

## CASE STUDY

# Effect of botulinum toxin type A, motor imagery and motor observation on motor function of hemiparetic upper limb after stroke

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### Abstract

**Background:** In rehabilitation settings, motor imagery, motor observation and mirror therapy serve as techniques for the recovery of paretic upper limb in patients with movement disorders after stroke, whereas botulinum toxin type A (BTX-A) offers the best treatment for focal spasticity.

**Case reports:** After haemorrhagic stroke, three patients (two men and one woman, mean age:  $61.2 \pm 7.03$ ) presented with hemiparesis of the left or right hand and arm with flexion of fingers, wrist and elbow, with no disturbance to sensitivity but with loss of use handoff the limb to write, eat or dress. After BTX-A injections, the patients underwent a daily rehabilitation programme based on motor imagery and motor observation for 1 month. Before and after the combined treatment, the motor function, spasticity and functional deficits of the patient were extensively measured. After a 3-month follow-up, upper limb spasticity measured with the Modified Ashworth Scale had worsened, yet the associated score remained lower than that at baseline. However, in these three patients a large improvement of motor function of the hemiparetic upper limb was observed.

**Conclusion:** Combined treatment may be a viable rehabilitation option in post-stroke patients with disability to upper-extremity motor function, however further investigations are needed to determine its reproducibility in larger case series or clinical trials.

**Keywords:** Stroke, functional status, rehabilitation, activities of daily living, botulinum toxin type A, motor imagery, motor observation, mirror therapy

### Introduction

Motor disorders and loss of functional movement are common consequences of stroke [1], related to

muscle over-activity and motor weakness following brain damage and compromising quality of life in turn. Many rehabilitation programmes for the upper

extremity in post-stroke patients have been proposed and functional recovery is dependent upon the nature and extent of brain damage. New techniques based on practical applications of the concept of post-stroke brain plasticity are still under evaluation. One such technique, ‘mirror therapy’, is based on the concepts of ‘motor imagery’ and ‘motor observation’ [2]. Mirror neurons discharged during the execution of hand object-directed actions and during the observation of the same actions performed by other individuals [3]. Related to the mirror therapy is the ‘motor imitation’, also linked to motor imagery. It is related to the mental rehearsal of simple or complex motor acts that are not accompanied by overt body movements. Motor imagery represents the voluntary effort of an individual to imagine himself/herself executing a specific action [3, 4]. Motor observation can be defined as the perception of the actions of others. It has been hypothesized that motor imagery and motor observation could be used to improve the recovery of motor functions after stroke [5]. One limitation of motor rehabilitation in neurological disease is spasticity, defined as a velocity-dependent increase of tonic stretch reflexes with exaggerated tendon jerks and which results from hyperexcitability of the stretch reflex [6]. Upper limb spasticity can impede activities of daily living, personal hygiene and functional improvement because paresis and increased muscle tone can also cause joint stiffness leading to contractures. Management of spasticity is considered essential in the prevention of deformities, to improve function and to relieve distressing symptoms. In recent years, botulinum toxin type A (BTX-A) has also been demonstrated to be effective in reducing post-stroke spasticity, by preventing the release of acetylcholine from pre-synaptic axons of the motor endplate and blocking signal transmission at the neuromuscular junction [7, 8]. However, there is controversy surrounding whether there is improvement in motor function relative to reduction of spasticity. In fact, reduction in spasticity does not necessarily translate into improved functional abilities [9].

**Case series**

The present report describes three patients (one woman and two men) affected by upper limb spasticity after haemorrhagic stroke with resultant hemiparesis in left and right upper limb. Table I summarizes the clinical and demographic characteristics of the three post-stroke patients concerned. The subjects presented with hemiparesis of the left (or right) hand and arm with flexion of fingers, wrist and elbow. They had difficulty in extending their fingers and their elbow, but all patients did

Table I. Demographic and clinical characteristics of the post-stroke patients.

