Abnormal central integration of a dual somatosensory input in dystonia
Evidence for sensory overflow

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Summary

Several observations suggest impaired central sensory integration in dystonia. We studied median and ulnar nerve somatosensory evoked potentials (SEPs) in 10 patients who had dystonia involving at least one upper limb (six had generalized, two had segmental and two had focal dystonia) and in 10 normal subjects. We compared the amplitude of spinal N13, brainstem P14, parietal N20 and P27 and frontal N30 SEPs obtained by stimulating the median and ulnar nerves simultaneously (MU), the amplitude value being obtained from the arithmetic sum of the SEPs elicited by stimulating the same nerves separately (M + U). Throughout the somatosensory system, the MU : (M + U) ratio indicates the interaction between afferent inputs from the two peripheral nerves. No significant difference was found between SEP amplitudes and latencies for individually stimulated median and ulnar nerves in dystonic patients and normal subjects, but recordings in patients yielded a significantly higher percentage ratio [MU : (M + U) × 100] for spinal N13 brainstem P14 and cortical N20, P27 and N30 components. The SEP ratio of central components obtained in response to stimulation of the digital nerves of the third and fifth fingers was also higher in patients than in controls but the difference did not reach a significant level. The possible contribution of subliminal activation was ruled out by recording the ratio of SEPs in six normal subjects during voluntary contraction. This voluntary contraction did not change the ratio of SEP suppression. These findings suggest that the inhibitory integration of afferent inputs, mainly proprioceptive inputs, coming from adjacent body parts is abnormal in dystonia. This inefficient integration, which is probably due to altered surrounding inhibition, could give rise to an abnormal motor output and might therefore contribute to the motor impairment present in dystonia.

Keywords: upper limb SEPs; somatosensory evoked potentials; dystonia; somatosensory system; muscle afferent input; surrounding inhibition

Abbreviations: M = median nerve; SEP = somatosensory evoked potential; U = ulnar nerve

Introduction

The pathophysiology of dystonia is still unclear. Neurophysiological studies in patients with dystonia disclose excessive co-contraction of antagonist muscles, difficulty in activating the appropriate muscles and an overflow of muscular activity into extraneous muscles (Sheehy and Marsden, 1982; Rothwell *et al.*, 1983; Hughes and McLellan, 1985; Cohen and Hallett, 1988; Marsden and Sheehy, 1990; Berardelli *et al.*, 1998). This lack of specificity during muscle activation could depend partly on reduced reciprocal inhibition (Rothwell *et al.*, 1983; Berardelli *et al.*, 1985;

Nakashima *et al.*, 1989; Panizza *et al.*, 1989, 1990; Priori *et al.*, 1995). Recent findings also suggest changes in cortical inhibitory circuits in dystonia (Ridding *et al.*, 1995). A second possible causative mechanism for dystonia that is still open to question is inefficient central sensory–motor processing (Odergreen *et al.*, 1996), because numerous clinical phenomena suggest the primary involvement of the somatosensory system (Hallett, 1995). For example, sensory tricks (Sheehy and Marsden, 1982; Marsden and Sheehy, 1990; Leis *et al.*, 1992) and peripheral afferent blockade

(Kaji *et al.*, 1995) can relieve dystonic spasms. Finally, patients with focal hand dystonia have an impairment of discriminative sensory processing (Byl *et al.*, 1996*a*) and an abnormal perception of movement (Grunewald *et al.*, 1997). Somatosensory evoked potentials (SEPs) assess the neural activity of dorsal horn (with recording of spinal N13 potential) and of dorsal column–lemniscus medialis (with recording of brainstem P14 and cortical N20, P27 and N30 potentials) systems of the lemniscal pathway. Routine SEP studies in dystonia have produced conflicting results. Some authors (Reilly *et al.*, 1992; Kanovsky *et al.*, 1997; Tinazzi *et al.*, 1999) found an increased amplitude of cortical components, possibly arising from motor cortices, in several patients, whilst others (Mazzini *et al.*, 1994; Grissom *et al.*, 1995) reported a decreased amplitude.

The interaction between afferent inputs coming from adjacent nerves at the spinal, brainstem and cortical levels of the somatosensory system has been evaluated in normal subjects by comparing SEP amplitudes obtained after stimulating the two nerves simultaneously with the arithmetic sum of SEP amplitudes obtained after stimulating each nerve individually (Burke *et al.*, 1982; Gandevia *et al.*, 1983; Okajima *et al.*, 1991; Huttunen *et al.*, 1992; Hsieh *et al.*, 1995). In normal subjects spinal, brainstem and cortical SEPs to dual input are smaller than the expected size calculated from the arithmetic sum of the two single inputs. The suppression of SEPs after dual input originates from the phenomenon of surrounding inhibition that is present at multiple levels of the somatosensory system (Burke *et al.*, 1982; Gandevia *et al.*, 1983; Okajima *et al.*, 1991; Huttunen *et al.*, 1992; Hsieh *et al.*, 1995).

