

# Abnormal interaction between vestibular and voluntary head control in patients with spasmodic torticollis

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## Summary

The functional status of vestibulo-colic reflexes in the sternocleidomastoid (SCM) muscles was investigated in 24 patients with spasmodic torticollis using small, abrupt 'drops' of the head. None had been treated with botulinum toxin injections during at least 4 months preceding the study. Eight of the patients, four of whom had been studied before surgery, were also studied after selective peripheral denervation of neck muscles. The reflex was of normal latency and duration in the 'passive drop' condition, in which subjects were instructed not to oppose the fall of the head. To study voluntary interaction with the reflex response, subjects were then asked to flex the neck as quickly as possible after onset of the head drop ('active

drop'). In this condition, voluntary responses in patients were delayed, smaller and less effective in counteracting the head fall than in normal subjects. The same abnormalities were also found in patients after surgery when the head posture was improved. Somatosensory/auditory voluntary reaction times in SCM were normal, as was the latency of the startle reflex. We conclude that voluntary interaction with the vestibulo-colic reflex is disrupted in patients with spasmodic torticollis, a finding which corroborates the patients' aggravation of their symptoms by head or body perturbations. Lack of effective interaction between two major systems controlling head position may contribute to torticollis.

**Keywords:** spasmodic torticollis; head drop; vestibulo-colic reflex; startle reflex; reaction time

**Abbreviations:** ANOVA = analysis of variance; RT = reaction time; SCM = sternocleidomastoid

## Introduction

The pathophysiology of spasmodic torticollis is unknown. However, several lines of evidence suggest that it is a form of focal dystonia caused by dysfunction of the basal ganglia. For example, it can be observed either in isolation or as part of a more widespread hemidystonia after structural lesions of the basal ganglia or its connections (Boisen, 1979; Marsden *et al.*, 1985; Isaac and Cohen, 1989; Bhatia *et al.*, 1994). In addition, spasmodic torticollis is often part of the clinical presentation in generalized primary torsion dystonia (Fahn *et al.*, 1988), in which functional imaging data and neurophysiological studies imply abnormalities in the basal ganglia and its projections (Eidelberg *et al.*, 1995; Ceballos-Baumann *et al.*, 1995; Ridding *et al.*, 1995; Eidelberg, 1998).

The main unresolved question at the present time is why spasmodic torticollis, like other focal dystonias, affects only one part of the body. Two types of explanation have been proposed. The first relies on the fact that there is a rough somatotopy within the sensory motor region of the basal ganglia, so that spatially limited damage might produce effects on only one part of the body (DeLong *et al.*, 1985). The second suggestion is that the basal ganglia damage may itself be more widespread, but that the deficit is clinically focal because of some secondary dysfunction in another part of the motor system. In other words, focal dystonia would occur only when there was a combination of a propensity towards dystonia produced by a basal ganglia deficit coupled

**Table 1** Characteristics of subjects who took part in the head drop experiment and the subgroups of subjects who took part in all three experiments (head drop, simple RT and startle RT)

	Healthy subjects		Patients before surgery		Patients after surgery
	HD only	All expts	HD only	All expts	HD only
Sex (M : F)	11 : 10	9 : 4	6 : 14	5 : 7	3 : 5
Mean age in years (range)	40 ± 9.4 (26–59)	43 ± 8.9 (30–59)	47 ± 9.2 (30–65)	44.6 ± 10.2 (30–65)	50.6 ± 8.4 (38–60)
Mean onset (years)			35.1 ± 11.7	34 ± 12	37.1 ± 13.8
Disease duration (years)			12.2 ± 7.8	11 ± 5.3	13.5 ± 10.4

All values are mean ± 1 SD. Note that group means of subjects are given in the table. For comparison of patients before and after surgery, see Results. M = male; F = female; HD = head drop; expts = experiments.

with a second insult. The nature of this second insult might be natural or pathological. For example, overuse or overtraining of muscle groups is often associated with dystonia (e.g. writer's cramp or musician's cramp) (Sheehy *et al.*, 1988). The plastic changes associated with such training in sensory and motor areas of the cortex (Byl *et al.*, 1996) may become unstable in the presence of subtle basal ganglia changes, and lead to dystonia. Alternatively, the second insult might be pathological. In a recent animal model, it has been shown that blepharospasm can be produced by the combination of a basal ganglia lesion (dopamine depletion in the substantia nigra pars compacta) and a peripheral lesion of the facial nerve, but by neither of these lesions in isolation (Schicatano *et al.*, 1997). There are also clinical examples of this phenomenon (Singer *et al.*, 1998). Indeed, torticollis has been described in some patients following unilateral lesions of the eighth nerve (Bronstein *et al.*, 1987).

Following this line of reasoning, there is some evidence that vestibular input to the ocular motor control system is abnormal in patients with torticollis (Bronstein and Rudge, 1986; Huygen *et al.*, 1989; Stell *et al.*, 1989). There is also limited evidence, from subtle asymmetries in click-evoked myogenic responses (Colebatch *et al.*, 1995), that there might be abnormalities in the vestibular control of the neck itself. Whether either of these would be sufficient to couple in some patients with underlying basal ganglia deficit to produce spasmodic torticollis is unknown. In this study, we sought further evidence for an abnormality of vestibulo-colic processing in patients with spasmodic torticollis. By perturbing the head with small 'drops' (Ito *et al.*, 1995, 1997), we showed that there was an abnormality in the way voluntary and reflex control systems worked together to control the neck, and that this persisted in patients in whom the neck position was improved after selective peripheral denervation.

## Material and methods

### Subjects

All subjects gave their informed consent to the study, which was approved by the local ethics committee. We studied 21 healthy subjects, 20 patients with spasmodic torticollis before

surgery (selective peripheral denervation), of whom four were also restudied after surgery, and an additional four patients only after surgery. The rationale for studying patients after surgery was twofold. First, we could test whether cutaneous or proprioceptive inputs, that were altered by surgery (see below), contribute significantly to the motor responses after the head drop. Secondly, we could evaluate whether normalization of head position by surgery changed the pattern of the dystonic activity that we evoked. The subject characteristics are summarized in Table 1.

Eleven of the 20 torticollis patients who were studied before surgery and two of the four patients who were studied only after surgery showed a combination of abnormal head rotation and head tilt. Seven patients in the preoperative group had a combination of abnormal head rotation, head tilt and neck extension. The remaining four patients (two studied only before and two only after surgery) had a predominant neck extension. Abnormal head position was measured using a goniometer. Muscle power was tested before the experiment. Patients with clinical weakness of neck flexion were excluded.

