning from (B), field ipsilateral to TC pulling; dashed curves = shifts into or returning from contralateral field. Positive values indicate contralateral positions, negative ipsilateral. Arrowheads mark final head position and symbolize direction of gaze shift. Hatched areas above and below heavy horizontal curves visualize extent of head movement during gaze shifts into contra- and ipsilateral hemifields, respectively. Likewise, areas between light curves (emphasized by lighter hatching where overlaying the head movement visualization) show final eye displacement. (C and D) Normal subjects; data plotted according to absolute direction. See text for further details.

Eccentricities in the ipsilateral field. Corresponding data for orbital eye position are represented by light curves. Initial eye position obviously mirrored initial head position (hence a 9.4° deviation in contralateral direction, light horizontal curves). Likewise, final eye position (thin curves diverging to the right) exhibited asymmetries complementary to those of the head as did total eye displacement (= final minus initial position); recall that this displacement is generally smaller than the amplitude of the primary eye saccade (cf. Fig. 1). Finally, in order to better visualize the relative shares of head and eyes in the total gaze displacement, the arrowheads mark the final gaze position (and therefore fall on 45° lines), and point into the direction of the gaze shifts.

Part B of Fig. 3 gives an analogous representation of our patients’ centripetal saccades, with the curve attributes final and initial being interchanged in comparison with part A. For example, the horizontal heavy lines across the hatched area now represent the final head positions after completion of the centripetal gaze movement. Remarkably, this position is virtually the same whether gaze returns from a large eccentricity (e.g. 60°) or a small one (e.g. 20°), or from the ipsilateral (continuous curve) or the contralateral (dashed) hemifield, and is similar to the position from where the head started during centrifugal movements (cf. corresponding horizontal curves in A). Taken together, parts A and B indicate that, regardless of the direction of the gaze shifts, patients’ head movements are smaller when the shifts occur in the ipsilateral field than when they occur in the contralateral one. To give a numerical example, 60° gaze shifts in the contralateral hemifield (pooled across centrifugal and centripetal direction) were accompanied by head displacements of 26.1 ± 11.9° whereas head displacements in the ipsilateral hemifield amounted only to 15.5 ± 9.7°, a difference which was statistically highly significant ($P = 0.0006$).

The lower two panels of Fig. 3, C and D show a similar analysis for our normal subjects, with directions now being discriminated according to right and left, instead of along and against TC pulling direction. As could be expected, there was an almost complete symmetry with regard to these directions. Comparing the hatched areas in parts A and B with those in parts C and D it becomes clear that patients’ head movements were smaller than those of normal subjects regardless of which hemifield is considered. As a corollary of this observation, we also note that, during the fixation at eccentric targets, patients incurred much larger orbital eye deviations than normal subjects did, most dramatically so for contralateral gaze shifts, but clearly also for ipsilateral gaze. For example, when fixing a target at 60° in the contralateral hemifield, patients maintained a lateral eye deviation of 38 ± 5° whereas normal subjects would exhibit only 23 ± 7° ($P < 0.001$).

**Head dynamics**

Figure 4A shows peak head velocity as a function of head displacement in normal subjects (hatched areas, ± 95% confidence intervals).
Fig. 4 Head and gaze velocities and primary saccade error. (A) Peak head velocity as a function of head displacement amplitude (presentation as in Fig. 2A). (B) Peak gaze velocity (= eye + head velocity) as a function of gaze amplitude (‘main sequence’; presentation as in Fig. 2A). (C and D) Frequency distribution of mean primary saccade error in patients during ipsiversive (C) and contraversive (D) gaze shifts; positive values indicate undershoot.

Confidence intervals) and the individual curves of patients (± standard error bars). As a group, patients had slower head movements than normal subjects. However, on an individual basis, four of our seven patients displayed ‘normal’ head velocities, while two of the remaining three were very slow in both the ipsilateral (−) and contralateral (+) directions (Patients 1 and 3, who were the two oldest; Methods). When the four possible combinations of ipsi- and contradirectional movements and ipsi- and contralateral hemifields are considered separately (not shown), one condition stands out: patients’ centrifugal head movements in the torticollis direction (i.e. into the ipsilateral hemifield) were significantly faster than the other three types (P < 0.0001 for 30° and 40° head amplitudes, respectively). However, in the two slow patients these head movements were slower than any type of similar sized head movement in normal subjects.