To assess the possible abnormal sensory processing of a dual input in dystonia, both in dorsal horn and in dorsal column systems, we compared (i) the amplitudes of the spinal, brainstem and cortical components of the SEPs recorded after stimulating the median and ulnar nerves simultaneously, and (ii) the arithmetic sum of the corresponding SEP amplitudes obtained by stimulating the two nerves individually.

Patients and methods
Patients
We studied SEPs in 10 patients (five men, five women, age range 28–58 years, mean age 45.3 years) who had dystonia involving at least one upper limb and in 10 healthy subjects matched for age and sex (five men, five women, age range 23–57 years, mean age 39.9 years). No patient had a family history of degenerative disorder or a personal history of cerebrovascular disease. Six patients had generalized dystonia, two had a segmental dystonia and two had focal dystonia of the hand (one patient had right-sided writer's cramp and the other had left-sided writer's cramp) (Table 1). All the patients underwent an extensive neurological examination that paid special attention to possible clinical

Table 1 *Clinical findings for the 10 patients with idiopathic dystonia*

Subject	Age (years)	Sex	Diagnosis
1	47	F	Generalized dystonia
2	52	F	Segmental dystonia
3	45	F	Segmental dystonia
4	50	M	Generalized dystonia
5	41	M	Left-sided dystonic writer's cramp
6	58	F	Generalized dystonia
7	39	M	Generalized dystonia
8	48	F	Generalized dystonia
9	28	M	Generalized dystonia
10	45	M	Right-sided dystonic writer's cramp

sensory abnormalities (tactile sensation and position sense). No patients had sensory abnormalities and none had tremor. The results of biochemical, CT and MRI examinations remained normal throughout the study period, and thus dystonia was considered to be idiopathic in all dystonic patients included in the study. Four patients had received treatment with botulinum toxin until 5 months before the SEP recording session, three had received treatment with anticholinergic drugs and the remaining three were untreated. All subjects gave written informed consent before participating in the study, and the protocol was approved by the local ethics committee of Verona.

SEP recordings procedure
In SEP recording sessions, subjects were instructed to lie down comfortably on an examination couch, relaxed and supine. Right and left median and ulnar nerve SEPs were recorded in all subjects. In order to also stimulate afferents from forearm muscles that are frequently involved in dystonia, we stimulated the ulnar and median nerves at the elbow. Stimuli consisted of electrical square pulses of 0.2 ms duration delivered at a rate of 2.2 Hz through Ag/AgCl surface electrodes (impedance <5 KΩ) attached to the skin overlying the nerves. Stimuli were delivered at motor threshold intensity. Three trials were carried out for left and right side stimulation: the median nerve stimulated individually (M), the ulnar nerve stimulated individually (U), and both nerves simultaneously (MU). In seven normal subjects and in seven patients (patients 1, 3, 4, 5, 6, 7 and 9), SEPs were also recorded by stimulating individually and then simultaneously the digital nerves of the third and the fifth fingers of the right hand with ring electrodes at an intensity of three times the sensory threshold. Sweeps containing EMG activity were rejected. Seven hundred sweeps were averaged for each trial. Each trial was repeated at least twice and the average of two reproducible trials was analysed. Sweep length was 50 ms and filtering bandwidth was 5–1500 Hz (–6 dB octave roll-off).

SEPs were recorded using Esaote Biomedica Reporter (Esaote Biomedica, Florence, Italy). Recording electrodes were placed over Erb's point, over the spinous process of

Table 2 *Mean amplitude (μV) and latency (ms) of right and left median and ulnar nerve SEP components in normal subjects and patients*

