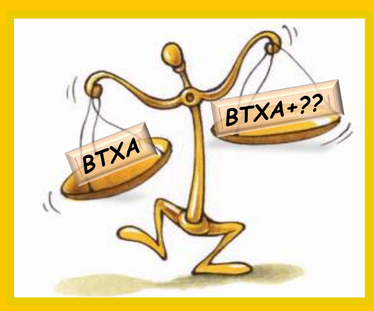
BOTULINUM TOXIN AND MIRROR THERAPY: A NEW APPROACH FOR POSTSTROKE SPASTICITY

Scalise A , Toffoli M, Grassetti L, Gentile C, Troiero K, Simeoni S, Rizzi L, Gigli GL

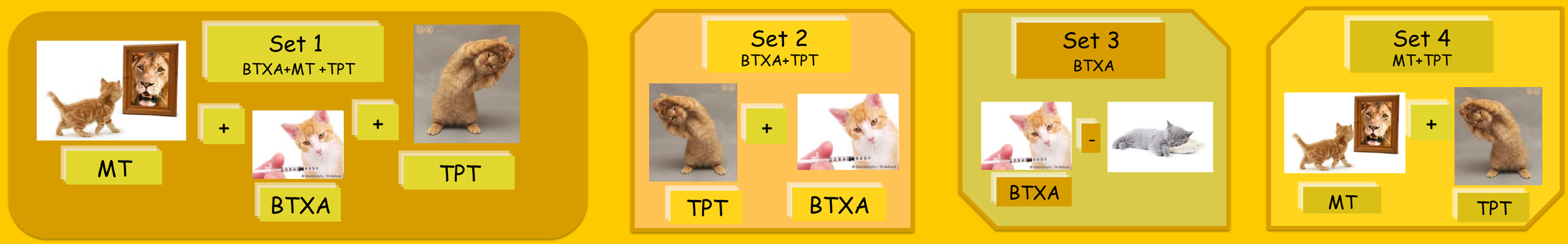
University Hospital of Udine, Italy

Introduction Stroke is one of the major causes of death and disability worldwide; this burden is increasing due to an aging population and unhealthy lifestyle habits. Paresis and spasticity of the upper limb are the most frequent and impacting consequences of stroke. Poststroke spasticity can develop as early as 1 week after stroke, and it is estimated to occur in up to half of stroke survivors, with social, medical, and economical burdens. The aim of the treatment in patients with post-stroke spasticity is focused on the reduction of muscle limb overactivity. Several types of treatments can be used to alleviate post-stroke spasticity, including physical therapy, systemic and intrathecal medications as well as surgery. The gold-standard therapy for focal spasticity after stroke is botulinum toxin type A (BoNT-A). After BoNT-A treatment, it is current practice to offer patients additional rehabilitation therapy, but the evidence supporting this multidisciplinary approach is not strong. There is growing evidence supporting mirror therapy (MT), a simple and inexpensive new technique of rehabilitation, as a useful tool in addition to traditional physiotherapy (TPT) in treating arm paresis in stroke patients.

Objectives In patients with upper-limb post-stroke spasticity, we compared BoNT-A, MT, and TPT treatments, applied individually or otherwise combined.
Our objective was to evaluate the gold-standard among the functional treatments of spasticity.



Subjects and Methods: We consecutively recruited 61 patients with post-stroke upper limb spasticity. Subjects were assigned to 1 of 4 treatment sets, according to their possibilities (logistics management of the rehabilitation program) to undergo a given treatment:
Patients in **set1** were treated with BoNT-A, MT and TPT, in **set2** were treated with BoNT-A and TPT, in **set3** were treated with BoNT-A alone, in **set4** were treated with MT and TPT.



