Quantification of long-term effects of botulinum injection in a case of cerebral palsy affecting the upper limb movement

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Introduction

In cerebral palsy, spasticity is often successfully treated with standardized botulinum toxin injection (BTI) [1–3]. Though, the limited duration of BTI effect, the need to repeat injections over time and the toxicity implications seriously require to face the matter of treatment optimization. For this reason, clinics are experiencing the emerging practice of combining BTI with several rehabilitative approaches, ranging from physical to occupational therapies and aiming at empowering and enduring the pharmacological profit given by botulinum itself [4].

We report the case of a female child affected by hemiplegia, due to cerebral palsy. After the admission, she underwent electroencephalographic (EEG) assessment, movement analysis (MA) and observational scoring of the upper limbs. After treatment with botulinum and physical rehabilitation, all the evaluations (thus including EEG and MA) were repeated.

We aim at illustrating how the single evaluative approaches contributed here to the final quantification and characterization of the long-lasting effects induced by the pharmacological treatment. We are aware that this specific case report provided evidence of striking improvement: we do not claim here that specific rehabilitation approaches can provide the described results; rather, we would like to put emphasis on the potentiality which rehabilitation had in this case of brain recovery, and even in the absolutely chronic stage.

Case report

Remote medical history

The subject is a female child now aged 10 years. Pregnancy evolved with hypertension. After fetal distress, she was born in emergency, with cesarean delivery at 42 weeks of gestation. Meconium aspiration occurred during the delivery. Apgar score 1 min after birth was 5, but a score of 7 was registered 5 min later. She then underwent 8 days of mechanical ventilation, after which pulmonary hypertension arose. Furthermore, a pulmonary infection (pathogenic agent not known) was treated with antibiotics.

At the age of 8 years, she started to suffer from involuntary movements of her right arm. A diagnosis of focal myoclonus was formulated, following which she started a treatment with Oxicodal® (active ingredient is oxcarbazepine, at present 150 mg/12 h). The treatment resulted in the complete extinction of dystonic movements.

Radiological history

The subject underwent Computerized Axial Tomography examination, showing left temporal frontal infarction. These findings were later confirmed by Magnetic Resonance Imaging, at the age of 8 years (Figure 1). Scans confirmed

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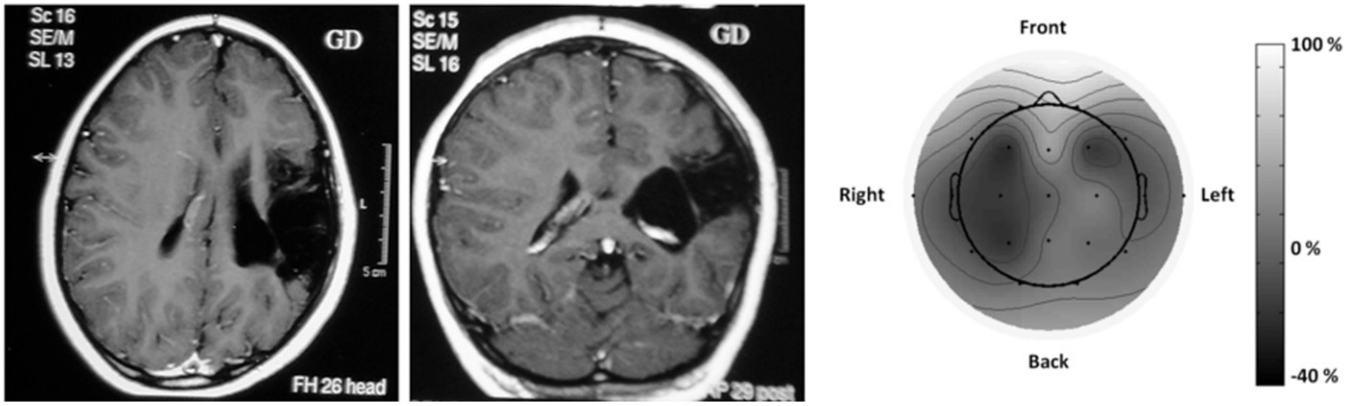

Figure 1. Axial (left) and coronal (center) MRI brain sections show altered structures in the left frontotemporal region. Such alterations manifest as a hypointensity area in the T1-weighted sequence. The extension of alteration was quantified in 5 cm on the axial plane, and in 3 cm on the coronal plane. Electroecephalographic map (right) of the brain in the mu frequency range (10–13 Hz) shows diffused desynchronization over the right (healthy) hemisphere; desynchronization is limited to the frontopolar region in the left (lesioned) hemisphere. Average map is drawn for 0.5 s latency after stimuli presentation and for pointing movements executed with both the right and left arms. All figures are shown in radiological convention (''Right is left'').

