FAMPRIDINE IN MULTIPLE SCLEROSIS PATIENTS: ACTIVITY ON UPPER LIMB FUNCTION EVALUATED BY KINEMATIC ANALYSIS

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INTRODUTION

Multiple sclerosis (MS) is one of the most common neurological diseases and involves inflammatory demyelination and axonal loss of the central nervous system.

Physiologically, myelin loss leads to changes inaxonal ion channels that cause conduction failure. Fampridine (4-aminopyridine, FA) is a potassium channel blocker that can increase action potential duration and amplitude, leading to improved conduction in demyelinated nerve fibers and to increased neurotransmitter release at synaptic endings.

The aim of the study is to assess the activity on upper limb function evaluated with a kinematics analysis of FA in patients with MS.

MATERIAL AND METHODS

25 patients were assigned to receive FA (10 mg twice daily) for 2 weeks.

A battery of tests including Symbol Digit (SD), Nine Hole Peg Test (9HPT), Fatigue Severity Scale (FSS), 12-item Multiple Sclerosis Walking Scale (MSWS-12), Two Minutes Walking Test (2MWT) and Timed 25-foot Walk (T25FW) was performed at baseline (T0), at the end of treatment (T1) and 2 weeks later (T2). Responders had been defined by the literature as subjects with an improvement at the 9 hole greater than 20%.

During kinematics analysis, subjects generated isometric force steps with their dominant hand, in one of 6 randomly selected directions on the horizontal plane, and under two conditions: (i) VISION, i.e. subjects could see on a computer screen both the target force and NO VISION, i.e. no monitoring of the instantaneous force. (Fig 1) In a second series of experiments, subjects performed planar arm movements (amplitude 10 cm) with an identical experimental design (6 different directions, two conditions); hand trajectories were sampled by a digitizing tablet. (Fig2) We then estimated the following indicators: reaction time (RTI, time between target onset and movement start); path curvature (LIN, percent increase of the length of the actual path, relative to the straight line); trajectory smoothness (SMO, integral of the norm of the jerk of the hand/force path); movement duration (DUR, total, acceleration and deceleration phase) and degree of asymmetry of the speed profile (DDU, ratio between the durations of deceleration and acceleration phases); aiming error (AAI, difference between target and starting trajectory direction).

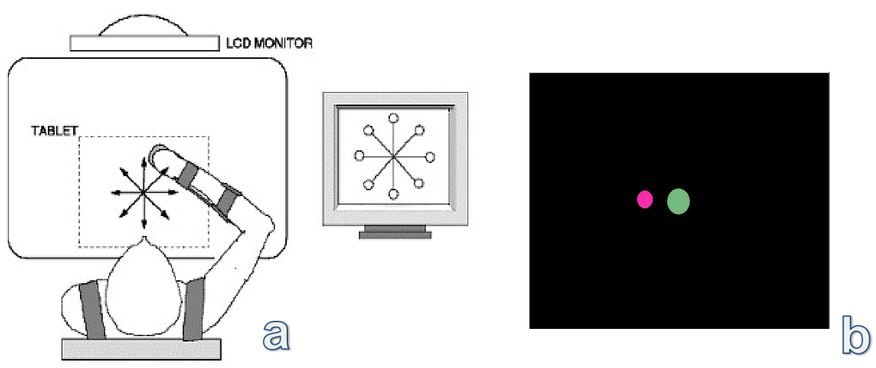

Fig 1: patient position (a), target (b), graphic tablet for kinematic analysis (c) and example of trajectories and speed profiles (d)

Kinematic and clinical evaluation at baseline (T0), at the end of treatment (T1) and 2 weeks later (T2)

RESULTS

Out of 25 subjects were 13 female and 12 male. Mean age was 51 ys, mean disease duration 14 years, 13 (44.8 %) subjects had relapsing remitting, 8 (27.6 %) secondary progressive and 8 (27.6 %) had primary progressive disease course.

8 patients reported a significant improvement (>20%) in walking speed (∆T25FW), 6 patients were “partial responders” with a subjective improvement in walking, 7 patients were “no responders”, 2 could not be tested and 2 patient dropped out from the study due to side effects (diffuse paresthesia and facial mioclonus).

Considering 9 HPT for right hand, 3 patients reported a a significant improvement >20%, 10 patients showed an improvement (< 20%) 8 patient were “no responders” and 2 patient could not be tested and 2 dropped out. Considering 9 HPT for left hand, 2 patients reported a a significant improvement >20%, 9 patients showed an improvement (>20%), 8 patient were “no responders”, 2 patients could not be tested and 2 patient dropped out. (see table 1). The correlation between the two tests is shown in Figure 2

N°	ΔT25FW%	Δ9HPT-DX%	Δ9HPT-SX%
S1	−12.40	−13.27	7.58
S2	**-26.75**	N.E	8.06
S3	2.44	12.82	2.17
S4	**-31.79**	−10.39	−8.14
S5	N.E	−14.43	4.60
S6	−10.00	0.89	3.80
S7	N.E	N.E	N.E
S8	23.66	21.89	−11.95
S9	N.E	N.E	N.E
S10	**-64.38**	−3.72	−3.68
S11	34.48	0.14	1.51
S12	−4.62	2.55	8.76
S13	5.51	28.86	4.86
S14	18.33	N.E	N.E
S15	**-50.38**	**-24.42**	**-27.00**
S16	N.E	−4.37	61.04
S17	**-26.00**	−5.32	−5.26
S18	−16.38	11.01	−19.75
S19	**-43.71**	−8.67	−11.64
S20	−10.11	**-24.96**	16.27
S21	0.00	17.86	−1.25
S22	−1.85	**-35.70**	−8.04
S23	**-26.21**	−12.38	**-20.44**
S24	**-44.56**	−7.20	−13.65
S25	18.18	−1.22	1.15

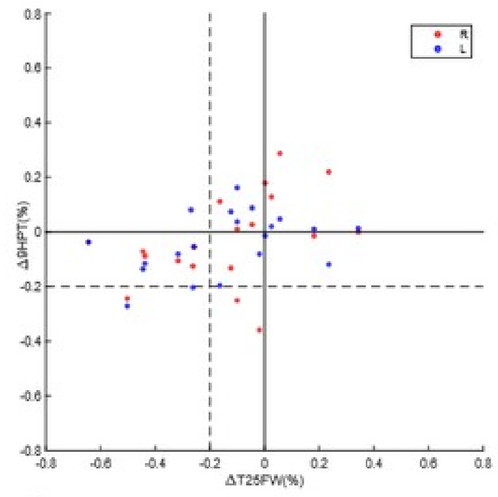

Fig.2: Correlation between the changes in T25FW and 9HPT

Regarding kinematic indicator : trajectory smoothness and movement duration were significantly affected by the administration of Fampridine overtime ($p < 0.05$) both considering the all group and the responders group when evaluating at walking speed. (See table 2)

INDICATOR	TREATMENT	VISION	TREATMENT:VISION
RTI	**0.0029**	**<0.0001**	**0.0050**
LIN	0.3470	0.6297	0.0639
AAI	0.1581	0.6103	0.3104
DUR	**0.0001**	**<0.0001**	**0.0017**
ADU	**0.0010**	**<0.0001**	**0.0041**
DDU	**0.0015**	**<0.0001**	0.2511
SMO	**<0.0001**	**<0.0001**	0.1007

Tab 2. result of the mixed effects model

CONCLUSION

The study showed an activity of Fampridine on upper limb motor performance when evaluated with kinematic analysis.