Mean age (SD) (years)	61.2 (7.03)
Mean time (SD) since onset of stroke (months)	6.3 (2.97)
Sex ratio	
Female/Male	0.5
Stroke type	
Thrombotic	0
Haemorrhagic	3
Side	
Right	1
Left	2

not have disturbed sensitivity. The three patients were cooperative, oriented well in time and space and without unilateral spatial neglect or aphasia. They were able to walk slowly without any walking aids. In the post-stroke period, the patients used their healthy upper extremity to perform daily activities almost exclusively. The patients reported they did not use their paretic arm or hand to write, eat or dress. After discharge, they undertook intensive rehabilitation programmes (1 hour three times/week for 12 weeks) to improve motor function of hemiparetic upper limb with few results. It was hypothesized these three patients would benefit from both BTX-A injections and a rehabilitation programme based on motor imagery and motor observation. Prior to this combined treatment, the patients were submitted to a comprehensive evaluation of their motor and functional deficits.

The Modified Ashworth Scale (MAS) [10] was used for grading the resistance encountered during passive muscle stretching. It is a 5-point ordinal scale: ranging from 0 = normal muscle tone up to 4 = limb rigid in flexion or extension. A supplementary level ‘1+’ between the scores of ‘1’ and ‘2’ was used to indicate slight increase in muscle tone, demonstrated by a catch, followed by minimal resistance throughout the remainder (less than half) of the range of motion. The Barthel Index and the Functional Independence Measure (FIM) were also used to measure activity (disability) which are widely used to score change in function. The Barthel Index is a 10-item instrument measuring functional independence in personal activities of daily living [11]. The FIM is an 18-item instrument also measuring functional independence in personal activities of daily living (13 items) and includes measures of communication and social cognition (five items), each item has a 7-point scale with which to respond [12]. Functional status was also assessed by the Activities of Daily Living (ADL) scale (scores ranging from 6 (all functions preserved) to 0 (all functions lost)), which determines the level of independence in six activities: bathing, dressing,

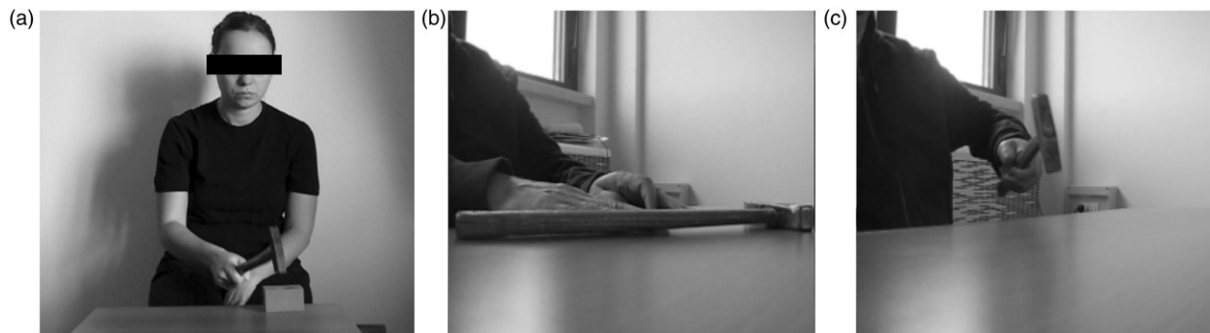


Figure 1. (a) The patient observes very carefully the physical therapist doing a motor act; (b) The patient imagines doing the motor act observed; (c) The patient reproduces the motor act just observed and imagined.