The severity at the time of the assessment was determined using the TWSTRS (Toronto Western Spasmodic Torticollis Rating Scale) (Consky and Lang, 1994), which includes assessment of the dystonic position of the head, neck and shoulder, effectiveness of any sensory gesture, how long the patient can keep the head in a straight position, and the range of head and neck movement. The maximum severity score on this scale is 35. Disability was rated according to the TWSTR disability subscales (maximum score of 30). Severity of head tremor was scored according to the validated clinical rating scale proposed by Bain and colleagues (Bain *et al.*, 1993). Additionally, patients were asked specifically whether their ability to control head movements was motion dependent. Based on estimates of the amount of acceleration or deceleration occurring in daily life, the following scoring system was used: 0 = no difference between static position (e.g. standing) and being in motion; 1 = greater difficulties in controlling head movements compared with a static position only during abrupt head/body acceleration or deceleration, e.g. caused by sudden jolts of a vehicle (trains, cars, etc.), while being in this vehicle, or an abrupt push

while being in a crowd; 2 = during minor head/body perturbations, e.g. during smooth bus or train rides.

All patients had received botulinum toxin injections in the past. The interval between the last botulinum toxin injection and the investigation before surgery was at least 4 months in all patients. The eight patients studied postoperatively were investigated within 3 months after surgery before possible functionally relevant reinnervation would have occurred.

The surgery carried out was a selective peripheral denervation which aims to denervate the muscles causing abnormal movements while preserving innervation to those that do not (Bertrand and Molina-Negro, 1988; Bertrand, 1993; Muenchau *et al.*, 1999). In principle, this involves section of branches of the accessory nerve supplying the sternocleidomastoid (SCM) muscle or of posterior rami of the roots C1–C5/6 uni- or bilaterally. The latter is called posterior ramisectomy and results in complete motor and sensory denervation of the corresponding posterior segments (posterior neck muscles and all sensory modalities from the posterior neck). The anterior rami that supply anterior neck muscles and form the cervical and brachial plexuses are spared.

Additionally, two patients aged 51 and 52 years, respectively, with bilateral severe reduction of vestibular function (>90%) to caloric and rotational testing (Rinne *et al.*, 1998) were studied to reconfirm the vestibular origin of the drop response in the current setting.

### **Recording system**

Head acceleration was monitored with a precision piezo resistive DC-coupled linear accelerometer mounted with surgical tape on the forehead with the sensitive axis aligned to earth vertically. Muscle activity in both SCM muscles was recorded with silver chloride surface electrodes with an impedance of typically 1 k $\Omega$ . They were placed in differential pairs on the belly of the muscle 5 cm apart. The earth was placed at the wrist. The EMG signals were amplified, analogue filtered (32 Hz to 3 kHz) and acquired at a sampling rate of 1 kHz as in previous studies using the head drop technique (Ito *et al.*, 1995, 1997). In one subject, we compared the latencies, duration and magnitude of the EMG reflex response after sudden head drop using a sampling rate of 10 kHz with those acquired at a sampling rate of 1 kHz, and found no differences.

### **Experimental setting**

Patients were lying supine and well supported on a platform. The head extended beyond the edge of the platform in longitudinal alignment with the body and was supported by a sling around the occiput (Fig. 1), positioned so that the head was held slightly flexed. The carry handles of the sling were restrained from above by a Martin Baker<sup>®</sup> electromechanical aerial bomb release with <1 ms release

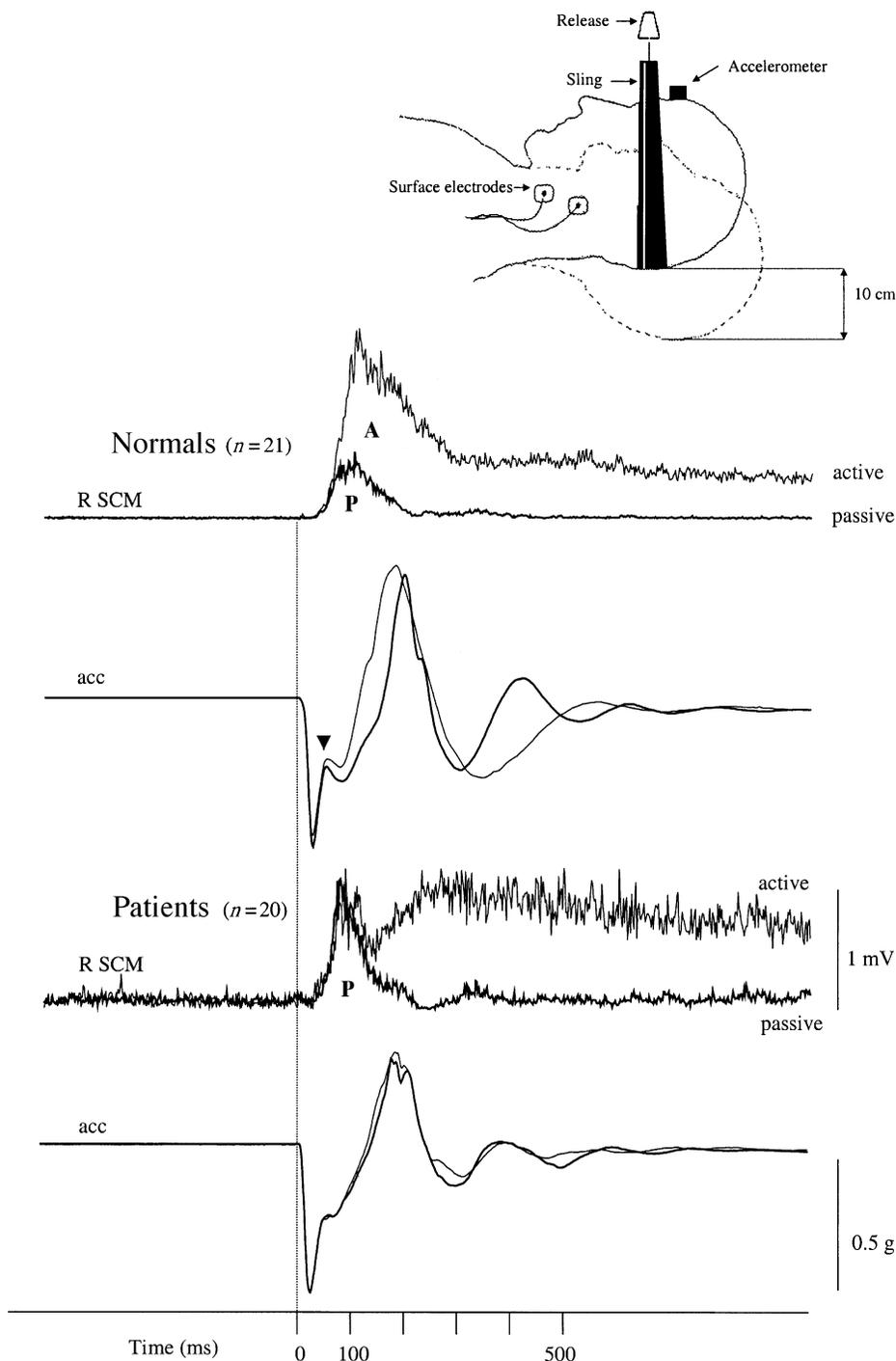
time. The bomb release was fixed to a frame at the end of the platform and could be activated manually by a switch. Activation of the bomb release at random intervals dropped the head, which then fell freely until it hit a cushioned surface 10 cm below the initial level of the occiput, so that the neck was extended briskly. Following the drop, the head was lifted by the examiner and the carry handles were reattached to the bomb release.

