Electrodiagnostic and nerve ultrasonographic features in upper limb spasticity: an observational study

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Summary

To better understand the effects of spasticity on peripheral nerves, we evaluated the electrodiagnostic and nerve ultrasonographic features of the median and ulnar nerves in adults with upper limb spasticity. Twenty chronic stroke patients with spastic hemiparesis underwent nerve conduction study and nerve ultrasonography of the median and ulnar nerves at both upper limbs. Affected *versus* unaffected upper limb comparisons showed significant differences in the median and ulnar nerve distal motor latencies, compound muscle action potentials and F-wave minimal latencies. Furthermore, we observed a significantly greater median nerve cross-sectional area at the elbow of the affected upper limb compared with the unaffected one. Our findings confirmed electrodiagnostic asymmetries and nerve ultrasonographic abnormalities in the affected versus the unaffected upper limb after stroke. Slight changes in lower motor neuron activity and spasticity might contribute to these alterations.

KEY WORDS: elasticity imaging techniques, electrodiagnosis, electromyography, muscle spasticity, rehabilitation, ultrasonography.

Introduction

Stroke is the second cause of disability in Europe (Bustamante et al., 2016). Damage to descending motor tracts results in the upper motor neuron syndrome (UMNS), which may bring about changes at the level of the lower motor neurons that innervate striated muscle (Hara et al., 2004; Lukács, 2005; van Kuijk et al., 2007; Picelli et al., 2014 d). Spasticity, defined as a state of increased muscle tone with exaggerated reflexes characterized by a velocity-dependent increase in the resistance to passive movement (Lance, 1980), is a positive feature of UMNS. Acute stroke commonly results in upper limb involvement with a 17-38% prevalence of spasticity one year later (Bhakta et al., 2000; Smania et al., 2009; Stinear et al., 2012; Picelli et al., 2014 c; Opheim et al., 2015). Stroke reduces arm function and independence, having an impact on self-estimated autonomy in activities of daily living; it also causes unpleasant sensations such as heaviness, rigidity and pain (Opheim et al., 2015; Baricich et al., 2016).

Spasticity leads to changes in the muscle structure by increasing intramuscular connective tissue and fat content (Gracies, 2005 a, b). This disruption of the normal muscle architecture increases spastic muscle echo intensity (Picelli et al., 2012), which correlates with muscle thickness, pennation angle and compound motor action potential (CMAP) amplitude in patients with chronic stroke (Picelli et al., 2014 b).

The nerve conduction study (NCS) technique has never been used in parallel with nerve ultrasound (US) in stroke patients, even though NCS parameters have been reported to be altered after stroke (van Kuijk et al., 2007; Paoloni et al., 2010) and the combined use of these techniques could offer complementary anatomical information. Thus, the main aim of this study was to evaluate NCS and US parameters of the median and ulnar nerves in chronic stroke patients with spastic upper limb. Our secondary aim was to examine the association between combined NCS and US measures and clinical features of post-stroke upper limb spasticity.

Material and metodhs

This was a single-center observational study. The inclusion criteria were: age over 18 years; first-ever unilateral stroke; spasticity of the forearm pronators, and wrist and finger flexors graded at least 1 on the modified Ashworth Scale (MAS) (Bohannon and Smith, 1987); time since stroke: at least 6 months; time since last botulinum toxin treatment: at least 5 months. The exclusion criteria were: inclusion in other trials; fixed contractures or bony deformities at the affected upper limb; previous treatment of upper limb spasticity with neurolytic or surgical procedures; other conditions affecting the upper limbs (bilateral stroke, peripheral neuropathy, peripheral nerve lesion(s), nerve compression syndrome, myopathy, severe osteoarthritis, recent muscle lesion(s), recent bone

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fracture, joint replacement). All participants were outpatients. Written informed consent for participation in the study was obtained from all of them. The study was carried out in accordance with the Declaration of Helsinki and approved by the local ethics committee.