Patients received IncobotulinumtoxinA (Xeomin®; Merz Pharma), the doses were determined by a neurologist, experienced in BoNT treatment, in agreement with the current guidelines and according to the needs of the individual patient. The MT intervention consisted in 20 minutes of MT treatment for session for a total of 20 sessions in one month. Patients were treated with TPT consisted of 20 minutes of treatment for session for a total of 20 sessions in one month. Given the transient effect and the reversibility of BoNT-A, with an interval of at least 4 months, patients were treated several times with a different treatment-set. For statistical purposes, each treatment was counted as an independent one for a total of 104 "observations". Shortly before and at the end of each treatment- set the following variables were evaluated in the affected arm: Ashworth Scale (MAS), the Motricity Index (MI), the EuroQOL-5D (EQ-5D), and the Barthel Index. The beneficial effects of different combination of MT, TPT, and BONT-A were analyzed by comparing the improvements in\between sets.

Results: Demographic data are reported in Table 1. Proportions of improved, unchanged, and worsened observations for each set are shown in Table 2. The results in Table 3 show the empirical significance levels for the Wilcoxon rank sum test for improvements in motor function. Patients in set 1 reached significant improvement ($P<0.05$) in all used scales. On the contrary, results for patients in set 4 were inconsistent in all used scales. Patients in set 2 and set 3 reached intermediate outcomes.

Tab.1 Sample Description

	Set 1	Set 2	Set 3	Set 4	Total
Observations	37	37	18	12	104
Males	25 (68%)	21 (57%)	13 (72%)	10 (83%)	69 (66%)
Females	12 (32%)	16 (43%)	5 (72%)	2 (17%)	35 (34%)
Age < 70 years	20 (54%)	18 (49%)	5 (28%)	7 (58%)	50 (48%)
Age > 70 years	17 (46%)	19 (51%)	13 (72%)	5 (42%)	54 (52%)
Stroke within 60 months from enrollment	17 (46%)	20 (54%)	7 (39%)	5 (42%)	49 (47%)
Stroke older than 60 months from enrollment	20 (54%)	17 (46%)	11 (61%)	7 (58%)	55 (53%)
Hemorrhagic stroke	12 (32%)	10 (27%)	3 (17%)	1 (8%)	26 (25%)
Ischemic stroke	25 (68%)	27 (73%)	15 (83%)	11 (92%)	78 (75%)
Dominant hemisphere affected	15 (44%)	9 (27%)	5 (33%)	4 (44%)	33 (36%)
Non dominant hemisphere affected	19 (56%)	24 (73%)	10 (67%)	5 (56%)	58 (64%)

	MI	MAS	BI	EQ-5D
Set 1	0,00069	0,00001	0,00088	0,0022
Set 2	0,05695	0,00221	0,01272	0,11773
Set 3	0,13591	0,00799	0,7818	0,09855
Set 4	0,53338	0,1421	0,6251	0,26431

Tab.2 Results of Treatment Sets on Conventional Outcome Measures

	MI			MAS			BI			EQ-5D		
	better	unchanged	worse	better	unchanged	worse	better	unchanged	worse	better	unchanged	worse
set1	48,6%	43,2%	8,1%	86,4%	2,7%	10,8%	43,2%	45,9%	10,8%	56,76%	27,0%	16,2%
set 2	16,2%	72,9%	10,8%	75,6%	8,1%	16,2%	35,1%	51,3%	13,5%	41,67%	36,1%	22,2%
set 3	22,2%	72,2%	5,5%	77,7%	5,5%	16,6%	11,1%	50,0%	38,8%	38,89%	38,8%	22,2%
Set 4	25,0%	41,6%	33,3%	50,0%	25,0%	25,0%	25,0%	50,0%	25,0%	33,33%	33,3%	33,3%

Tab.3 Significance Levels in Wilcoxon Rank Sum Test for Improvements in Motor Function

Conclusion: To our best knowledge, the beneficial effects of the combination of MT, TPT, and BONT-A in poststroke spasticity have never been assessed before. Moreover, given the different mechanisms of action, we hypothesized that MT, BoNT-A, and TPT may have a synergistic effect in the treatment of motor function in stroke patients that goes beyond the effect of each individual treatment. In particular, MT and BoNT-A may have a synergistic effect in modulating maladaptive cortical plasticity, which may contribute to poststroke plasticity. We conclude that a multimodal neurorehabilitation strategy is more effective than a single therapy to promote recovery of function and reduce spasticity of the upper extremity in chronic stroke patients.