Two different conditions were studied in all subjects (a set of 10 drops each). In the 'passive drop', subjects were told to close their eyes and relax as much as possible while the head was dropped. In the 'active drop', subjects were also instructed to relax before the drop but then to flex the neck as quickly as possible when it was released. For both instructions, several minutes elapsed between each drop, which gave the patients the opportunity to relax.

Background EMG activity was monitored continuously before the drop. To study the influence of pre-innervation on the neck reflex response, the passive drop of four healthy subjects was studied additionally under the following conditions: complete relaxation, slight bilateral SCM contraction or unilateral SCM contraction by rotating the head against mild resistance (counterpressure of the subject's hand that was placed at the chin) to the right and left, respectively.

To determine whether the responses in the active drop task are different from a simple neck flexion task or a neck flexion task modified by startle, we also carried out a simple reaction time task (simple RT; neck flexion after an auditory 'go' signal) and a reaction time task after a startling stimulus (startle RT; neck flexion after a loud sound). These tasks were studied in 12 patients (non-operated) and 13 healthy subjects. Characteristics of this group are given in Table 1.

In the RT experiments, subjects were lying supine on the platform with their head resting on a firm pillow in the same slightly flexed and relaxed position as in the head drop experiment. Head acceleration and EMG activity were recorded as mentioned above. In the simple RT, they were instructed to flex their neck as quickly as possible and hold the head against gravity for several seconds after an acoustic 'go' signal (opening click of the aerial bomb release, free field intensity 30 dB above ambient noise, measured at a distance of 1 m from the source with a CEL Instruments Digital Impulse Sound Level Meter, accuracy  $\pm$  1dB at reference level). In order to produce a similar sensory stimulus to the trigeminal nerve as during the head drop (due to sudden release of the sling around the head), a painless electrical stimulus (twofold the sensory threshold) was applied to the right supraorbital nerve at time zero (opening click). In the startle RT, subjects were warned that in some of the RT trials there could be a startling stimulus linked to the auditory 'go' signal but they were also encouraged to react to the simple 'go' signal as before. In random trials, the 'go' signal was combined with a loud sound, capable of eliciting a startle reaction. The sound was obtained by discharging a magnetic coil of a magnetic stimulator over a metal filing



**Fig. 1** Grand average of rectified EMG envelopes of the right sternocleidomastoid muscle (R SCM) and head acceleration traces (acc) of the active and passive head drop experiment in healthy subjects (*top*) and patients with spasmodic torticollis (*bottom*). The EMG and corresponding acceleration traces of the passive drop are drawn in bold. The first part of the acceleration trace is similar in healthy subjects and patients. In healthy subjects, but not in patients, the acceleration trace of the active drop diverges from the acceleration trace of the passive drop before onset of the decelerative phase of the passive drop (arrowhead). The early extra EMG in the active condition (A) is significantly smaller and delayed in patients. The experimental set up is illustrated in the inset (*top right*).

cabinet (intensity 130 dB, measured at a distance of 1 m from the source). In each individual, a minimum of 10 trials containing the ‘go’ signal (control) and 10 trials containing

both the ‘go’ signal and the startling stimulus (test) were obtained. As for the simple RT, a painless stimulus was given to the supraorbital nerve at time zero of each trial.

### Data analysis

In all experiments, onset of head movement was taken from the acceleration records. In the head drop experiment, the amplitude and latency of the initial peak acceleration after release of the sling were also determined.

EMG responses of 10 trials were rectified and averaged. Non-averaged individual pre- and postoperative head drops additionally were compared in the four subjects who were studied both before and after surgery. Background EMG activity was determined for 500 ms before the onset of the stimulus. The total sweep length was 1500 ms. In healthy subjects, the right SCM was measured; in patients with spasmodic torticollis, both SCMs were measured.

In the passive head drop experiment, latencies of onset and duration of the passive reflex response (P) in SCM were determined (see Fig. 1). To assess the modulation of the reflex response in the active drop, the acceleration trace and rectified averaged EMG of the active drop were superimposed on the acceleration and EMG recordings of the passive drop (Fig. 1). Onset of the active EMG in the active drop was defined as the point of divergence of the active and passive EMG envelope.

In order to determine whether the vestibular stimulus elicited by the head drop would modify the active task studied (neck flexion), we compared the EMG onset latencies, EMG peaks and acceleration traces of the active head drop experiment with those of the simple neck flexion experiment (simple RT). In the simple RT, onset latency of voluntary EMG activity after the 'go' signal was measured. Additionally, we studied whether the neck flexion was altered by a startling stimulus by comparing the EMG onset latencies, EMG peaks and acceleration traces of the simple RT with those of the startle RT.

In the head drop experiment, EMG latencies were measured from onset of head acceleration. The mean latency between opening of the bomb release and onset of head acceleration was  $8 \pm 0.9$  ms (mean  $\pm$  standard deviation) and  $8.3 \pm 1.5$  ms in healthy controls and patients, respectively [one-way analysis of variance (ANOVA); n.s.]. In the simple and startle RT, latencies of EMG and acceleration traces were measured from time zero (opening click of bomb release and electrical stimulus over supraorbital nerve). In our experimental setting, the loud sound in the startle RT had to travel a distance of 3 m from the place where it was generated to the subject's ear. This would take  $\sim 9$  ms which we subtracted from the latencies measured in the startle RT. Data of each subject were measured separately, and calculated means of the groups were compared. To illustrate group differences, the grand averages of the groups are also shown in Figs 1 and 4.