toileting, transferring from bed to chair, continence and feeding [13]. Moreover, the Frenchay Arm Test (FAT), a 'focal' disability measure for stroke patients was also used. This test assesses the ability of the hemiparetic arm to perform five functional activities (stabilize a ruler, grasp a cylinder, pick up a glass, remove and replace a sprung clothes peg and comb one's hair) [14]. Finally, the Nine-Hole Peg Test (NHPT), an evaluation method that uses the interval scale of dexterity, was performed. In this test, the time required to place pegs in nine holes arranged at 15-mm intervals in three rows and to remove them is measured [15]. After completing this clinical evaluation, the patients gave written informed consent to be submitted to the combined treatment. The patients were treated with intramuscular administration of BTX-A (NT 201 XEOMIN, Merz Pharmaceuticals GmbH, Frankfurt, Germany). The toxin was reconstituted with 1 ml of saline solution and under electromyographic guide, using a 26 gauge needle, 30 units of BTX-A were injected into the flexor pollicis longus, 100 units were injected into the muscle belly of the biceps brachii muscle at two sites (each site received 50 units), as well as 100 units into the flexor digitorum superficialis muscle at one site. After botulinum toxin injections, the patients were submitted to a daily rehabilitation programme based on motor imagery and motor observation for 45 minutes, each day of the week for a period of 1 month. Thirty-seven video-sequences, each lasting ~1 minute, were prepared. Every video-sequence reproduced a movement carried out by a healthy subject (a physical therapist) and performing a different daily action (e.g. having a coffee, using a hammer). Each session contained a variable number of video-sequences (from five to 10) and three phases. The first phase involved motor observation where patients were asked to carefully observe short movies (Figures 1 and 2). The second phase involved motor imagery where the physical therapist instructed patients to close their eyes and imagine themselves performing

the movement just observed (Figures 1 and 2). In the third phase, the patients were required to use the impaired upper limb to execute the movement just observed and imagined (Figures 1 and 2). Table II summarizes test and scale performance for the post-stroke patients at the baseline, after 1 month and after a 3-month follow-up. After 1 month, the patients performed a post-treatment assessment. This follow-up period was chosen as the optimal time for the first outcome assessment because the clinical effect of BTX-A is said to peak around this period [7]. In all patients, after the BTX-A injections, the MAS scores indicated a reduction of wrist, fingers and elbow's spasticity and reduction of flexor synergies; the patients could voluntarily extend their wrist, fingers and elbow (Table II). This improvement facilitated the performance of motor actions with the impaired upper limb. After a 3-month follow-up, the MAS score had increased, but it remained lower than that at baseline level for all patients. The upper limb dexterity had also improved (FAT score) and the patients were able to perform movements such as grasp a cylinder and pick up a glass (Table II). Furthermore, after the combined treatment, in all patients the NHPT score had increased and the extent of disability had reduced (FIM score, Barthel Index and ADL score) (Table II).

## Discussion

In the present report, clinical improvement in the motor function of upper limbs of three patients after haemorrhagic stroke following combined treatment of BTX-A injections and a rehabilitation programme based on motor imagery and motor observation is described. The traditional treatment approach for motor deficits after stroke is mainly based on techniques aimed at stimulating the use of the paretic limb during supervised training sessions [16]. It has been suggested that repetitive, active



Figure 2. (a) The patient observes very carefully the physical therapist doing a motor act; (b) The patient imagines doing the motor act observed; (c) The patient reproduces the motor act just observed and imagined.

Table II. Test and scale performance for the post-stroke patients at the baseline ( $t_0$ ), after 1 month ( $t_1$ ) and after a 3-month follow-up ( $t_2$ ).

