# Fampridine improves horizontal eye movements in patients with multiple sclerosis and internuclear ophthalmoplegia: a double-blind, placebo-controlled crossover study

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## INTRODUCTION

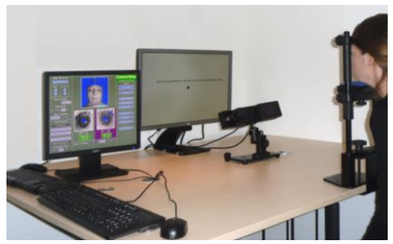
Internuclear ophthalmoplegia (INO) is a common cause of visual symptoms in patients with multiple sclerosis (MS). It is characterized by slowing of eye adduction during horizontal saccades. Recent studies suggest fampridine may improve nerve conduction in MS patients. We performed a study in MS patients with INO to determine effects of fampridine on eye movement speed.

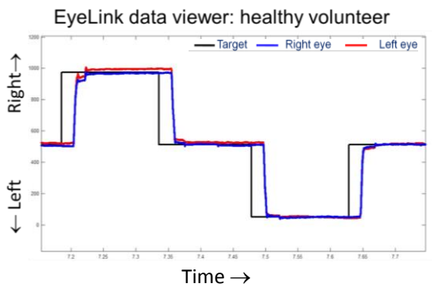
## METHODS

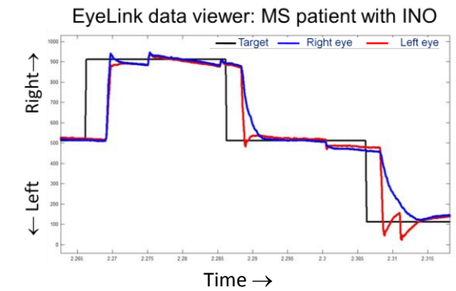
This was a randomized, double-blind, placebo-controlled, cross-over study with fampridine in 24 MS patients with INO. Patients received a single dose of 20 mg fampridine or placebo on two separate occasions. We analyzed eye movements recorded by the EyeLink1000 at baseline and at 1.5, 2.5, 3.75 and 5.5 hours post-dose. Subjects made saccades in response to a target jump from the center to an eccentric location, either left or right from the center binocularly with a frequency of 1000 Hertz.

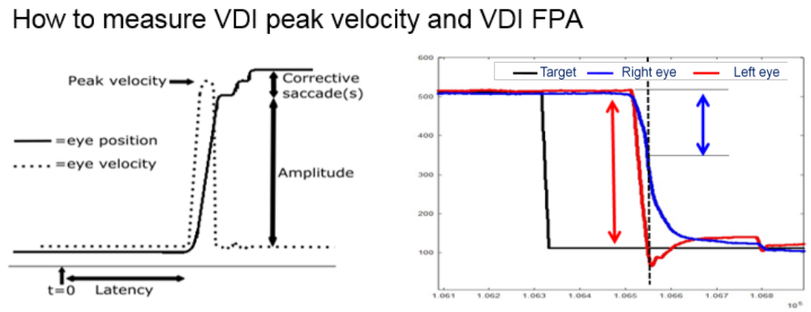
The primary outcome measure was the Versional Dysconjugacy Index (VDI), peak velocity. Secondary outcome measure was the VDI First-Pass Amplitude (FPA). Higher VDI and FPA values indicate a delay in eye adduction associated with INO. The VDI and FPA were compared with a mixed model analysis of variance; patients served as their own control-group.

CNS tests performed in this study were adaptive tracking, body sway, rapid visual information processing (RVIP), simple reaction time task, symbol digit substitution test and a pharmaco-EEG. These CNS tests showed to be able to measure cognitive function. These tests were performed predose and 3.5 and 4.6 hours after dosing.



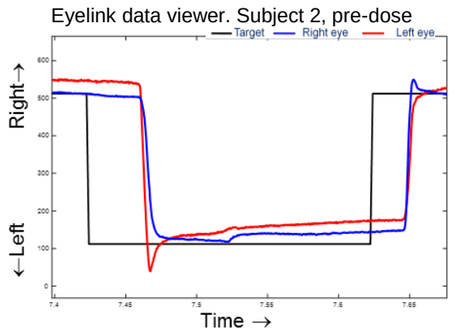


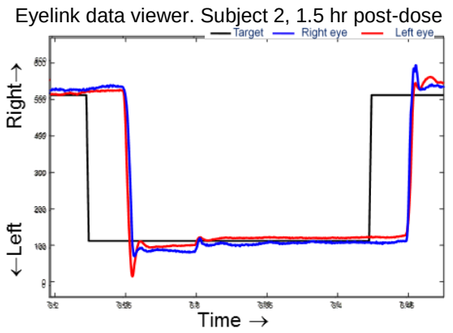




## RESULTS

All patients completed the study, one patient was excluded from the analyses (no INO diagnosis in retrospect). A significant change of -17.4% (95% CI: -22.4%, -12.1%; p<0.0001, see figure 1) in VDI and -12.5% (95% CI: -18.9%, -5.5%; p<0.01, see figure 2) in FPA were observed after fampridine administration compared with placebo, indicating a significant improvement in eye adduction. The main adverse event reported after administration of fampridine was dizziness (61%).



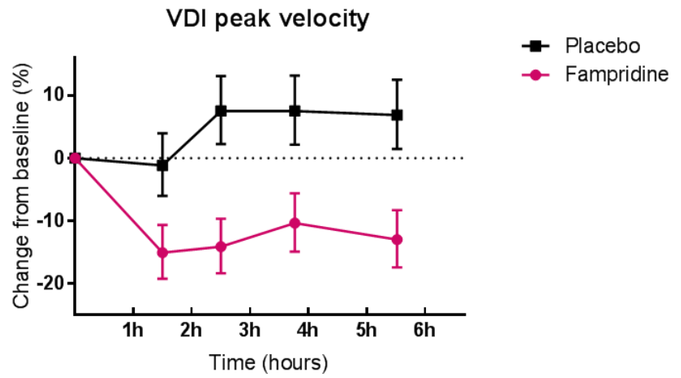




*Figure 1: VDI peak velocity of placebo and fampridine*

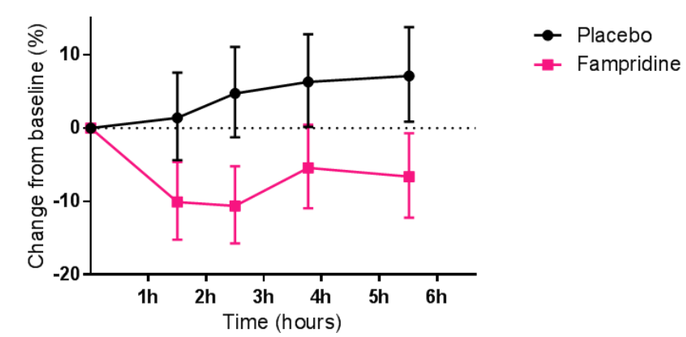



*Figure 2: VDI first pass amplitude of placebo and fampridine*

## CONCLUSIONS

Fampridine was associated with a significant decrease in VDI, corresponding with an improvement in INO severity.

Whether fampridine also improves the symptoms of patients with MS and an INO with vision disturbance will need to be determined in future clinical studies.

This model may also be used to preselect INO patients with a fampridine response for studies that investigate remyelinating drugs, as the EyeLink device was shown here to be very sensitive to even small improvements in nerve conduction.

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