Table I. U.E.R.S., S.H.U.E.E., EEG and MA scores.

U.E.R.S.	A: shoulder	B:elbow	C: forearm	D: wrist	E: hand
Pre-treatment score	3	2	0	1	1
Post-treatment score	3	3	1	1	1
S.H.U.E.E.	SFA	DPA	GRA	Stereoagnosis	
Pre-treatment score	38%	51%	33%	2	
Post-treatment score	62%	57%	100%	3	
Electroencephalography	Alpha ERD	Mu ERD	Beta ERD	Rebound	
Pre-treatment score (%)	−15	−10	−10	+25	
Post-treatment score (%)	−50	−40	−50	+40	
Movement analysis	ADJ% (%MC)	RP% (%MC)	NMU	MV (m/s)	
Pre-treatment score AA	26.94 ± 8.25	34.04 ± 5.36	5.60	0.40 ± 0.05	
Pre-treatment score LAA	15.26 ± 7.09	44.98 ± 2.80	3.30	0.56 ± 0.03	
Post-treatment score AA	23.06 ± 3.28	37.91 ± 2.78	6.78	0.53 ± 0.06	
Post-treatment score LAA	13.17 ± 2.73	43.82 ± 4.42	4.10	0.60 ± 0.06	
Score normality range	15.38	41.40	2.00	0.59	

SFA, spontaneous functional analysis; DPA, dynamic posture analysis; GRA, grasping and release; ERD, event-related desynchronization; ADJ%, percentage adjusting phase; RP%, percentage returning phase; NMU, number of movement units; MV, mean velocity; AA, affected arm; LAA, less-affected arm. Improvements are highlighted in light blue.

the presence of a large region of hyperintensity in the left hemisphere, located frontotemporally. The extension of alteration was quantified in 5 cm on the axial plane (ranging from the pre-central to the central and lateral sulci), and in 3 cm on the coronal plane (involving the inferofrontal gyrus).

Recent medical history and treatment

The child entered the Instituto de Rehabilitacion Infantil Teleton of Santiago de Chile at the age of 2 years. At the neurologic examination the patient was alert, responsive and able to establish social interaction, accordingly with her age. Later, school performance resulted regular, even though supported for the management of psychomotor hyperactivity. The girl showed hypertonia of the right side of the body, resulting in motor impairment. The right upper limb resulted to be more affected than the right lower limb, presenting mixed tone and poor integration in the motor schemas. Adducted shoulder, flexion of the elbow and wrist, together with contraction of the hand fingers and thumb-in palm, were observed in the posture of the right upper extremity. Ashworth rating, according to the Modified Ashworth scale, was 2 for the majority of the right upper limb muscles [5, 6]. Diagnosis of spastic hemiplegia was thus formulated (Gross Motor Function I).

Recently, the right upper limb was evaluated by the kinesiologist, by means of the U.E.R.S. scale for the range of motion quantification [7]. Results are shown in Table I, first row (U.E.R.S. ranges from 0 to 3. 0: severe restriction; 1: moderate restriction; 2: mild restriction; 3: no limitation). With reference to normality, the right limb showed reduced range of motion: the elbow presented mild restriction of movements (scoring 2/3), the forearm showed severe restriction (0/3), while the wrist (1/3) and the hand (1/3) were classified in moderate restriction. Last, the occupational therapist applied the S.H.U.E.E. scale for everyday activities [8]. She rated the spontaneous function (38%), the dynamic posture (51%) and the grasping (33%): she assigned a final score of 2 to stereoagnosis. Results are shown in Table I, third row.

After the consent of the girl's parents, EEG data were recorded synchronously with the MA system, while the patient was performing a repeated pointing task, consisting in hitting with the forefinger a clown's nose on a touch-screen. EEG was then processed for the extraction of event-related synchronization and desynchronization (ERS/ERD). The processing method is fully described in Molteni et al. [9, 10]. Over the left brain motor area (C3 standard position: site of cerebral lesion) desynchronization reached −15% in the low alpha (8–10 Hz), −10% in the mu (10–13 Hz) and −10% in the low beta (13–22 Hz) frequency bands for pointing tasks with the right (i.e. contralateral) hand; rebound reached +25% in the mu band.

In order to collect movement data during the pointing task, reflective markers were placed on the shoulders and the upper limbs of the girl, according to reduced Rab protocol [11]. Each movement was segmented into three sequential phases: the going (GP), adjusting (ADJ) and returning (RP) phases [12]. To evaluate differences between the girl's affected and less-affected limbs, and deviations from the normality range, some kinematic parameters were computed: the duration of the three movement phases expressed as the percentage of total movement duration (GP%, ADJ%, RP%), the index of curvature (IC), number of movement units (NMUs), average jerk (AJ), peak velocity (PV) and mean velocity (MV) as described in literature [12, 13].