	N13		P14		N20		P27		N30	
	Median	Ulnar	Median	Ulnar	Median	Ulnar	Median	Ulnar	Median	Ulnar
Normal subjects										
Amplitude	1.35*	0.96	0.84*	0.49	2.16*	1.31	2.32*	1.61	2.07*	1.35
SD	0.52	0.44	0.27	0.19	0.69	0.55	0.8	0.56	0.8	0.7
Latency	9.47	9.61	10.73	11	15.19	15.41	19.7	19.85	22.72	22.7
SD	0.53	0.43	0.83	1.03	0.73	0.76	2.19	1.93	2.58	3.08
Patients										
Amplitude	1.38*	0.89	0.85*	0.46	2.31*	1.41	2.64*	1.85	2.43*	1.49
SD	0.41	0.29	0.3	0.23	0.8	0.57	0.87	0.51	0.92	0.52
Latency	9.03	9.33	10.2	10.51	15.13	15.26	21.07	21.16	23.68	24.21
SD	0.83	0.94	0.9	0.91	1.02	1.06	2.85	2.28	3.02	2.93

Median nerve versus ulnar nerve: $*P < 0.05$.

the sixth cervical vertebra and over the parietal (P3, P4) and frontal (F3, F4) scalp regions contralateral to stimulation. The Erb's point electrode was referred to an electrode located on the shoulder of the non-stimulated side and the sixth cervical vertebra electrode was referred to an electrode located immediately above the thyroid cartilage. Parietal and frontal electrodes were referred to the earlobe of the stimulated side. To ensure full muscle relaxation, muscular activity was monitored through surface EMG recordings from the forearm flexor and extensor muscles of the stimulated arm. In six normal subjects, SEPs were also recorded while the subject maintained tonic isometric wrist flexion at 5–10% of maximum EMG activity level. Acoustic EMG feedback helped the subjects to maintain a constant level of contraction.

We identified and analysed the following SEP components: the peripheral N9 from the brachial plexus; the N13 potential originating in the dorsal horn of the cervical spinal cord (Desmedt and Cheron, 1981); the far-field P14 potential, which originates from the cuneatus nucleus (Tinazzi *et al.*, 1996); the parietal N20 and P27, which arise in the S1 (Desmedt *et al.*, 1987; Allison *et al.*, 1991); and the cortical N30 potential, probably originating from multiple generators located in the frontal lobe (Mauguière *et al.*, 1983; Desmedt *et al.*, 1987; Rossini *et al.*, 1989) and in the posterior wall of the central sulcus (Rossini *et al.*, 1987; Allison *et al.*, 1991).

Amplitudes were measured peak-to-peak and latencies at the peak of each component.

We evaluated the ratio MU/(M + U) × 100, where MU is the SEP amplitude obtained after simultaneous stimulation of the median and ulnar nerves and M + U is the arithmetic sum of the SEPs obtained by individual stimulation of the two nerves.

Statistical analysis

For statistical analysis we used non-parametric tests that can control the effect of non-normal distributions and non-homogeneous variables. In the experiment studying latencies, amplitudes and the ratio MU/(M + U) × 100

of SEPs obtained in response to median and ulnar nerve stimulation and to digital nerve stimulation, we used the unpaired Mann–Whitney test to compare the data between patients and controls. We used the paired Wilcoxon test to compare data obtained in response to median and ulnar nerve stimulation between the two sides in the patients and in the controls, and to compare the SEP ratio to median and ulnar nerve stimulation during wrist flexion with that obtained at rest in normal subjects. We calculated a Spearman rank order correlation coefficient to compare the SEP amplitude of brainstem P14 and cortical N20, P27 and N30 in patients. $P < 0.05$ was taken as the significance threshold. Values in the text are means ± standard deviation.

Results

In normal subjects and in patients, the amplitudes of SEP responses evoked by stimulating the median nerve were significantly greater than those obtained in response to ulnar nerve stimulation, while latencies did not differ (Table 2). Individual stimulation of the patients' median and ulnar nerves elicited SEPs that did not differ significantly in latency and amplitude from those of the controls, although cortical SEPs were slightly larger in patients (Table 2).

In normal subjects, simultaneous stimulation of the median and ulnar nerves elicited SEPs of which the amplitudes of N13, P14, N20, P27 and N30 were always smaller (<100%) than the amplitude of the arithmetic sum of the individual SEPs. The N9 behaved differently: its amplitude after simultaneous stimulation of the median and ulnar nerves was equal to the expected value (Fig. 1). There were no ratio differences between right and left arms (Table 3).