Gaze dynamics

Peak gaze velocity as a function of gaze amplitude is shown in Fig. 4B. In all patients this velocity, which is almost fully dominated by eye peak velocity, was within the normal range. Moreover there was no difference between ipsilaterally and contralaterally directed saccades or between saccades executed in the ipsilateral and contralateral hemifields (not shown).

Accuracy of primary gaze saccades and occurrence of corrective saccades

The primary gaze saccades of normal subjects consistently undershot the target and so did those of patients. On average the mean undershoot of patients and normal subjects was similar (e.g. with 60° gaze shifts, normal subjects: 3.3 ± 2.9°; patients: 3.2 ± 6.3°; P = 0.88). However, patients exhibited a larger scatter and required more secondary saccades to reach target (mean difference of frequency, 0.32; P < 0.01 for each target amplitude after Bonferroni correction). Figure 4C and D, plots the frequency distribution of the errors remaining after the primary gaze saccade for contraversive
(part C) and ipsiversive (part D) gaze shifts, pooled together for the seven patients. With the exception of Patient 3, no significant difference between the mean accuracy of primary gaze saccades into the contralateral and ipsilateral directions could be detected (e.g. 60°, ipsilateral: 3.5 ± 7.2°, contralateral: 3.0 ± 3.5°; P = 0.76). Centrifugal gaze saccades in patients undershot the target more than centripetal ones, similarly to those in normal subjects. Furthermore, when restricting the analysis to centrifugal and centripetal movements and sorting these according to hemifields as in Fig. 3, no significant differences for the ipsilateral field versus the contralateral field were found.

**Gaze latency**
Gaze latency was significantly increased in patients compared with normal subjects. For example, with target displacements of 60°, normal subjects started their gaze saccade 193 ± 21 ms after the target displacement, whereas patients showed a latency of 290 ± 18 ms (P < 0.0001). Latencies for ipsilateral and contralateral directions, as well as hemifields, showed no significant differences in torticollis patients. As in normal subjects, centrifugal saccades started later than centripetal saccades (40°, P = 0.0005; 60°, P = 0.0001).

**Head latency**
As can be expected from the differences in gaze latency, head latency was also significantly larger in patients than in normal subjects. For example, with target displacements of 60° head latency of normal subjects was 215 ± 41 ms, whereas in patients it amounted to 349 ± 31 ms (P < 0.0001). Thus, the increase of head latency in patients compared with normal subjects (134 ms) was much larger than that of gaze latency (97 ms), reflecting the fact that the delay of the head with respect to the eye (or gaze) saccade is also significantly larger in patients than in normal subjects (e.g. for 60° gaze shifts, 54 ± 38 ms versus 22 ± 43 ms; P < 0.0001). Within patients, the latency of ipsiversive head movements was longer than that of the contraversive ones (P < 0.05 for each target amplitude) as were the eye–head delays (e.g. 60°, ipsiversive: 71.2 ± 58.7 ms; contraversive: 37.5 ± 34.2 ms, P = 0.03). The hemifield had no significant effect upon head latency or eye–head delay.

**Total acquisition time**
Total acquisition time, i.e. the time elapsing after the target step until the eye ultimately settles on target, was clearly longer in patients than in normals. For example, with target displacements of 60°, normal subjects needed 460 ± 95 ms to reach final target position, whereas patients showed a total acquisition time of 703 ± 164 ms (P < 0.0001). About one-half of this difference is due to the increased reaction time in patients, the rest being caused by the increased number and the longer latencies (not shown) of secondary saccades. Acquisition times for ipsilateral and contralateral directions as well as for the two hemifields showed no significant differences in torticollis patients.

**Eye movement parameters**

**Head free condition**
As already noted above, because of the reduced contribution of the head to gaze movements, the orbital eccentricity of the eye during eccentric gaze position was increased in patients compared with normal subjects, particularly in the contralateral hemifield. In contrast, the dynamics of eye saccades were similar in normal subjects and patients; saccade velocity as a function of eye saccade amplitude as well as duration did not differ between patients and normal subjects.

**Head fixed condition**
When subjects were asked to stabilize their heads in space and to perform gaze shifts only with the eyes, normal subjects and patients performed similarly with one notable exception: in patients, the latency of the eye saccades was again clearly longer than in normal subjects. For example, with target displacements of 60°, normal subjects’ gaze saccade latency was 179 ± 7 ms, whereas patients showed a latency of 376 ± 67 ms (P < 0.0002).