The affected arm evidenced longer ADJ phase (ADJ%: 26.94 ± 8.25) and shorter RP (RP%: 34.04 ± 5.36) with respect to the less-affected arm and to the normality range. A more segmented kinematics was observed for the affected arm (NMU: 5.6) and a slower movement (MV: 0.40 ± 0.05) than the less-affected arm and normality range. No differences emerged in the comparison between affected arm and less-affected arm in GP%, IC, AJ and PV indexes.

The girl then underwent electromyography-guided muscular BTI. The following doses of Botox® (Allergan) were administered to muscles of the right upper limb: anterior brachialis 40U, flexor carpi ulnaris 40U, pronator teres 40U, pronator quadrates 25U, opponens pollicis 10U.

After the BTI, the girl attended 20 sessions of physical therapy, lasting 40 min each and occurring twice a week. Each session focused on limb preparation (consisting in muscle stretching and proprioceptive work), strength training (consisting in progressive resistance exercise, in which workload was determined for each muscle) and task-oriented functional activities (consisting in functional tasks that involve a whole limb, such as reaches, transfers, pushes and object manipulation) and was followed by occupational therapy.

After the conclusion of therapy, and 4 months after BTI, the kinesiologist repeated the U.E.R.S. scoring. Improvements in the range of motion of the right upper limb were recorded, with the elbow passing from 2 to 3, and with the forearm passing from 0 to 1 (Table I, second row). Moreover, spontaneous functional analysis, dynamic posture, grasping and release all increased, with stereoagnosis score turning from 2 into 3 (Table I, fourth row).

EEG and MA assessments were simultaneously repeated with the same procedure described above. Over the left brain motor area (C3 position) desynchronization reached −50% in the low alpha, −40% in the mu and −50% in the low beta frequency bands for pointing tasks with the right hand. A map of mu band desynchronization is depicted in Figure 1 right. Rebound exceeded +40% in the mu and low beta bands.

In the comparison between pre- and post-treatments, the affected arm pointed out faster movement (affected arm MV POST: 0.53 ± 0.06; resulting in the normative band), while no differences emerged for the less-affected arm. The differences between affected arm and less-affected arm concerning the movement duration were maintained. In the post-treatment assessment, the less-affected arm presented the same differences showed in the pre-treatment assessment, in comparison with normality range.

Discussion

This work aimed to report the effects of the BTI in the upper limb, performed in accordance to the standards [2]. We assessed the movement capabilities of a 10-year-old girl, so as to fulfill a number of requirements. First, we were interested to apply quantitative evaluations, for providing objective measures. Second, we aimed to explore movement manifestation by investigating all its components: (i) the mechanical aspect, studied by means of the U.E.R.S. scale, (ii) the generative facet, studied at a cognitive level by means of electroencephalography, (iii) the executive feature, investigated through MA and (iv) the contextual side, evaluated through the S.H.U.E.E. scale for finalized activities. Third, we aimed to quantify the changes/improvements brought to movement performance by BTI in long-term effect. This motivated a double assessment of the four movement components, performed once before and then repeated after the BTI. The last and most ambitious scope of the work was the comparison of the different results, provided by the various evaluations and by the repetition of the assessments, so as to infer knowledge about movement integration and compensation following BTI.

Results confirmed that BTI long-term effects were present, though playing a marginal role: indeed, only the elbow and forearm of the affected limb could get durable benefit, in terms of increased range of motion. Even though marginally supported by mechanical improvement, at a cognitive level we could observe substantial modification of the EEG correlates of upper limb movement, pointed out by consistent increase of desynchronization in alpha, mu and low beta frequencies, and of the beta rebound, and indicating deep cerebral changes. This fact astonishingly resulted in much better scores of the S.H.U.E.E. scale, thus indicating general quality increase in the performance of everyday activities.

Overall, we deem that these results opened wide perspectives on the girl's rehabilitation potentiality. Indeed, even small long-lasting improvements – induced on biomechanics by BTI – triggered wide cerebral modification, well reflected in improved contextual movements and motor strategy. This fact underpins the human capability to amplify the effects of rehabilitation, even in the presence of small improvement of the end-effector performance, and especially in paediatric age. In fact, given that the botulinum toxin effect blows over after 3 months, during which the sprouting induced muscle reinnervation, MA in post-session revealed no differences (excepted for the MV index) in comparison with pre-session while the cerebral activity modification endured, revealing the maintenance of rehabilitation effects.

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Declaration of interest

The authors declare that no commercial or financial conflict of interest exists for any of them, in connection with the submission of the present draft. The authors alone are responsible for the content and writing of this article.

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