In patients, simultaneous stimulation of the median and ulnar nerves elicited SEPs in which the amplitudes of N13, P14, N20, P27 and N30 were often larger (>100%) than the amplitude of the arithmetic sum of the individual SEPs. All central SEP responses obtained by simultaneous stimulation of the median and ulnar nerves were larger in patients than in controls but this difference was statistically significant
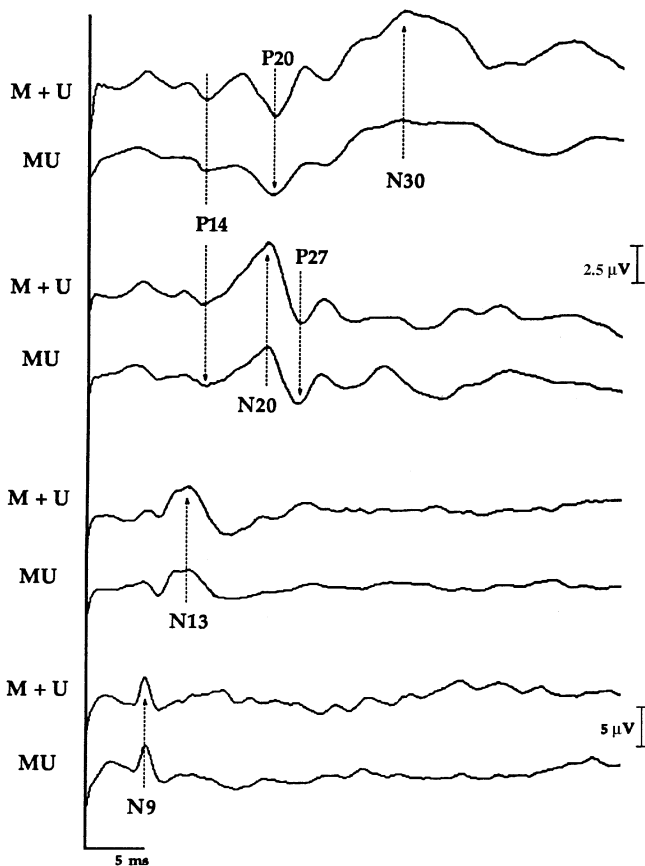
Fig. 1 SEP traces for simultaneously stimulated right median and ulnar nerves (MU) and summed SEPs for individually stimulated median and ulnar nerves (M + U) in a 32-year-old healthy male subject. Peripheral potentials are recorded at Erb's point (N9). Note that the peripheral potentials N9 (MU) and N9 (M + U) have the same amplitude. The N13 potential is recorded with a sixth cervical vertebra–thyroid cartilage montage. Over the scalp, the N20 potential recorded over the parietal electrode (P3) contralateral to the stimulation side is preceded by a P14 potential and followed by a P27 potential. The N20 potential exhibits a reversed-phase P20 potential over the frontal electrode (F3) followed by a large negativity (N30 potential). Note that the amplitude of spinal N13, brainstem P14, parietal N20, P27 and frontal N30 potentials evoked to simultaneous (MU) median and ulnar nerve stimulation is lower than that given by the algebraic summing of the two individually stimulated nerves (M + U).

only for cortical SEPs. The mean ratios [MU/(M + U) × 100] of spinal N13 (97 ± 10% in patients versus 87 ± 5% in normal subjects), of the brainstem P14 (98 ± 21% versus 80 ± 17%) and of cortical N20 (95 ± 20% versus 76 ± 13%), P27 (92 ± 22% versus 66 ± 10%) and N30 (104 ± 20% versus 78 ± 13%) components were significantly ($P < 0.05$) larger in patients than in controls (Table 3 and Figs 2–4). There were no differences in the mean ratio of the N9 component between patients and control subjects (101 ± 3% versus 100 ± 3%).

In some patients (cases 1, 3, 4, 5, 6, 7, 8 and 9) one or more components of SEPs for right and left forearm stimulation were larger for MU than for M + U SEPs. This was found in eight sides for N13, 11 sides for P14, 10 sides for N20, nine sides for P27 and 12 sides for N30, but was never observed in normal subjects (Table 4). Abnormalities were concomitant in the dorsal horn system (as reflected by the N13) and in the dorsal column system (as reflected by the P14, N20, P27 and N30 potentials) on eight sides, and they were either in the dorsal horn or the dorsal column system in the other eight sides. Within the dorsal column system, a SEP pattern of facilitation (as reflected by a ratio > 100%) of brainstem P14 and cortical N20, P27 and N30 potentials was concomitant in seven sides and was either in the brainstem or in the cortex in nine sides. In addition, there was no significant correlation between brainstem P14 and cortical N20, P27 and N30 SEP abnormalities (Spearman correlation: $r = 0.37$ for N20; $r = 0.39$ for P27; $r = 0.11$ for N30).