Nerve conduction study

Nerve conduction studies were performed using an Oxford Medelec Synergy electromyograph (Viasys Healthcare, WI, USA; filter = 10-5000 Hz) according to current guidelines (American Association of Electrodiagnostic Medicine, 1999; American Association of Electrodiagnostic Medicine, 2002). For the median nerve, the following NCS parameters were assessed: abductor pollicis brevis muscle (APB) wrist-thenar distal motor latency (DML) and CMAP amplitude, elbow-wrist motor nerve conduction velocity (MNCV), and F-wave minimal latency. For the ulnar nerve, the following parameters were assessed: abductor digiti minimi muscle (ADM) DML, CMAP amplitude, below elbow-wrist and above elbow-below elbow MNCVs, and F-wave minimal latency. The same physician (blinded to the other evaluations) examined all the patients.

Ultrasonographic evaluation

We performed B-mode real-time nerve US using a MyLab70 XVision system (Esaote, Genoa, Italy) equipped with sonoelastography and interfaced with an 18 MHz linear transducer. The cross-sectional area (CSA) of the median and ulnar nerves was calculated at the wrist and elbow excluding the hyperechoic perineurium (Heinemeyer and Reimers, 1999; Peer and Bodner, 2003; Schreiber et al., 2013). Sonoelastography was performed in the transverse view at the wrist and elbow for the median and ulnar nerves by applying vertical rhythmic compression with the transducer (the quality of the examination was guaranteed by the "optimal compression scale", a function of the sonoelastography software). On sonoelastography images, nerve hardness percentage was calculated in order to measure nerve stiffness (Picelli et al., 2017). The same physician (blinded to the other evaluations) examined all the patients.

Clinical evaluation

We measured the tone of the forearm pronators and wrist and finger flexors at the affected upper limb using the MAS, a 6-point scale that grades resistance to rapid passive stretch from 0 (no increase in muscle tone) to 5 (joint is rigid) (Bohannon and Smith, 1987; Picelli et al., 2014 a). The same physician (blinded to the other evaluations) examined all the patients.

Statistical analysis

Statistical analysis was carried out using the Statistical Package for the Social Sciences for Macintosh, version 20.0 (SPSS Inc, Chicago, Illinois). The Wilcoxon signed-rank test was used to compare the US and NCS parameters between upper limbs (affected vs healthy) within the same individual. The Spearman rank correlation test was performed to assess the association between the instrumental features (US and NCS) of the median and ulnar nerves and the clinical characteristics of the spastic muscles (MAS scores) at the affected upper limb. The alpha level for significance was set at $p<0.05$.

Results

Twenty adults with upper limb spasticity due to chronic stroke were recruited from among 78 outpatients consecutively admitted to our clinical unit. The enrolment period was from November 2015 to May 2016. Table I shows the patients' clinical features.

No NCS measure fell outside our normal range of values, which was in line with that reported by others (Puksa et al., 2003; Qrimli et al., 2016; Alber, 2017), at either affected or unaffected upper limbs (Table II). For the median nerve, affected vs unaffected upper limb comparisons showed significant differences in the APB DML (affected 3.9±0.5 ms *vs* unaffected 3.5±0.5 ms; p=0.047), CMAP amplitude (affected 12.1±2.2 mV *vs* unaffected 14.6±2.9 mV; p=0.013), F-wave minimal latency (affected 22.7±2.2 ms *vs* unaffected 25.3±3.2 ms; p=0.045) and nerve CSA at the elbow (affected 8.6±2.1 mm^2 *vs* unaffected 7.6±1.7 mm^2; p=0.045). For the ulnar nerve, affected *vs* unaffected upper limb comparisons showed significant differences in the ADM DML (affected 2.8±0.5 ms *vs* unaffected 2.6±0.3 ms; p=0.018), CMAP amplitude (affected 10.7±2.9 mV *vs* unaffected 13.4±2.4 mV; p=0.001) and F-wave minimal latency (affected 23.5±2.5 ms *vs* unaffected 25.7±3.1 ms; p=0.045).

The Spearman correlation showed a significant inverse association between wrist flexor MAS score and ulnar nerve ADM CMAP (ρ=-0.504; p=0.033), as well as a significant direct association between finger flexor MAS score and ulnar nerve ADM DML (ρ=0.474; p=0.047). Furthermore, we found a significant direct association between forearm pronator MAS score and median nerve CSA at the affected elbow (ρ=0.489; p=0.042). Table III shows the results of correlation analysis.