### Statistical analysis

In patients who were studied after surgery, pre- and postoperative mean head rotation and head tilt were compared using a Wilcoxon signed ranks test. Independent samples

*t* test was performed to compare results of the head drop experiment between (non-operated) patients with and without retrocollis. A paired samples *t* test was carried out to compare EMG activity between normal and dystonic SCM in patients. A one-way ANOVA was used for each experiment to compare the results between healthy subjects and patients (preoperative data). A two-way repeated-measures ANOVA was used to compare the onset latencies of the EMG components in these groups between the RT tasks and the head drop experiment and to compare the onset latencies of head movement between the simple RT and the startle RT. When a significant difference was found in the ANOVA, a pair-wise comparison was made using Bonferroni's correction. Mean pre- and postoperative data of the patients who were studied both before and after surgery ( $n = 4$ ) were compared with the Wilcoxon signed ranks test. The same test was used to compare individual pre- and postoperative head drops ( $n = 10$ ) case by case. Additionally, head drop data were compared between the eight patients studied after surgery and a group of eight patients studied before surgery who were matched for sex, age, onset age and preoperative head position (degree of head turn and head tilt) using the Mann-Whitney test. To measure a possible correlation between different variables, the Spearman rank-order correlation coefficient was used. For all statistical analyses, an adjusted value of  $P < 0.05$  was considered to be significant.

### Results

In patients, separate measurements were made from the dystonic and non-dystonic SCM muscle. No differences were noted in the responses from each side. Thus, as in healthy subjects, measurements from the right-sided SCM were used and compared with those of the right-sided SCM in healthy subjects.

### Head drop task

Figure 1 shows the grand average responses in healthy subjects and in patients with spasmodic torticollis following head drop in the passive and active conditions. Table 2 summarizes the detailed measurements based on individual measurements.

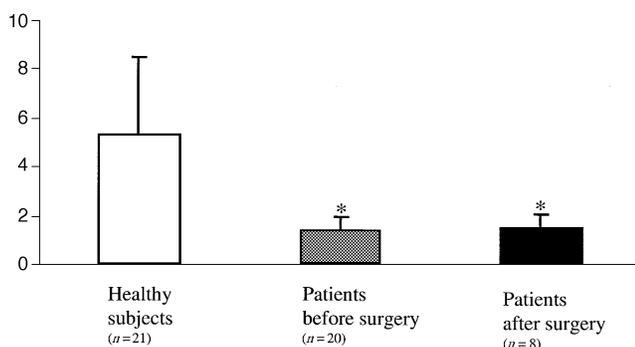
### Healthy subjects

After release of the sling in the passive condition (passive drop), the head made a rapid entry into the fall, with a peak acceleration of  $\sim 0.5 g$ . After the initial acceleration peak, the pattern of acceleration fluctuated with wide inter-subject variability. As described previously (Ito *et al.*, 1995, 1997), the head drop produced an early reflex burst of EMG in the SCM muscle (passive reflex response P) that had a mean latency of 23 ms and a duration of 175 ms. If subjects were instructed to react to the drop by flexing the neck as quickly as possible (active drop), then this response was larger and

**Table 2** Data on head acceleration and EMG responses in the head drop experiment

	Healthy subjects ( <i>n</i> = 21)		Patients before surgery ( <i>n</i> = 20)		Patients after surgery ( <i>n</i> = 8) ( <i>n</i> = 8)*	
	Passive	Active	Passive	Active	Passive	Active
<b>Acceleration</b>						
Time of peak (ms)	14.8 ± 2	14.4 ± 2	15 ± 2 (14.5 ± 1)	14.8 ± 2.4 (14.1 ± 2)	13.0 ± 1.4	13.5 ± 1.8
Peak amplitude (g)	0.45 ± 0.16	0.46 ± 0.1	0.49 ± 0.17 (0.45 ± 0.14)	0.5 ± 0.15 (0.43 ± 0.1)	0.42 ± 1.1	0.43 ± 0.2
<b>EMG</b>						
Onset of P (ms)	22.9 ± 5	22.7 ± 4.8	24.7 ± 5.5 (24.1 ± 5)	24.5 ± 4.7 (23.8 ± 3.4)	25.6 ± 5	24.3 ± 4.5
Duration of P (ms)	175 ± 27	–	172 ± 45.8 (180 ± 28.5)	–	182.8 ± 42	–
Latency active response		69 ± 23†		132 ± 45.2† (121.8 ± 28.3)		137 ± 64†

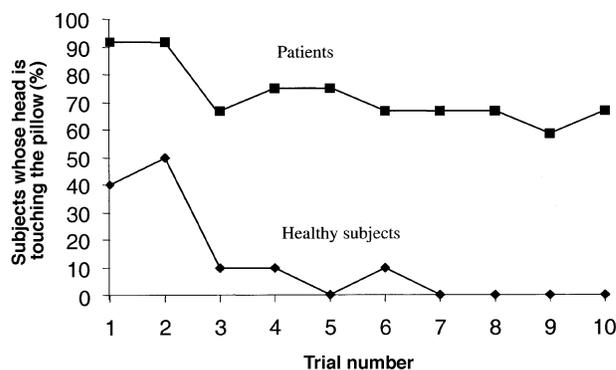
All values are mean ± 1 SD. P = reflex response. \*Values in parentheses are from the eight unoperated patients who were matched for sex, age and (preoperative) degree of head displacement with the eight patients after surgery. †*P* < 0.001 (comparison between healthy subjects and patients).



**Fig. 2** A/P ratio indicating active modulation of the reflex response during the first 175 ms of the active head drop experiment. Data of the right SCM muscle are shown. Error bars indicate 1 SD. \**P* < 0.001 (comparison with healthy subjects).

was followed by a prolonged period of tonic EMG activity. The mean duration of the initial peak of extra EMG activity in the active condition from onset of the first response in SCM to the onset of the tonic EMG activity was 313.2 (range 256–340) ± 40 ms (mean ± standard deviation). We related this EMG peak (labelled A for active in Fig. 1) to the reflex response in the passive condition by calculating the ratio A/P. A was defined as the area under the curve from onset of EMG activity until 175 ms thereafter in the active drop, and P as the area under the curve from onset of reflex EMG activity until 175 ms thereafter in the passive drop (corresponding to the mean duration of the reflex response in the passive drop). The data in Fig. 2 illustrate that the initial peak A in the active condition was some five times larger than the reflex response in the passive condition. Extra EMG activity in the active condition began an average of 69 ms after the onset of the head drop (see Fig. 1).