To assess whether our findings in patients could have originated from a possible facilitation of the segmental motor system, we studied the SEP ratio at rest and during voluntary contraction in the six normal subjects. The ratio did not differ significantly (Wilcoxon test, $P > 0.05$) at rest and during voluntary contraction (85 ± 7% during contraction versus 85 ± 5% during relaxation for N13; 74 ± 12% versus 73 ± 11% for P14; 76 ± 7% versus 77 ± 9% for N20; 66 ± 7% versus 67 ± 7% for P27; 77 ± 14% versus 78 ± 12% for N30).

To assess whether the SEP ratio abnormalities involved all the afferents or a selective group of afferents, in seven patients (cases 1, 3, 4, 5, 6, 7 and 9) and in seven normal subjects we compared the ratio after mixed nerve stimulation

Table 3 *Mean amplitude measured peak-to-peak (μV) and standard deviation (in parenthesis) of simultaneous (MU) and summed (M + U) median and ulnar nerve SEPs in normal subjects and in dystonic patients*

	N9		N13		P14		N20		P27		N30	
	MU	M + U	MU	M + U	MU	M + U	MU	M + U	MU	M + U	MU	M + U
Right arm												
Controls	4.4 (1.56)	4.47 (1.53)	2.21 (0.94)	2.54 (1.09)	1.08 (0.36)	1.34 (0.39)	2.73 (0.87)	3.63 (1.21)	2.79 (1)	4.08 (1.26)	2.76(0.75)	3.72 (1.71)
Patients	4.05 (1.44)	4 (1.47)	2.28 (0.68)	2.33 (0.65)	1.36 (0.62)	1.37 (0.5)	3.64 (1.03)	3.85 (1.41)	4.28 (1.25)	4.68 (1.27)	4.56(1.47)	4.25 (1.34)
Left arm												
Controls	4.21 (1.38)	4.16 (1.36)	1.81 (0.57)	2.08 (0.63)	1 (0.33)	1.33 (0.42)	2.42 (0.76)	3.31 (1.07)	2.39 (0.81)	3.79 (1.31)	2.43 (1.29)	3.14 (1.46)
Patients	3.92 (1.62)	3.89 (1.67)	2.04 (0.45)	2.21 (0.56)	1.19 (0.53)	1.24 (0.47)	3.21 (1.14)	3.58 (1.05)	3.77 (1.41)	4.3 (1.29)	3.45 (1.23)	3.58 (1.33)
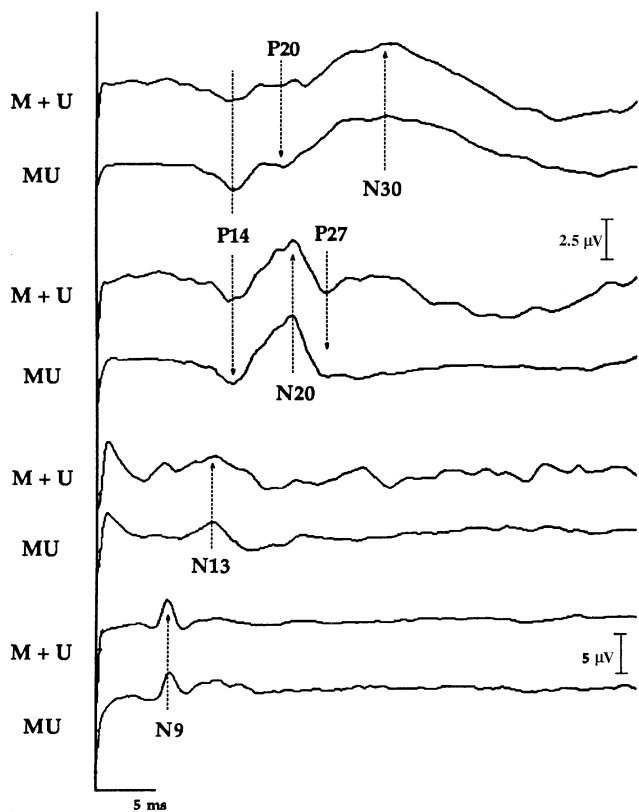
Fig. 2 SEP traces for simultaneously stimulated right median and ulnar nerves (MU) and summed SEPs for individually stimulated median and ulnar nerves (M + U) in a 47-year-old female patient with generalized dystonia. Note that the amplitude of spinal N13, brainstem P14, parietal N20, P27 and frontal N30 potentials evoked to simultaneous median and ulnar nerve stimulation (MU) is higher than that given by the algebraic summing of the two individually stimulated nerves (M + U), whereas peripheral potentials N9 (MU) and N9 (M + U) have the same amplitude.
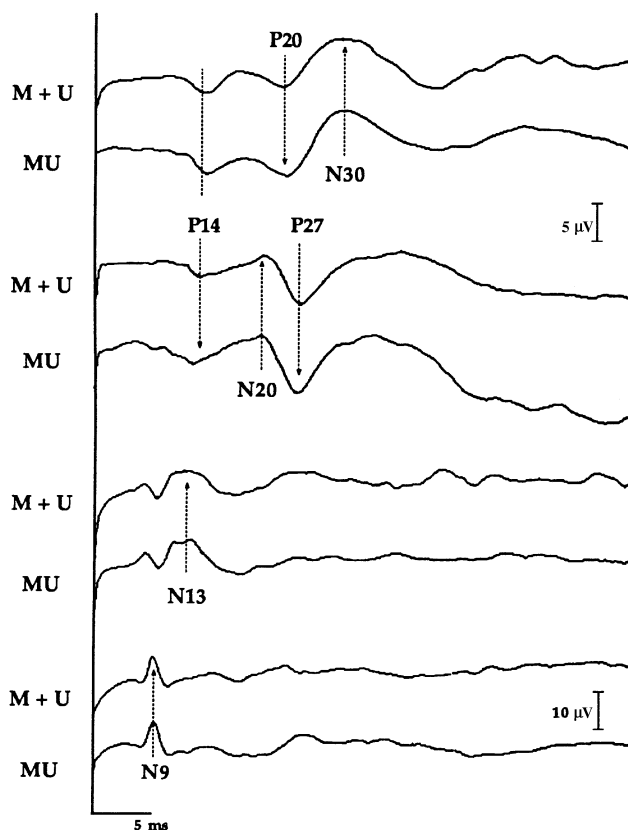