Discussion

The main finding of this study is that some median and ulnar nerve NCS measures (DML, CMAP amplitude and F-wave minimal latency) significantly differed between the affected and unaffected upper limbs in chronic stroke patients.

Our results are in keeping with previous reports of NCS alterations after stroke (Paoloni et al., 2010). Decreased ADM CMAP amplitude was found in acute/subacute stroke patients, sometimes as early as 4 days after onset, and was associated with poor motor recovery (van Kuijk et al., 2007). To explain those data, a lower motor neuron involvement was suggested to occur in stroke patients as a sort of "dying back" neuropathy due to motor unit deafferentation (van Kuijk et al., 2007; Paoloni et al., 2010). The hypothesis was that UMNS results in a loss of synaptic input to the spinal alpha motor neurons, which become functionally inactive or undergo transsynaptic degeneration leading to disturbances of the axonal flow, axonal degeneration, dysfunction of neuromuscular transmission at the motor endplate, and re-

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duction of functionally active motor units (van Kuijk et al., 2007). Similarly, decreased ADM CMAP amplitude and pathological spontaneous activity were found after stroke, and reported to correlate with the time after onset and stroke severity (Lukács, 2005). Collateral reinnervation was suggested to start in the acute phase after stroke with enlarged motor units occurring during the chronic phase (Lukács, 2005). In keeping with the hypothesis of trans-synaptic degeneration of alpha motor neurons, the number of motor units estimated by F-wave analysis was reported to be reduced as early as 2 weeks after stroke in the affected upper limb (Hara et al., 2000; Hara et al., 2004). At variance, significant changes of the ulnar sensory nerve action potential and MNCV were found in the unaffected side of stroke patients, suggesting an increased risk of NCS abnormalities due to risk factors for polyneuropathy, such as diabetes mellitus (Paoloni et al., 2010).

In our view, although none of the NCS measures recorded in this study in the two upper limbs fell outside the normal range values (Puksa et al., 2003; Qrimli et al., 2016; Alber, 2017), it is plausible that all the above-mentioned mechanisms, and in particular the "subclinical" involvement of the lower motor neuron in UMNS (Hara et al., 2000), might have contributed to the NCS asymmetries here detected. Furthermore, we also argue that spasticity might not have played a crucial role in the NCS differences observed between the upper limbs, given that we detected only a significant inverse correlation between wrist flexor MAS score and ulnar nerve ADM CMAP, and a significant direct correlation between finger flexor MAS score and ulnar nerve ADM DML.

Interestingly, we also found a greater median nerve CSA in the affected elbow in comparison with the unaffected one. Enlargement of nerve CSA results from nerve demyelination, interfascicular epineurial fibrosis and perineural thickening as a consequence of chronic nerve compression (Grimm et al., 2014; Hunkar and Balci, 2012). In the elbow region, the most common median nerve compression syndrome occurs when the nerve passes between the humeral and ulnar heads of the pronator teres muscle, through the so-called "pronator canal" (Vymazalová et al., 2015). The main causes of median nerve compression at the elbow usually include pronator teres muscle hypertrophy or excessive tension (Vymazalová et al., 2015; Gurses et al., 2016). On these bases, we argue that the enlargement of median nerve CSA at the affected elbow, observed in the present study, might be due to a "subclinical" pronator teres syndrome probably caused by increased stiffness of the spastic pronator teres muscle. This would be in keeping with the significant direct association between the median nerve CSA at the elbow and spasticity of forearm pronators observed at the affected upper limb.

This study has several limitations. First, the sample size was small. Second, we did not explore NCS and US features normalized in parallel with spasticity after treatment. Third, other causes of spasticity than stroke were not considered. Fourth, we did not investigate other nerves of the upper limb in addition to the median and ulnar ones. Fifth, we did not perform any needle EMG evaluation, or consider other useful neurophysiological parameters such as the H-reflex.

In conclusion, our findings confirmed electrodiagnostic asymmetries and nerve ultrasonographic abnormalities in the affected upper limb compared with the unaffected one after stroke, and may help in the interpretation of NCS and US in patients with chronic stroke. Future studies are needed to further confirm our findings and overcome our limitations.

Acknowledgements

We thank Dr. Maurizio Osio for his helpful suggestions.

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