In order to quantify the functional effectiveness of the subjects' reaction, we noted the percentage of trials on which their head hit the restraining pillow after it had been released. In the passive condition, the head hit the pillow on every



**Fig. 3** Proportion of subjects whose head hit the pillow during each of the 10 trials of the active head drop experiment. The head of healthy subjects (*n* = 10) sometimes hit the pillow during the first six trials but not thereafter. Very few of the patients (*n* = 12) ever managed to prevent their head from hitting the pillow.

trial. On the first two trials of the active condition, 50% of the subjects' heads did not hit the pillow. After the sixth trial, none of the subjects' heads hit the pillow, indicating that the voluntary reaction had a functionally significant effect on early head position (Fig. 3).

#### Patients with spasmodic torticollis

Release of the head produced the same initial acceleration as in healthy subjects (Table 2 and Fig. 1). In the passive condition, the reflex response had the same latency and duration as normal, although the mean amplitude appeared to be slightly larger. We have not quantified the absolute sizes of EMG responses because it is difficult to normalize data between different subjects. However, it seems likely that this amplitude difference was caused by the higher level of background EMG in the patients' SCM prior to head drop (area under the curve, 12.1 ± 12 mV/ms as compared with 2.2 ± 2.3 mV/ms in healthy subjects; one-way ANOVA,

$P < 0.001$ ). This was confirmed by asking four healthy subjects to increase the background level of EMG activity prior to head drop which caused an increase in the amplitude of the reflex response.

The main difference between patients and normal subjects was the later onset of extra EMG activity in the active trials. Not only did this happen some 60 ms later in the patients (Table 2), but the amount of extra EMG over and above that evoked in the passive condition (reflected in the A/P ratio) was less than one-third of that seen in healthy subjects (Fig. 2). The net result was that very few of the patients ever managed to prevent their head from hitting the pillow in the active condition (Fig. 3). Both onset latency of extra EMG activity and the A/P ratio were significantly correlated with the percentage of 'pillow hits' during the 10 active head drop trials (Spearman rank-order correlation coefficient  $r = 0.65$ ,  $P = 0.04$  and  $r = -0.86$ ,  $P = 0.001$ , respectively).

#### *Clinical correlates (non-operated patients)*

In patients, the onset latency of extra EMG activity and the A/P ratio were not correlated with the patients' age, duration of symptoms, overall severity or disability scores (as determined by the TWSTRS), magnitude of head rotation or head tilt (in degrees), head tremor scores (Bain *et al.*, 1993) or background EMG activity in SCM. Onset latency of extra EMG activity and the A/P ratio were also not significantly different in patients with retrocollis as compared with those without retrocollis. However, the score for motion dependency of neck symptoms was significantly correlated with both onset latency of extra EMG activity (Spearman rank-order correlation coefficient  $r = 0.46$ ,  $P = 0.041$ ) and the A/P ratio ( $r = -0.49$ ,  $P = 0.03$ ).

#### *The effect of surgery*

Of the eight patients we studied postoperatively, a right selective accessory nerve denervation and left posterior ramisectomy was carried out in three, a right accessory nerve denervation and bilateral posterior ramisectomy in one and a bilateral posterior ramisectomy in four patients. In these eight patients, the degree of head displacement before and after surgery was as follows:  $38^\circ \pm 18^\circ$  (mean  $\pm$  standard deviation) and  $11^\circ \pm 4^\circ$  mean head rotation and  $22^\circ \pm 16^\circ$  and  $12^\circ \pm 4^\circ$  mean head tilt before and after surgery, respectively (Wilcoxon signed rank test,  $P = 0.004$  and n.s.). Results (mean data) of the head drop experiments are shown in Table 2. Only data from the intact SCM are presented. We compared the data with those of unoperated patients in two ways. First, four of the eight patients had been studied prior to surgery. Comparison of group means and of data of individual head drops before and after surgery on a case by case basis (see Material and methods) did not show a significant difference of head acceleration and EMG data. We also performed a second comparison between all eight operated patients and eight patients from the unoperated

group who were matched for age, sex and preoperative degree of head displacement. Head acceleration and EMG data also did not differ between these two groups.

#### *Labyrinthine-defective patients*

Two patients with defective labyrinthine function were studied. The acceleration traces did not differ from those of healthy subjects and patients with spasmodic torticollis. As has already been described by others (Ito *et al.*, 1995), the reflex response in the passive condition was delayed (onset latency: 51 and 52 ms, for each patient; mean of healthy controls:  $22.9 \pm 5$  ms). The onset of extra EMG activity in the active condition was also delayed compared with the mean normal data (96 and 163 ms, respectively; healthy controls:  $69 \pm 23$  ms).

#### *Reaction time tasks*

The RT time for neck flexion was measured in 13 of the healthy subjects and 12 of the patients. The mean data from all subjects are shown in Fig. 4 for both the simple and startle RT tasks.