Fig. 3 SEP traces for simultaneously stimulated right median and ulnar nerves (MU) and summed SEPs (M + U) in a 50-year-old male patient affected by generalized dystonia. Note that in this patient also the amplitude of spinal N13, brainstem P14, parietal N20, P27 and frontal N30 potentials evoked to simultaneous median and ulnar nerve stimulation (MU) is higher than that given by the algebraic summing of the two individually stimulated nerves (M + U), whereas peripheral potentials N9 (MU) and N9 (M + U) have the same amplitude.

at the elbow and after cutaneous afferent stimulation at the fingers. The ratio of all central SEP responses obtained in both conditions was higher in patients than in the control group, but in the first condition (mixed nerve stimulation) this difference was statistically significant while in the second condition (digital nerve stimulation) it was not (Fig. 5).

Discussion

Our data show that SEPs evoked by dual nerve input in dystonic patients show significantly impaired suppression at the spinal, brainstem and cortical levels of the lemniscal pathway. These SEP abnormalities were unrelated to peripheral factors, since the peripheral N9 response was normal. A defect of surrounding inhibition probably accounts for this finding, but there are several points that need to be discussed.

Previous routine studies in dystonia showed that in some patients the median nerve-derived N30 potential has an increased amplitude (Reilly *et al.*, 1992; Kanovsky *et al.*, 1997), though others failed to replicate this finding (Mazzini *et al.*, 1994; Grissom *et al.*, 1995). The only available SEP
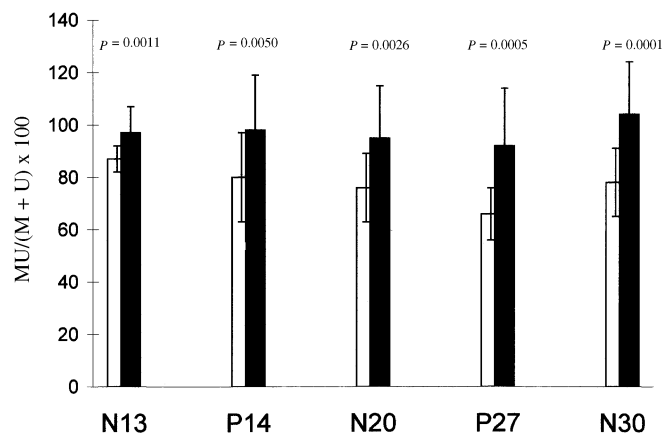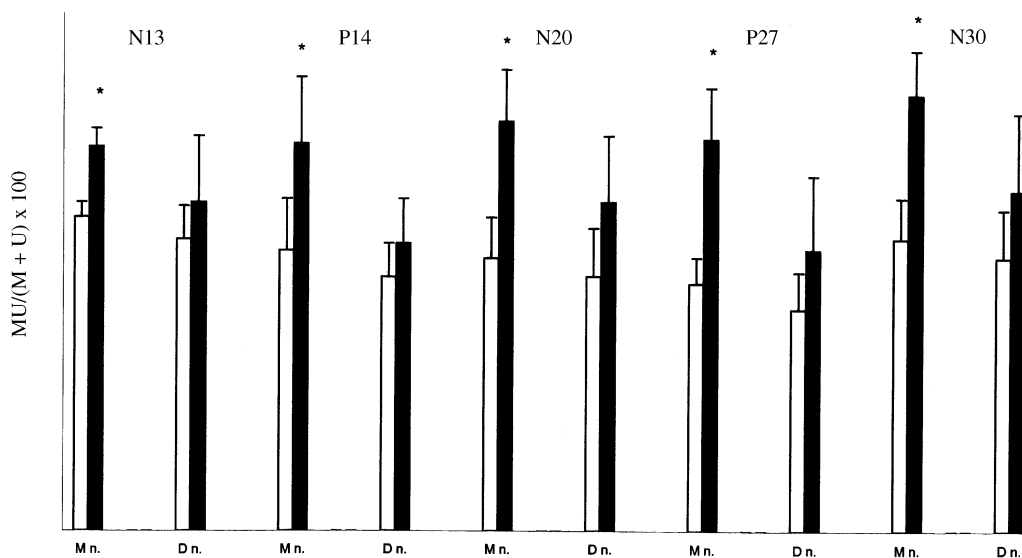

