ASYMMETRY IN BRAINSTEM REFLEX EXCITABILITY IN CERVICAL DYSTONIA

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ABSTRACT

Objective: Our objective was to search for any asymmetry in brainstem interneuronal excitability, and its correlation with the features of involuntary movement and EMG (electromyography) activity.
Methods: We studied blink reflex and recovery of the late component (R2) with paired stimuli in patients with cervical dystonia. Thirty-one cases were included in the study.
Findings: Enhanced recovery of R2 was observed in 27 cases (87%) at interstimuli intervals of 200 and 600 ms, and it was asymmetric in 24 cases.
Discussion and Conclusion: This finding was found to be localized contralateral to the direction of torticollis in cases with simple rotational torticollis, and with tonic EMG activity. The asymmetry was less pronounced or absent in cases with involuntary head rotation in more than one plane, symmetric involvement of cervical muscles, and with choreic and/or tremulous dystonic EMG pattern.
Keywords: brainstem reflex, blink reflex, cervical dystonia, torticollis, reflex asymmetry, interneuronal excitability.

SERVİKAL DİSTONİDE BEYİNSAPI REFLEKS ASİMETRİSİ

ÖZET

Amaç: Bu çalışmada servikal distonili olgularda beyinsapı refleks asimetrisinin varlığı ve bu bulgunun distoninin kliniği ve EMG aktivitesi ile ilişkisi araştırılmıştır.
Yöntem: Servikal distonili 31 olgunun göz kırpma refleksi ve bu refleksin geç yanıtının (R2) toparlanması incelendi. Sonuçlar 20 sağlıklı gönüllünün bulguları ile karşılaştırıldı.
Bulgular: Yirmi yedi olguda (%87) 200 ve 600 msn'lik intervallik stimulus ile R2'de artmış toparlanma ve 24 olguda asimetri gözlendi.
Tartışma ve Sonuç: Servikal distonili olgularda başın çevrilme yönüne ters lokalizasyonda hipereksitabilite mevcuttur.
Anahtar Kelimeler: beyinsapı refleksi, göz kırpma refleksi, servikal distoni, tortikolis, refleks asimetri, internöronal eksitabilite

INTRODUCTION

Increased excitability of the central interneuronal connections in patients with primary dystonia has been described (Tolosa et al. 1988, Berardelli et al. 1988, Nakashima et al. 1990, Carella et al. 1994). Electrophysiological reflex studies such as H-reflex recovery curve, recovery of the late component (R2) of the blink reflex (BR), and the masseter inhibitor reflex showed that the location of dystonia determines which reflex study is expected to be most abnormal (with most enhanced excitability). The enhanced excitability shows some extention if one regards the exact localization of the dystonic muscle; however this tends to be limited. This finding led to the notion that the enhanced excitability bears somatotopic features (Deuschl et al. 1992, Nakashima et al. 1989, Rotwell et al. 1983). Enhanced recovery of R2 after a prior conditioning stimulus that was first shown to occur in patients with blepharospasm was also detected in patients with cervical dystonia (Berardelli et al. 1985, Eekhof et al. 1996).

Considering the data presented above, we have tested the presence of any asymmetry in the excitability of the neuronal network mediating BR in patients with cervical dystonia, and discussed the possible contributing factors.

METHOD

A total of 31 patients with cervical dystonia (aged from 21 to 70 years), and 20 healthy volunteers as controls (aged from 24 to 45 years) were studied. The duration of illness ranged from 1 month to 15 years. All patients gave informed consent before the study. Table 1 and 2 summarizes general, clinical and electrophysiological features of the patients.

Long-lasting recordings of the EMG activity were obtained from both sternocleidomastoid (SCM), and posterior group muscles (splenius capitis, and trapezius muscle in some of the patients) using surface electrodes placed 2-3 cm apart over the muscle bellies. Action potentials were amplified by an amplifier with a bandwidth of 20 Hz to 5 kHz, and input sensitivity was kept between 100 and 500 (V. The BR was elicited percutaneously with stimulation of the superior orbital nerve using stimuli 2.5 to 3 times the threshold of R2 component. The recovery cycle of R2 was studied using paired shocks (conditioning and test stimuli) of equal intensity at three different interstimuli intervals (200, 600, and 1000 ms). Three consecutive trials were recorded for further analysis. The area of the response to the test stimulus, measured by area

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Table 1: General characteristics of the patients

Female/male	16/15
Age range	21- 70 years
Duration of illness	1 mo.-15 years
Focal	24
Segmental	5
Generalized	2
Primary	22
Secondary*	9

*8 subjects with tardive dystonia.