**Discussion**

**Asymmetry of head contribution to gaze reorientation**
Intuitively, one might expect that it is easier for patients to move their heads into the direction of the torticollis, rather than into the opposite direction. Hence, one might be tempted to conclude that ipsiversive movements are larger than contraversive ones (a hint at the occurrence of an ipsiversive ‘extra pull’ could be the larger velocities of ipsiversive head movements observed in the ipsilateral hemifield). As a consequence, during the periods of fixation between steps, the head would have to make additional contraversive movements (e.g. in the form of drifts or jerks) because otherwise the difference in amplitude would accumulate with each cycle of ipsi- and contraversive gaze shifts and continuously increase the head’s position bias. Alternatively, one could argue that during periods of fixation, the head might drift, under the influence of the torticollis, into the ipsilateral direction; if this were so, ipsilateral head movements accompanying gaze shifts should be smaller than contralateral ones (otherwise the ipsilateral bias in head position would again increase with repetitive ipsi- and contraversive gaze shifts). However, neither of these two scenarios applied. The head displacements during fixation periods were small and exhibited no consistent directional preponderance, on average. Furthermore, if gaze shifts executed within a given hemifield are considered, no conspicuous differences between the
amplitudes of the accompanying ipsi- and contraversive head movements are observed [cf. for example, the ipsiversive (centrifugal) head movements within the ipsilateral hemifield of Fig. 3A with the corresponding contraversive (centripetal) ones in Fig. 3B].

As was shown in Fig. 3A and B, the main asymmetry observed in patients concerns the hemifield within which a gaze shift is executed, with the head movement being larger when accompanying a gaze shift within the contralateral field (be it a centrifugal shift into, or a centripetal one returning from that field) than within the ipsilateral one. In Fig. 3A and B this difference is visualized by the different sizes of the hatched areas above and below the horizontal curves representing head offset for primary gaze. We interpret this asymmetry as a consequence of the head position bias in conjunction with the limited eye-in-orbit motility (ocular motor range) and a behavioural preference for a restricted range of eye-in-head eccentricities. The anatomical oculomotor range is in the order of ± 55°, but in the context of eye–head coordination there seems to be a neurally encoded limit of ~45° (Guitton and Volle, 1987). The preferred range (in normal subjects) for static eye excursion during fixation appears to be limited to ± 22° (‘customary ocular motor range’; Stahl, 1999). Clearly, the contralateral bias of the eyes in patients (which mirrors their ipsilateral head offset) restricts their contralateral eye movement range and enlarges the ipsilateral one. Hence, the larger head amplitudes during centrifugal gaze shifts into the contralateral hemifield (as compared to the ipsilateral field), can be viewed as a compensatory measure preventing the eyes from ‘hitting’ their limits of motility or exceeding a preferred orbital eccentricity range (as will be discussed below, this goal is only partially achieved). Note that a similar asymmetry can be instantly provoked in normal subjects whose heads have been purposely turned away from the imminent target position at the outset of a centrifugal gaze shift. Hence, it is probably not correct to qualify the asymmetric head amplitudes of patients as adaptive in the sense of a slow compensation of the type known to occur, for example, in eye saccade amplitude after a tenotomy of an extraocular muscle (e.g. Scudder et al., 1998).

**Reduced magnitude of head contribution**

Besides the asymmetric involvement of the head there is a second clear difference between the head movements of patients and normal subjects, which concerns the magnitude of the head displacements during gaze shifts of given amplitude. As demonstrated by Fig. 3, irrespective of the hemifield, the head displacements of patients (parts A and B) were smaller than those of normal subjects (parts C and D). As a consequence, even for gaze shifts into the ipsilateral hemifield, head eccentricity was smaller in patients than in normal subjects (except for gaze shifts ≤ 20° where TC head bias exceeded the eccentricity observed in normal subjects). Because of the overall reduction of head amplitude in patients, the hemifield-dependent asymmetry of the head amplitudes can only reduce, but not eliminate, the problem of very large orbital eye eccentricities occurring during contralateral gaze. Indeed, Fig. 3 indicates that, when gazing at a 60° contralateral target, patients maintained a tonic eye deviation of ~40°, a value that is close to the ‘neural’ limit of 45° in normal subjects reported by Guitton and Volle (Guitton and Volle, 1987). In summary, patients incur, and apparently tolerate (or have to tolerate), larger eccentricities of orbital eye position during eccentric gaze fixation than normal subjects do; in other words, their customary ocular motor range is enlarged.