Patient	MAS $t_0$	MAS $t_1$	MAS $t_2$	BI $t_0$	BI $t_2$	FIM $t_0$	FIM $t_2$	ADL $t_0$	ADL $t_2$	FAT $t_0$	FAT $t_2$	NHPT $t_0$	NHPT $t_2$
a	2	1	1+	55/100	65/100	98/126	106/126	3/6	4/6	2/5	4/5	4/9	8/9
b	1+	1	1	84/100	97/100	100/126	110/126	4/6	5/6	3/5	4/5	5/9	7/9
c	2	1	1+	65/100	77/100	96/126	107/126	3/6	4/6	2/5	4/5	3/9	6/9

MAS = Modified Ashworth Scale; BI = Barthel Index; FIM = Functional Independence Measure; ADL = Activities of Daily Living; Table shows the ADL preserved; FAT = Frenchay Arm Test; NHPT = Nine-Hole Peg Test.

movements of a paretic limb could have positive effects on neuronal plasticity [17]. Current neuro-rehabilitative techniques still under evaluation have brought to light the concept of post-stroke brain plasticity. Several studies have been based on the hypothesis that motor areas are recruited not only when actions are actually executed, but also when a subject imagined or simply observed an action [18]. The neurophysiological basis for this recruitment relies on the discovery of so-called ‘mirror neurons’ [3]. Mirror neurons are activated during the execution of hand object-directed actions and during the observation of the same actions performed by other individuals [4]. The observed action seems to be ‘reflected’, as in a mirror, in the motor representation for the same action of the observer. Related to the mirror therapy is the motor imitation which implied motor imagery and motor observation. Indeed the activation of motor areas by the observation of actions becomes reinforced by the concomitant active execution of the observed actions [19].

In the present report, several tests and scales were used to evaluate the improvement of motor function of hemiparetic upper limbs in three post-stroke patients after BTX-A injections and a rehabilitation programme including motor imagery and motor observation. The observed changes in test and scale scores may be attributed to several factors. They could reflect improvement in strength and coordination in the hemiparetic upper limb, a change in ‘learned non-use’ behaviours or use-dependent

cortical changes after the combination of BTX-A injections and motor imagery and motor observation. Spasticity interferes with movement in a complex manner and can affect activities of daily of living. The use of botulinum toxin to reduce spasticity is sometimes used, but does not necessarily translate into better functional abilities [8]. This study treated the spasticity to enable the performance of more complex movements and to reduce the interactions that prove to be obstacles to executing extension movements. During the phase of motor imagery in the rehabilitation programme, small movements of hemiparetic hands were observed, reproducing the motor act imagined, as if the hand prepared itself to take something. It is possible that during the motor act and its imagination the same brain structures were activated. During the first rehabilitation sessions, at the end of each session, the patients reported having some difficulties in imagining the movement observed. These difficulties became less with more sessions, suggesting that the imagination or visualization could be improved with the performance of the motor acts. Moreover, the patients reported they had dreams about being able to perform some motor acts with the hemiparetic arm. The combined treatment in these patients served to improve motor ability with no other therapeutic interventions.

It is known that post-stroke patients display greater motor disability related to learned non-use phenomena [2, 20]. In this report, the post-stroke patients were asked to observe everyday life actions

and some aspects of the observed actions possibly triggered brain areas belonging to the mirror neuron system. In fact, complementary to these findings are those that suggest how action observation may interact with the mirror neuron system in acquiring new motor skills. The improvement of motor ability can be related to the positive effect of action observation therapy, as suggested by other functional magnetic resonance imaging (fMRI) studies [21]. Whether changes occurred at the cortical level is not known, because neuroimaging techniques were not included in this protocol, but the additional component of action observation contributed to a significantly higher impact of this rehabilitation programme than physical training alone. The increased activation of the mirror neuron system as a specialized physiological motor network in the course of this new treatment suggested that this improvement relies on reactivation of motor representations related to the observed actions [21]. One possible mechanism for the benefit of motor imagery and motor observation was the potentiation of synaptic transmission that occurs during both motor imagery and actual execution. These observations raise the possibility that improved motor performance could be achieved through systematic exercises based on careful observation and imitation of everyday actions [4]. The combined treatment of BTX-A injections and a rehabilitation programme based on motor imagery and motor observation may be a viable therapeutic alternative in post-stroke patients with disabling upper-extremity motor function, however further investigations are needed to determine its reproducibility in larger case series or clinical trials.

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