Table 2: Clinical and electrophysiological features of patients

Simple torsional	19
Multiplanar	12
Tonic Cervical Dystonia	24*
Predominantly Choreic and/or Tremulous Cervical Dystonia	7

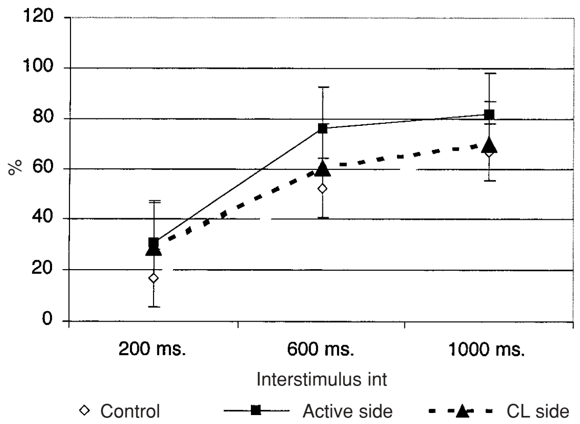
*7 of the 24 cases had dystonic head tremor accompanying cervical dystonia.

cursor, was expressed as a percentage of the area of the response to the conditioning stimulus. SPSS program was used for statistical analysis.

FINDINGS

The latencies of the early and late components of the BR were found to be normal in patients we have studied. We presumed the side with dystonia is where the leading muscle is located; the muscle with maximal activity, and responsible for the abnormal dystonic movement in all recordings was determined

Figure 1: R2 revovery curves of patients with cervical dystonia and control subjects



CL: Contralateral

to be the leading muscle.

The recovery of the late component of the BR is found to be significantly different in patients with cervical dystonia, when compared to that of control subjects. This finding was obtained on both sides, regardless of the direction of head turn. It was significant on the side contralateral to the direction of torticollis at all interstimuli intervals tested (p(0.001); whereas statistically significant enhancement of recovery was found at all intervals other than 1000 ms on the other side.

We found prominent enhancement of the recovery of R2 component in 27 patients. The enhancement was asymmetric in 24 patients. It was more prominent at the side contralateral to head turn in 19 of these patients, and the leading muscle in this group was either SCM contralateral to the direction of head turn, or SC ipsilateral to the direction of torticollis. The side with more prominent enhancement of R2 recovery was ipsilateral to the head turn in 5 patients.

Table 3: The occurrence of the enhanced recovery of R2 at the side contralateral and ipsilateral to the direction of head turn

R2 Recovery	Number	More prominent enhancement contralateral to the direction of head turn	More prominent enhancement ipsilateral to the direction of head turn
Enhanced / Total	27 / 31		
Lateralization (+)	24 / 27	19 / 24 (79.1%)	5/24 (20.8 %)
Symmetric enhancement	3 / 27		
Normal recovery		4* / 31	

*More prominent enhancement seen in the contralateral sides of head turn either in 2 cases of which R2 recovery was normal.

We noted that there was not any single muscle with more prominent dystonic contraction in this group of patients; bilateral SC in 4 patients, and bilateral SCM in 1 patient were found to be equally active.

The occurrence of enhanced recovery and dystonic contraction on the same side is seen tonic-dystonic EMG activity. Choreic or tremulous EMG activity is accompanied with localization of the side with enhanced recovery of R2 ipsilateral to head turn.

Regarding the group of 3 patients with symmetric enhancement of the recovery of R2 component, bilateral and symmetric involvement of SC was the prominent finding.

DISCUSSION

We have found enhanced recovery of the R2 component of BR in 25 patients with cervical dystonia (87%) using paired-stimuli technique. Previous work has shown that this finding indicates that interneuronal network at the brainstem mediating this reflex is intact; whereas the excitability of the suprasegmental structures exerting control on this reflex is altered (Berardelli et al. 1988). Our results also denote that the enhanced recovery of R2 is asymmetric in some patients with cervical dystonia.