It is not obvious what causes the reduction of head displacements to almost half the value of normal subjects. In principle, patients could make quite large head movements, e.g. of ~30° in the context of a centrifugal 60° contralateral gaze shift. Why did they not use this ability when gaze shifts of, say, 40° were required, thereby reducing their final eye-in-head position to an approximately normal value? It could be that the same displacement as in normal subjects is intended, but not realized, because of a deficient head motor control (such as a bilaterally enhanced muscle tone and a failure to silence antagonistic muscles) and/or because of alterations in peripheral mechanics (e.g. hypertrophic changes in affected muscles; Stark et al., 1988; Zangemeister et al., 1982). However, in view of the observation that four of our seven patients showed head velocities comparable to those of normal subjects, this notion must be questioned. Also, additional observations made during the clinical examination of a number of later patients showed that, when instructed to perform externally triggered gaze shifts towards visual targets mainly with the head, patients would make larger head movements than demanded (compare below). Thus, their head movements appeared not to be restricted per se by a ‘hard’ limit, a conclusion which is also supported by the lack of an obvious saturation in patients’ curves of head versus gaze position. Finally, it seems unlikely that the signal of intended head displacement would remain rigidly the same in the course of the disease, instead of being adjusted to compensate for the changes in motor controller and plant characteristics.

Fuller concluded from a survey of normal subjects that there are ‘head movers’ who consistently use large head movements when shifting gaze, and ‘non-movers’ who try to avoid head movements or make only small ones (Fuller, 1992). As a criterion of ‘head movement propensity’, Fuller used the ratio of head to gaze displacement during gaze shifts of 40°; by this criterion, most of our patients are ‘moderate non-movers’ (propensity 0.2–0.5). The phenomenological similarity, with regard to the extent of head participation, between the non-movers among healthy subjects and our patients suggests that patients’ reluctance to move their heads does not have its primary root in a motor deficit. This suggestion concurs with the observation made above that patients can, in principle, make large head movements. Also, the experience that head movers once in a while can become
Fig. 5 Model and simulations of head and eye movement fields in torticollis patients. (A) Model: $te$, internal representation of target-to-eye position; $eh$, eye-in-head; $th$, target-to-head; $hb$, head-to-body; $tb$, target-to-body. Eye and head plants (Eye, Head) modelled by two time constants each ($T1$, $T2$ and $T3$, $T4$, respectively). Upper part of circuit, including $PGE$ (pulse generator for eye saccades), $NI$ (neural integrator), $NI^*$ (replica of NI) and Latch, is a saccade generator of the local feedback type suggested by Robinson (1975) as modified by Jürgens et al. (1981). Gain of $PGE$ is reduced by oculomotor range when the eyes approach their limits of motility. Local feedback of eye position (through $NI^*$) is complemented by feedback of currently achieved head position vestibulosaccadic reflex (VSR); Laurutis and Robinson, 1986. The vestibulo-ocular reflex (VOR) is transiently inactivated during the eye saccade. Lower part, including $PGH$ (pulse generator for head movements) followed by a direct ($T3$) and an integrating ($1/p$) pathway. Via $gH$ (gain of head response to $tb$) and $SH$ (sample and hold element for $tb$) head movements are driven by $tb$ (angular distance of target from anterior–posterior body axis). The model differs from that of a normal subject by (i) the $10^\circ$ displacement of the head motor circuit’s set point (‘head offset’); (ii) a smaller and asymmetric gain of head response ($gH = 0.45$ for movements in the contralateral hemifield; 0.35 for ipsilateral field); and (iii) a symmetrically enlarged oculomotor range ($\pm 50^\circ$). No attempts have been made to simulate the difference in reaction time between normal subjects and patients (i.e. the triggering of the saccade, $Trig$). (B) Simulations of the experimental results depicted in Fig. 3A and B for both centrifugal and centripetal gaze shifts (grouped together because essentially identical).

non-movers for fear of dizziness or even for only an ill-defined feeling of uneasiness may be relevant here. An extreme example is patients with loss of vestibular function, in whom a very similar reduction in the range of head movements is observed (Maurer et al., 1998). Could it be that TC patients simply experience unpleasant sensations when they make head movements? We explored this possibility by explicitly asking later patients, on the occasion of clinical examinations, whether they consciously avoided head movements or whether head movements caused them any discomfort. However, unless severely affected, they denied this was the case. At present, we can only therefore advance the tentative hypothesis that patients obey a subconscious ‘head-avoidance’ behaviour, but have to leave open which consequences of large head movements they try to avoid.