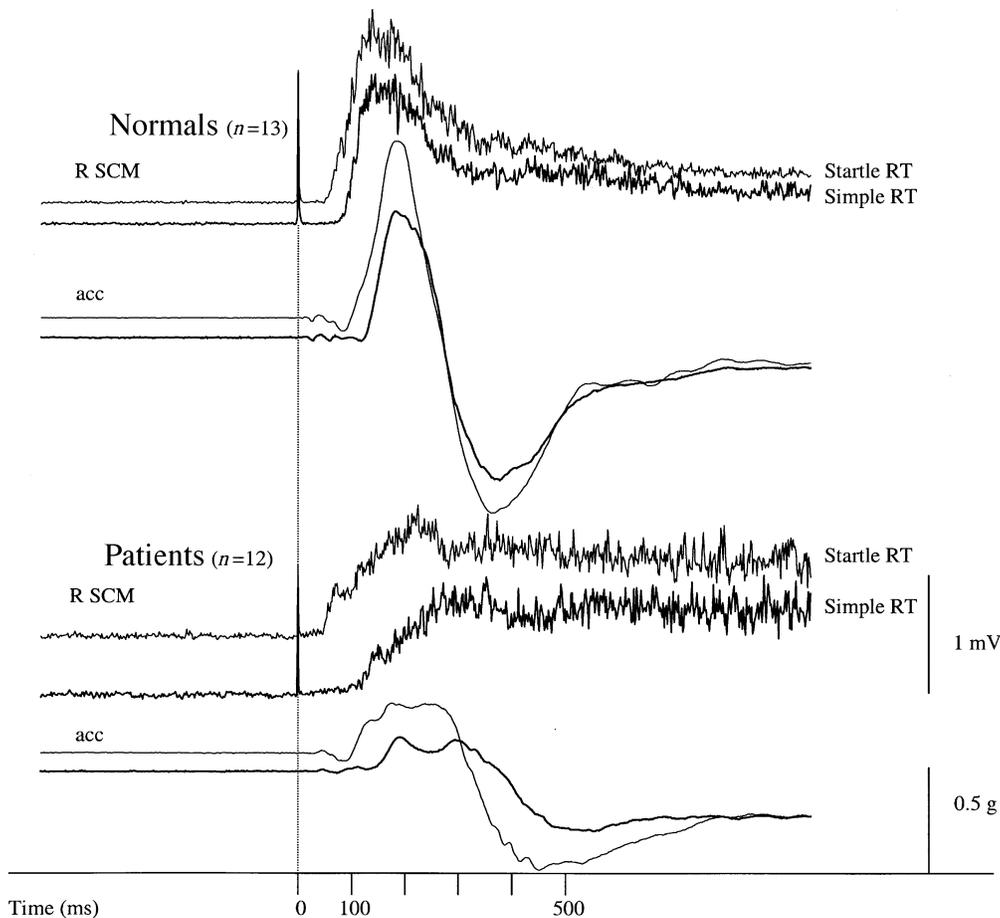
#### *Healthy subjects*

When healthy subjects reacted to the opening click of the bomb release plus a small electrical stimulus to the supraorbital nerve, the RTs measured from the EMG and acceleration traces were 88 ms and 132 ms, respectively (for details, see Table 3). If a loud startling sound was given, then both the EMG response and the head movement began some 40 ms earlier. Presumably the response to the startle was a compound of a true startle reflex in the SCM and a volitional response.

#### *Patients with spasmodic torticollis*

Responses in the patient group had the same latencies as in healthy subjects. The variability in simple RT was larger in the patients, but the latency was shortened by the startle in the same way as in healthy subjects (Table 3, Figs 4 and 5). The mean EMG data shown in Fig. 4 suggest that the speed with which the patients could recruit EMG activity in the SCM was slower than in normal subjects. This was confirmed by measuring the slope of the initial part of the EMG response (Table 3), which was significantly less steep in the patient group.

Frequently, both in healthy subjects and patients, a small acceleration towards the pillow was detected before the onset of the main acceleration peak away from the pillow (Fig. 4), which indicates initial brief neck extension. This was observed in five healthy subjects and six patients in the simple RT and in 10 healthy subjects and seven patients in the startle RT. It was much more pronounced in the latter task both in healthy subjects and in patients when it was present in both tasks.



**Fig. 4** Grand average of rectified EMG envelopes of the right SCM muscle (R SCM) and acceleration traces (acc) of the simple and startle RT in healthy subjects and patients. EMG and the corresponding acceleration traces of the simple RT are drawn in bold. Onset latencies of EMG responses and head flexion are taken from time zero (click of the electromechanical release in the simple RT and click plus loud sound in the startle RT, indicated by the dotted line). The stimulation artefact at time zero in the EMG traces is caused by the electrical stimulus given to the supraorbital nerve. The small-amplitude oscillations before the onset of the head movement were caused by perturbations of the accelerometer by contractions of the orbicularis oculi muscles due to stimulation of the supraorbital nerve (electrically elicited blink reflex). Peak EMG and acceleration amplitudes are smaller in patients, and onset slopes of EMG and acceleration traces are less steep, but onset latencies are similar in both tasks. Note that the response occurred earlier in the startle RT in both healthy subjects and patients.

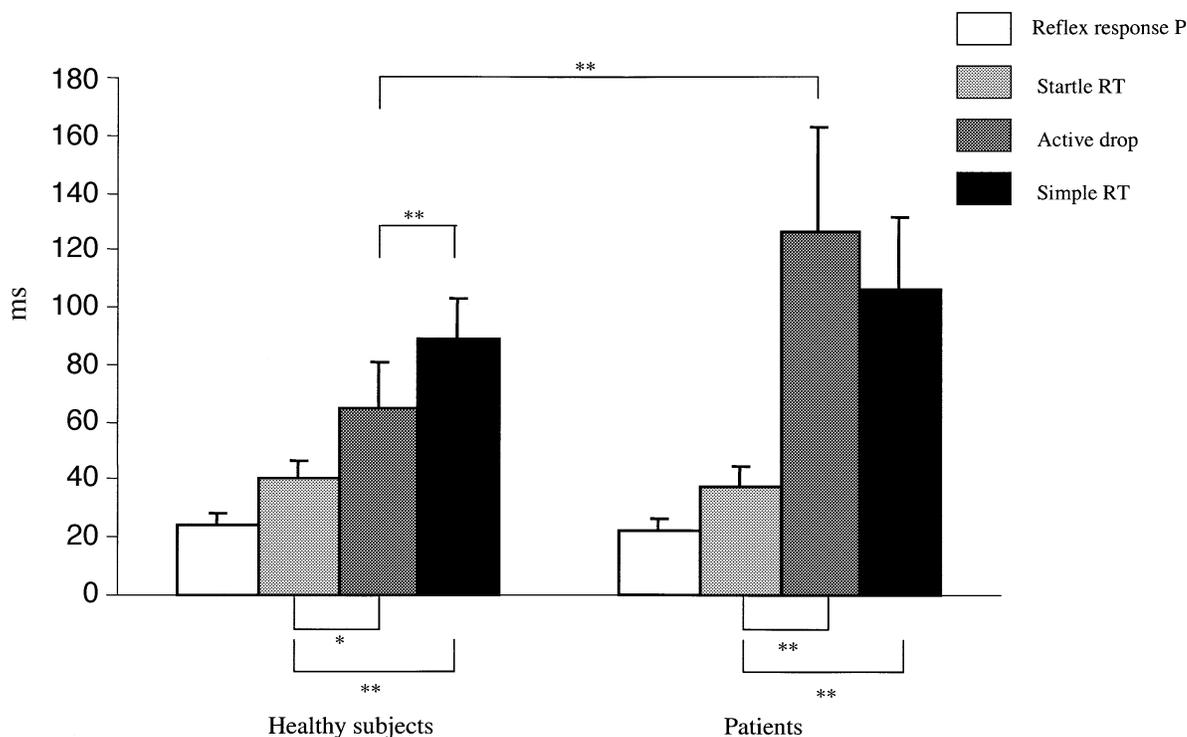
**Table 3** Data on head acceleration in the reaction time tasks and EMG responses in the three different tasks

	Healthy subjects ( $n = 13$ )			Patients ( $n = 12$ )		
	Simple RT	Startle RT	Act. head drop	Simple RT	Startle RT	Act. head drop
Acceleration						
Onset of neck flexion (ms)	132 ± 24	93.1 ± 28	–	150 ± 33	104 ± 28	–
EMG						
Onset of EMG activity (ms)	88.4 ± 15	41 ± 6.5	62.5 ± 15.4*	106 ± 27	38 ± 6.1	127 ± 37*
Slope of initial EMG (µV/ms)	3.5 ± 1.3†			2.2 ± 1.2†		
Peak amplitude of initial EMG (mV)	1.6 ± 0.6†			1 ± 0.5†		

All values are mean ± 1 SD. RT = reaction time task; Act. head drop = onset of extra EMG activity in the active condition measured from the onset of head acceleration. \* $P < 0.001$ ; † $P = 0.02$ .