Fig. 4 Histogram of mean amplitude ratio, expressed as [MU/(M + U) × 100], of N13, P14, N20, P27 and N30 potentials obtained in response to stimulation of the right and left median and ulnar nerves in patients (20 sides) and in control subjects (20 sides). The mean ratio of all SEP potentials in patients is significantly greater than that of SEP potentials obtained in normal subjects. Open columns = controls; filled columns = dystonic patients.

Table 4 *SEP findings in dystonic patients*

Patient	N13		P14		N20		P27		N30	
	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
1	>	>	>	>	>	>	>	>	>	>
2	–	–	–	–	–	–	–	–	–	–
3	>	–	>	>	>	–	>	–	>	–
4	>	>	>	>	>	>	>	>	>	>
5	–	–	–	–	–	>	–	–	>	>
6	>	–	–	>	>	>	>	>	>	>
7	>	–	>	>	>	–	>	–	>	–
8	–	–	>	–	–	–	–	–	–	>
9	>	–	–	>	>	–	>	–	>	–
10	–	–	–	–	–	–	–	–	–	–

Symbols for ratios: > = more than 100%; – = less than 100%.

Fig. 5 Histogram of mean amplitude ratio, expressed as [MU/(M + U) × 100], of N13, P14, N20, P27 and N30 potentials obtained in response to stimulation of the right mixed nerves (Mn.) and of the digital nerves (Dn.) in seven patients (filled columns) and in seven normal subjects (open columns). Note that the ratio of all central SEP responses obtained in both conditions was higher in patients than in the control group, but in the first condition (mixed nerve stimulation) this difference was statistically significant whereas in the second condition (digital nerve stimulation) it was not.

study from the lower limb also showed an increased amplitude of some cortical components (Tinazzi *et al.*, 1999). In the present study, stimulation of a single upper limb nerve elicited a slightly but not significantly larger N30 in the patients. These discrepancies in results between our study and previous investigations may reflect methodological differences. We delivered stimuli at a higher rate and to a more proximal site than other workers. These variables are both inversely related to the amplitude of the N30 SEP component (Fujii *et al.*, 1994).

On the other hand, a dual sensory input elicited a significantly higher ratio of SEP suppression, i.e. less inhibited SEPs, in patients than in normal subjects. Our control recordings in normal subjects during a slight voluntary contraction and the careful control of relaxation in dystonic patients exclude the possibility that the abnormal SEP suppression in dystonic patients reflected a different state of excitability of the segmental motor system.