Model description of head contribution
As a means to summarize the findings discussed so far, we have modified a descriptive model of eye–head coordination which we had previously used to compare patients suffering from a loss of vestibular function to normal controls (for details, see Maurer et al., 1999). The model (Fig. 5A) represents signal processing that must occur downstream of the SC; its input signal can be thought of as originating in the SC and represents the angular distance between the target and the line of sight ($te$; tantamount to desired gaze displacement). It comprises an eye movement branch (upper part in Fig. 5A) and a head movement branch (lower part). At the heart of the eye movement branch is a pulse generator ($PGE$) with local feedback that converts desired gaze displacement into a pulse of appropriate intensity and duration as described in a study by Robinson and later modified by Jürgens and colleagues among others (Robinson, 1975; Jürgens et al., 1981). To account for the limited range of eye-in-orbit motility, the pulse generator is inhibited (via oculomotor range) once eye position approaches these limits. The head movement branch is a servo that adjusts head-on-body position; the desired value of this position is a function of the angular target-to-body distance ($tb$; for simplicity, a constant fraction of $tb$ is used in the present model). During saccadic gaze shifts the head and eye movement branches interact in two ways: (i) orbital eye
position (\(eh\)) is summed with \(te\) to derive target-to-head distance (\(th\)); and (ii) a vestibular image of the current change in head position is subtracted from \(te\) (vestibulossaccadic reflex) to complement the local feedback of eye displacement (via NI*) in determining current gaze motor error (which drives the pulse generator). Finally, during periods of steady fixation the two branches are coupled through the action of the VOR which stabilizes gaze in the presence of ongoing head movements. [Note that the model ignores the conceivable role of neck proprioceptive and efference copy signals for saccade generation and gaze stabilization (Mergner et al., 1998).]

Only three of the model parameters used to describe the eye–head movement pattern of normal subjects had to be modified to yield head and eye movements which closely resemble those of our TC patients: specifically, we (i) added a head offset; (ii) reduced the head gain (\(g\)) and made it asymmetric (smaller for targets in ipsilateral field than in contralateral field); and (iii) enlarged the tolerated range of orbital eye positions (OMR). As shown in Fig. 5B, with these changes the model produces static characteristics of gaze reorientation (head versus body position and orbital eye position before and after gaze shifts which, in turn, determine the ranges of head and eye movements) that are very similar to those observed experimentally.

**Reaction time of eyes and head**

Another intriguing feature of TC patients (which is not addressed by the above model) has also been observed previously in patients with loss of vestibular function (Maurer et al., 1998). In comparison with normal subjects, both gaze saccade latency and head versus eye delay are increased. Moreover, a similar increase also affects the latency of eye saccades made with the head stationary. With regard to this phenomenon, it is difficult to continue the analogy, invoked above, with the ‘non-movers’ among normal subjects. The few published data (Bard et al., 1992), comparing eye and head movement latencies of head movers and non-movers in a paradigm somewhat similar to ours, indicate no difference in eye latency between ‘movers’ and ‘non-movers’ and the trend, at best, was for longer head latencies in ‘movers’ as compared with ‘non-movers’, contrary to the present observations.

The observed increase in the delay of the head upon the eyes in patients might be taken to suggest that the primordial problem underlying the increased gaze latency is a large increase in head latency related to TC. The increase in eye (gaze) latency might then be a secondary, adaptive effect. Conceivably, in order to avoid long-lasting extreme or even impossible orbital eccentricities, the eyes would wait until the head is ready for movement. Such a ‘beneficial’ increase in eye saccade latency has been observed in normal subjects when the eyes face a reduced range of orbital motility because at the outset of the gaze shift they are already deviated towards the target (Becker and Jürgens, 1992). The increase in head latency, in turn, might reflect a disturbed pattern, or an impaired processing, of the proprioceptive afferents signalling the initial head position. This information (\(hb\) in Fig. 5A) is required to specify the desired post-saccadic head position; indeed, as shown in Fig. 5A, signal \(tb\) which determines this position is obtained by summing \(te + eh + hb\).