A brief neck extension at the onset of a voluntary neck flexion task was also observed in another study of neck flexion kinematics in healthy subjects (Margulies *et al.*,

1998). There are two possible explanations for this initial brief neck extension. First, it could be caused by the action of the SCM muscle. This muscle is the principal and strongest



**Fig. 5** Mean onset latencies of EMG responses in the different tasks. Note that onset latencies of the reflex response P and of the active response in the startle and simple RTs are similar in both groups. Also, responses in the startle RT are faster than in the simple RT and in the head drop task in both groups. In healthy subjects, but not in patients, neck flexion EMG occurs earlier in the active head drop as compared with the simple RT. Onset of neck flexion EMG in the active head drop is significantly delayed in patients as compared with healthy subjects. Error bars indicate 1 SD. \* $P = 0.001$ ; \*\* $P < 0.001$ .

head flexor but, due to its insertion behind the pivot for head rotation, it can act as a head extensor when the head is in longitudinal alignment with the body (Machado De Sousa *et al.*, 1973), as in our experiment. Thus, activation of the SCM may result in a brief neck extension that is then followed by flexion. Alternatively, other neck extensors not recorded in the experiment might have been activated in the tasks studied, particularly in the startle RT.

### **Comparison of the reaction time tasks with the head drop experiment**

It has to be noted that the onset of the active response in the active head drop was taken from the EMG traces. It is not possible to determine unequivocally the beginning of neck flexion after the fall of the head from the acceleration traces. In healthy subjects, the EMG peaks of the active head drop and the RT tasks did not differ. Comparing the latencies of the different active tasks (see Fig. 5 and Table 3; mean values calculated from measurements of individual subjects' records), the fastest response occurred in the startle RT (41 ms). It was significantly faster than both the active response in the head drop experiment [62.5 ms in the healthy subjects in whom all three tasks were studied ( $n = 13$ )] and the response in the simple RT (88.4 ms) (repeated-measures

ANOVA,  $P = 0.001$  and  $P < 0.001$ , respectively). The active response in the head drop occurred significantly earlier than that in the simple RT ( $P < 0.001$ ).

In patients, the response in the startle RT (38 ms) was significantly faster than both the active response in the head drop [127 ms in the patients in whom all three tasks were studied ( $n = 12$ )] and the response in the simple RT (106 ms) ( $P < 0.001$ ). However, onset of the active response in the head drop was significantly delayed compared with healthy subjects ( $P < 0.001$ ) and occurred later than the response in the simple RT, albeit not significantly later ( $P = 0.12$ ) (Fig. 5 and Table 3).

### **Discussion**

The main finding of the present experiments is that although vestibulo-collic reflexes in the SCM are intact in patients with torticollis, their interaction with voluntary mechanisms of neck control is impaired.

### **Reflex responses to passive head drop in subjects lying supine**

As described by Ito and colleagues (Ito *et al.*, 1995), we found that passive head drop could readily elicit a short

latency (25 ms) reflex response in the SCM muscles of all healthy subjects. Consistent with their hypothesis that this component has a vestibular origin, we found that the early part of the reflex was absent in two patients with deficient vestibular function but that it was unaffected in patients after uni- or bilateral surgical denervation of posterior cervical segments including the sensory supply. The latency and duration of this early vestibulo-colic reflex were the same in patients with torticollis as in normal subjects.

### ***Interaction between reflex and voluntary responses to head drop***

The most important finding in the present experiments was that the interaction between reflex and voluntary responses to head drop was impaired in torticollis patients. When subjects tried actively to resist the head drop by flexing their neck voluntarily, extra EMG occurred over and above that seen in response to passive head drop alone. In patients, this extra EMG occurred some 60 ms later than in healthy subjects, and was significantly smaller in amplitude. The effect was not limited to the dystonic SCM, but was also found in the contralateral SCM. Latencies and amplitudes of extra EMG were correlated with patients' ability to prevent their head from hitting the pillow, confirming that the abnormal EMG responses were of functional importance. The net result was that, whereas healthy individuals could always manage to break the fall of their head before it touched the pillow, few of the patients were able to do this (Fig. 3).

Abnormalities of vestibulo-voluntary interaction in torticollis patients demonstrated in this experimental setting also appear to be of clinical relevance. Scores for motion dependency of symptoms reflecting difficulties in controlling head movement to natural head or body perturbations were correlated with abnormal EMG responses in the active drop.

The voluntary reaction to the head drop was also delayed in our two labyrinthine-defective patients, as previously reported (Ito *et al.*, 1997). Thus, although short-latency vestibulo-colic reflex pathways are normal in torticollis patients, their voluntary responses after the head drop resemble that of labyrinthine-defective patients, as if vestibular information was ignored in them or not fully integrated at higher CNS levels. This could explain the ineffective head control to head or body perturbation.

Voluntary activation in the head drop was also delayed and small in patients after posterior ramisectomy. Since surgery had a substantial corrective effect on head posture, we conclude that abnormal head position *per se* does not explain the changes in the active head drop condition. Also, we did not find a correlation between the results of the head drop and abnormal neck extension (retrocollis). Moreover, the duration and severity of symptoms, or the amount of dystonic EMG activity were not correlated with abnormal responses to head drop. It is therefore likely that abnormal

vestibulo-voluntary interaction is a primary problem in torticollis rather than being secondary to long-standing abnormal head movements.

### ***Rapid voluntary flexion of the neck (simple RT)***

Two sets of control experiments were performed to explore possible reasons for the abnormal vestibulo-voluntary interaction in the torticollis patients. In the first, we tested voluntary reactions of subjects to a non-vestibular (somatosensory plus auditory) input. Unlike the head drop condition, the RT to the onset of voluntary SCM activity in this task was not significantly different between healthy subjects and patients. As reported by other authors during studies of limb movement RTs (e.g. Ghez *et al.*, 1988; see review by Berardelli *et al.*, 1998), the initial rate of recruitment of EMG activity was less steep in patients than in normal subjects (Fig. 4). This may contribute to slowness of voluntary movements in dystonia (Oppenheim, 1911; Fahn, 1988). Although the same phenomenon may account for the smaller size of the patients' volitional response in the active head drop condition, it could not account for the delay in its onset.