Under normal conditions, lateral surrounding inhibition and possibly occlusion phenomena account for the suppression, in the CNS, of afferent signals coming from adjacent body parts (Burke *et al.*, 1982; Gandevia *et al.*, 1983; Okajima *et al.*, 1991; Huttunen *et al.*, 1992; Hsieh *et al.*, 1995). The increased ratio of all central SEP components elicited by dual input in dystonia therefore indicates an abnormality of the intrinsic inhibitory interactions within the somatosensory system, and hence a defect of lateral surrounding inhibition. This finding is in line with data obtained from animal studies which suggest that cortical reduction of inhibitory functions explain the altered differentiation of normally separate representations of the body maps in the primary sensory cortex in dystonia (Byl *et al.*, 1996*b*), and with the observation of an altered

representation of the fingers in S1 of dystonic musicians in a recent magnetoencephalography study (Elbert *et al.*, 1998). The abnormal cortical response to a dual input seemed not to be related to brainstem abnormalities, since there was no significant correlation between abnormalities of the P14, N20, P27 and N30 SEPs, and there was a dissociated SEP pattern of facilitation between brainstem P14 and cortical potentials in some cases. Our data showing that spinal suppression mechanisms were also impaired suggest that abnormal inhibition in dystonia is not restricted to the dorsal column system, and a parallel situation occurs at the dorsal horn level. This finding of abnormal inhibition at multiple levels of the somatosensory system is of particular interest when compared with a recent study that demonstrated abnormal inhibition within the motor cortex in patients with focal hand dystonia, using the technique of transcranial magnetic stimulation to paired stimuli (Ridding *et al.*, 1995), which was apparently not dependent on possible changes at the subcortical level of the motor system (Sheehy and Marsden, 1982; Marsden and Sheehy, 1990).

A striking finding was that abnormal SEP suppression was more prominent when stimulating mixed rather than digital nerves. This finding agrees with the presence of fairly specific impairment of muscle spindle input in patients with focal dystonia (Panizza *et al.*, 1989, 1990; Priori *et al.*, 1995; Kaji *et al.*, 1995; Grunewald *et al.*, 1997). This abnormal input enhances the tonic vibration reflex (Kaji *et al.*, 1995) and probably accounts for the reduced presynaptic inhibition of primary muscle afferents (Nakashima *et al.*, 1989; Priori *et al.*, 1995). The reduction of this inhibition by botulinum toxin (Priori *et al.*, 1995) or anaesthetic block (Kaji *et al.*, 1995) would explain the clinical improvement of dystonia after these treatments. In line with these observations, our results suggest a disinhibited input in dystonia arising from spatially segregated proprioceptive afferent fibres. The presence of altered SEP suppression when stimulating the digital nerves suggests, however, that disinhibition might also involve cutaneous inputs, although to a lesser extent. Hence, besides excessive afferent input arising from a single source, there is also reduced reciprocal gating of multiple and spatially separate inputs, which result in the spatial summation of already singularly abnormal multiple inputs from skin–muscular territories.

Whatever the mechanism may be, our data imply impaired afferent–input gating in dystonia. In other words, two inputs that engage the sensory system under normal conditions have a reciprocally inhibitory action that gates the total amount of signal at all central levels, spatially and temporally limiting the amount of input engaging the CNS. This appears not to be the case in dystonia. Although the functional importance of this gating remains unclear, this mechanism could play an important role in preserving the spatial separation of the two stimuli (Mountcastle and Darian-Smith, 1968). In this way, reciprocal sensory inhibition enhances the contrast between stimuli, so that information from adjacent body parts is perceived and, more importantly, processed separately. The

more immediate and challenging question is precisely what does muscle input overflow determine? A possible answer is incomplete processing of the incoming signal, resulting not only in excessive, but also in spatially distorted information. In dystonia, impaired spatial gating of multiple afferent inputs would ultimately result in a sensory overflow engaging the CNS. Disinhibition of afferent inputs could give rise to abnormal influences on motoneuronal excitability, resulting in dystonia. This hypothesis is in line with the observation that dystonic co-contraction is produced by abnormal synchronization of presynaptic inputs to antagonist motoneuronal pools (Farmer *et al.*, 1998). In other words, the influence of muscle input from a given muscle spreads over the antagonist motor neuron pool, suggesting reduced spatial filtering of muscle afferents in dystonia.

In normal conditions, afferent input to the motor system leads to finely tuned activation of neural elements and ultimately results in the correct execution of movement, and multiple experimental and clinical evidence confirms the importance of sensory feedback to the motor system (Hikosaka *et al.*, 1985; Alloway *et al.*, 1991; Porter and Lemon 1993; Rothwell, 1994; Bertolasi *et al.*, 1998). Our data did not allow us to establish if the abnormal central processing of somatosensory inputs is causally involved in the development of dystonia. However, these data do suggest that dystonia might, at least in part, depend on the fact that the motor system transforms distorted and excessive (i.e. not spatially filtered) afferent inputs into abnormal motor outputs.

Acknowledgements

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