However, the above hypothesis does not explain why patients had longer eye movement latencies than normal subjects also in the head fixed condition, i.e. when their heads were held intentionally stationary (since we did not use a biteboard to stabilize subjects’ heads, we can exclude from our measurements that there were attempted, but mechanically suppressed, head movements). An increase in eye latency of TC patients to random target steps in a head fixed situation was also observed by Stell and co-workers, but did not reach statistical significance (Stell et al., 1990). Thus, we are left with speculations: either the above hypothesis holds and the increase in eye latency is also carried over as a ‘habit’ to situations which do not require a co-ordination with the head or, alternatively, the TC condition entails a general increase of visuomotor latencies. The observation of a similar phenomenon in labyrinthine defective patients (Maurer et al., 1998) gives some credit to the ‘carry-over speculation’, whereas the notion of a general latency increase is not supported by the currently available literature according to which head and arm movement reaction times are normal in dystonic patients (Inzelberg et al., 1995; Kaji et al., 1995a; Currá et al., 2000).

**Dynamic versus static head impairment: a difference between voluntary and reflexive actions?**

Four of our seven patients made head movements of normal velocity during gaze reorientation, yet exhibited clearly abnormal head positions which they were apparently unable to correct by voluntary action. (Similar observations can be made in a simple bed-side test by comparing instructed voluntary head turns with reflexive head movements during reorienting gaze shifts towards the snapping finger of the examiner.) We would like to speculate that these differences reflect two different types of behavioural involvement of the head motor system. The head movements accompanying gaze shifts are particular in that they constitute a sub-element of a complex orienting behaviour in external space which is mostly elicited in a reflexive manner by external stimuli. In contrast, the patients’ unsuccessful attempts to correct for the abnormal head deviation by the TC are internally initiated and refer to body-referenced co-ordinates. In other words, the issue might not only be one of posture versus movement, but also of external versus internal initiation (note that in the work of Stell et al., 1990, which found no difference between internally driven versus reflexive saccade, the head was not involved in the task). In support of such a speculation one
can cite the observation that dystonic disorders are indeed restricted sometimes to a functional subset of the motor repertoire, like for instance, writer’s cramp (Fahn, 1988).

Oculomotor adaptation to deficient head contribution

Our results testify to the large degree of independence and flexibility of the oculomotor system which almost perfectly compensates for the asymmetry and the reduced gain of the head displacements as well as for its delayed occurrence. This compensation is likely to be instantaneous, as it can also be seen in normal subjects instructed to imitate the asymmetric head position of patients at the start of a head free gaze shift. For the compensation to be ideal (i.e. for the gaze parameters proper to be indistinguishable from those of normal subjects) three prerequisites must be met: (i) the oculomotor system proper must not be affected by the TC condition; (ii) there must be sufficient orbital headway so that the eye saccade initiating the gaze shift can acquire the target without being mechanically blocked; and (iii) the mechanisms mediating the orbital return movement (VOR, visual pursuit), by which gaze is stabilized on target while a head movement is going on, must be functional. Condition (i) is met as indicated by the observation that eye saccades have normal dynamics in patients, in accordance with earlier reports (Stell et al., 1990), and also condition (iii) appears to be met in many TC patients (cf. also Stell et al., 1990). However, the reduction of free orbital space on the ipsilateral side caused by the tonic head deviation may violate condition (ii), if not to the point of risking an arrest of the eyes, at least in such way as to force the eyes into an uncomfortable eccentricity. This creates the only constraint for the eye movement component, which appears to be delayed because it ‘waits’ for the head movement in order to reduce the period of uncomfortable lateral deviation. The surprising fact is that this delay appears to apply to all situations, whether implying a risk of large eye eccentricity or not.

Conclusions

Tonic and dynamic head motor control associated with visual orientation appears to be differentially affected in TC. Whereas all patients of this study incurred a laterally deviated head position while gazing at a target aligned with their anterior–posterior trunk axis, many made head movements of normal velocity during gaze reorientation. Moreover, all patients were, in principle, able to make large head movements, although they would make smaller ones than normal subjects for gaze shifts of given magnitude. Thus, to give a simplistic phenomenological description of TC, it can be said that the disease leads to a change of the tonic set point for static head position (with fluctuations of this signal possibly being responsible for the phasic head jerks that occur in some patients) and to a reduced gain of head displacement, but it does not necessarily impair the motor programme executing these displacements. These findings apply to head movements performed during externally triggered gaze shifts and must be contrasted to the high and often frustrative effort of patients to correct their tonic head deviation by a voluntary head movement.

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