### ***Responses to a startling stimulus (startle RT)***

In a second set of experiments, we tested whether abnormal vestibulo-voluntary interaction could have been due to a defect in the patients' startle reflex rather than in their voluntary RTs. The reason for testing the startle is as follows. An unexpected head drop can give rise to a startle reflex but, under passive conditions, this habituates rapidly with repeated trials, and does not contribute to the average response to head drop (Ito *et al.*, 1995). However, Valls-Solé and colleagues have shown that if subjects are required to react voluntarily to the startling stimulus, then the startle reflex itself does not habituate (Valls-Solé *et al.*, 1999). Thus, it is possible that in healthy subjects, the initial part of the voluntary response in the active head drop condition consists of a non-habituated startle that merges into later voluntary activity. If this were the case, then the late onset of volitional activity in patients could be due to an abnormal startle reflex rather than any defect in vestibulo-voluntary interaction.

There are three reasons why this is unlikely to be true. First, the onset latency of the startle reflex in SCM [ $\sim 40$  ms in the present and other experiments (Wilkins *et al.*, 1986)] is earlier than the onset of additional EMG activity in the active head drop task in healthy subjects ( $\sim 60$  ms), suggesting that the latter is not a startle response. Secondly, when we tested the interaction between a startle reflex and a voluntary reaction, by asking subjects to flex the neck in response to a very loud startling stimulus, EMG latencies were the same in patients as in healthy subjects (Figs 4 and 5 and Table 3). Thirdly, the startle elicited by whole-body drop (Bisborff *et al.*, 1999) is preserved in patients with torticollis (Stell *et al.*, 1990). We conclude that the abnormal response

of patients in the head drop condition is due to a specific deficit in vestibulo-voluntary interaction.

### ***Comparison of voluntary responses to head drop with the simple RT***

There is one final point to note about vestibulo-voluntary interaction in the active head drop task. In healthy subjects, the latency of the extra EMG activity over and above that seen in the passive condition was some 25 ms shorter than the usual simple RT. Indeed, the latency could be as short as 45 ms from onset of head acceleration. We can only speculate on why the latency was so short. It could be that the intention to respond voluntarily to the head movement increased the gain of the vestibular reflex, so that the onset of extra activity represents the onset of extra reflex activity rather than voluntary input from the brain. If so, then the problem in patients would lie in the voluntary modulation of short latency reflex responses. Alternatively, as suggested by Valls-Solé and colleagues (Valls-Solé *et al.*, 1999), it may be possible in certain RT tasks to release a well-prepared voluntary response from a subcortical rather than a cortical store, in which case the RT might be much shorter than normal. If this were true, then patients with torticollis might have a defect in this rapid response system. Unfortunately, the present data do not allow us to distinguish between these alternatives.

### ***Abnormal vestibulo-voluntary interaction in patients with torticollis***

Whatever the nature of the interaction between vestibular and voluntary systems, it is easy to see how a failure to integrate two major systems controlling head position could lead to functional problems in neck control, and perhaps contribute to the emergence of torticollis. However, it is less easy to understand how this relates to a presumed basal ganglia deficit. One possibility is that a focal part of the basal ganglia, affected by disease in torticollis, influences vestibular processing in the brainstem. The basal ganglia project via the pedunculo-pontine nucleus to the nucleus reticularis gigantocellularis (Garcia-Rill and Skinner, 1987), which receives strong projections from the vestibular system (Carleton and Carpenter, 1984). The interstitial nucleus of Cajal also has connections with both basal ganglia and vestibular systems (Fukushima *et al.*, 1983). Electrical stimulation in this region produces ipsilateral head rotation in monkeys and cats (Hassler and Hess, 1954; Malouin and Bedard, 1982). It is possible that the abnormal basal ganglia output disrupts vestibular processing in such a way as to leave simple vestibulo-collic reflexes intact, but interferes with vestibular input to voluntary and other high level systems. If this were the case, then perhaps other forms of focal dystonia might have similar abnormalities of volitional-reflex interaction.

Another possibility is that, in torticollis, basal ganglia pathology is more widespread and affects processing in several systems but its clinical expression is limited by other factors. Evidence in support of this comes from the fact that in several forms of focal dystonia, careful testing can often reveal neurophysiological abnormalities in parts of the body without clinical symptoms. For example, forearm reciprocal inhibition or blink reflex recovery can be abnormal in patients with torticollis who have no arm dystonia or blepharospasm (Tolosa *et al.*, 1988; Deuschl *et al.*, 1992). In these cases, it could be that dystonia expresses itself clinically in the neck because there is an additional secondary deficit in systems controlling neck movement. A possible candidate would be the vestibular system since mild vestibular deficits have been described many times in patients with torticollis who have no overt vestibular disease. These include subtle abnormalities in vestibulo-ocular testing (Bronstein and Rudge, 1986; Huygen *et al.*, 1989; Stell *et al.*, 1989; Benabou *et al.*, 1999), perception of verticality (Anastasopoulos *et al.*, 1997a, b) and postural control (Lekhél *et al.*, 1997; Moreau *et al.*, 1999; Müller *et al.*, 1999). Indeed, in occasional patients, spasmodic torticollis apparently is triggered by a vestibular insult (Bronstein *et al.*, 1987). Under normal circumstances, such deficits may produce no long-standing problems but, when combined with basal ganglia defects, they may focus clinical symptoms to the neck. In effect, a subclinical basal ganglia deficit is exposed by a secondary physiological problem (Schicatanò *et al.*, 1997). A final consideration is that, with either of these possibilities, the nervous system may try to compensate by reducing the gain of vestibular input to higher order systems controlling the neck. This lack of vestibular input can then explain the abnormal vestibulo-voluntary interaction.

### **Conclusion**

The impairment of the interaction of volitional control with vestibulo-collic reflexes adds new insight to the problem of vestibular function in torticollis. First, it shows that there is abnormal use of vestibular signals at the highest levels of the motor system, which we have referred to as abnormal vestibulo-voluntary interaction. Secondly, it shows that this abnormal vestibulo-voluntary interaction has functionally significant consequences in terms of head stability for these patients which correlated with the aggravation of their symptoms during motion. In addition, the findings may have broader significance for the neurophysiology of dystonia in general. The response we studied is vestibular in origin, but it is possible that abnormal voluntary interaction with short-latency reflex responses is a more widespread neurophysiological deficit in dystonia.

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