Asymmetry of functional changes and neurophysiological findings in cervical dystonia has been addressed in several studies. Data obtained using blood flow positron emission tomography indicates dysfunction of the structures such as supplementary, and primary sensorimotor cortex, and lentiform nucleus contralateral to the direction of the torticollis in these patients (Cebellos-Baumann et al 1995, Naumann et al. 2000). The analysis of recordings of long latency responses in cervical dystonia led some searchers to ascribe abnormal findings to the overactivity of the supplementary motor cortex (Naumann and Reiners 1997). The most relevant of these studies to our study is the one by Kanovsky et al. These authors found that the amplitudes of the precentral P22/N30 component of SEP responses were larger on the hemisphere ipsilateral to the dystonic SCM, or larger on the contralateral hemisphere to the dystonic splenius capitis muscle respectively when either one of these is the leading muscle (Kanovsky et al. 1997). These authors explained the asymmetry they noted by considering the suprasegmental control of the SCM and SC muscles; SCM is controlled by impulses originating in both hemispheres, and ipsilateral component may be more prominent. SC is also controlled by both hemispheres; however contribution of the contralateral hemisphere is much more prominent (Kanovsky et al. 1997). They reported later that this asymmetry is seen in patients with tonic cervical dystonia; lateralization was not detected in patients with tremulous form of torticollis (Kanovsky et al. 1997). They also showed that Botulinum toxin a treatment decreased the asymmetry detected in precentral P22/N30 component in their patients with tonic cervical dystonia (Kanovsky et al. 1997, Kanovsky et al. 1999).

Our findings are in accordance with the results presented by Kanovsky et al. We found that the side at which more prominent enhancement is localized contralateral to the direction of torticollis in 19 of our patients in whom there is a leading dystonic muscle. The side with more prominent enhancement of the precentral P22/N30 components is also the side contralateral to the direction of torticollis. The motor neurons of the accessory nucleus at the brainstem constitute the final common pathway to SCM, and their control on the muscles is ipsilateral. The SC is innervated by motor neurons located at the ipsilateral upper cervical spinal cord. If we consider the fact that the side with more prominent enhancement of the recovery of R2 is the side opposite to the direction of head rotation, than it can be proposed that a functional vector is present at the brainstem level that is linked to which side the head is to be turned. This "functional vector" may originate in the neuronal-interneuronal network at the brainstem, and control the muscles that determine the position of the head. This mechanism may coordinate the concomitant contraction of the muscles functioning to support each other such as SCM and contralateral SC. This control might be guided by suprasegmental structures including basal ganglia, and supplementary motor cortex. We propose that the mechanism of cervical dystonia involves a neuronal network that code specific postural or movement patterns. Further, it can be proposed that the codes that represent complex head movements are stored at the brainstem level as templates. The results of the study by Kanovsky et al. also support this notion.

The decrease of enhancement of the recovery of R2 in patients treated with Botulinum toxin may support the role of peripheral inputs in the pathophysiology of dystonia. The impulses originating in the periphery may trigger, or enhance the cascade of events in the central nervous system responsible for the development of dystonia.

In 5 patients in whom asymmetric enhancement of the recovery of R2 component was noted, the side of more enhanced recovery was ipsilateral to the direction of torticollis. Bilateral involvement of the SCM and/or SC, and choreic or tremulous dystonic activity was the prominent finding in this group of patients. In all 3 patients with symmetric enhancement of the recovery of R2, bilateral dystonic contraction of the SC muscle was noted.

Our results indicate that concomitant side preference or lateralization of both enhancement of excitability of BR, and dystonic contraction is seen in patients with tonic-dystonic EMG pattern. In only one patient with choreic-dystonic EMG pattern such concomitant side preference is detected. The same observation is true also for patients with dystonic head tremor. There seem to be no movement vector pointing to a particular direction in case of patients with either choreic and/or tremulous dystonic activity. In this case the functional disorder may involve both sides of the brainstem structures, or it may begin at one side, and the function of the other side may change in an effort to suppress the pathological activity of the contralateral side, which contradicts the learned patterns stored as templates in the brainstem neuronal network.

We observed that cervical dystonia accompanying generalized dystonia is more frequently characterized by choreic activity, and it seems meaningless to expect lateralization in such a case; our experience also supports this assumption.

CONCLUSION

In conclusion our results indicate that:

An asymmetry exists in enhanced excitability of the late component of the BR, which represents excitability of the interneurons at the brainstem in cases with cervical dystonia,

This asymmetry is more prominent if there is a discernable leading muscle responsible for the involuntary movement,

The lateralization of the enhanced excitability is contralateral to the direction of head turn; at the same side with the dystonic muscle if the leading muscle is SCM, or at the opposite side to the dystonic muscle if the leading muscle is SC (and vice versa for SC). Considering the fact that the suprasegmental control of the SCM muscle is provided by both hemispheres, and of the SC muscle predominantly from contralateral hemisphere, and SCM and contralateral SC turn the head to the same direction, led us to propose the existence of a network producing a hypothetical movement vector which is located at the brainstem, and where processing of commands from both hemispheres takes place,

Asymmetric excitability, and concomitant side preference of the localization of the leading muscle is noted in cases with tonic cervical dystonia.

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