# POSSIBLE EFFECTS OF CANNABINOID OROMUCOSAL SPRAY ON ANXIETY, DEPRESSION AND COGNITIVE FUNCTIONS IN MULTIPLE SCLEROSIS PATIENTS.

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## BACKGROUND

9-δ-tetrahydocannabinol and cannabidiol (THC:CBD) oromucosal spray (Sativex) is a cannabis-based drug derivative approved for the management of treatment-resistant multiple sclerosis spasticity. Recent studies have shown a possible role of the endocannabinoid system on anxiety and depression, as well as have been suggested a possible effect on cognitive functions. The aim of this study was to evaluate the possible effects of Sativex on cognitive function, anxiety and depression in a group of patients with multiple sclerosis (MS).

# **METHODS**

A total of 8 MS patients (4 female, mean age  $51.9 \pm 6.0$  years, mean EDSS  $5.31 \pm 2.7$ ), with moderate-to-severe spasticity due to MS, coming from the Santa Corona Hospital were included in the study and assessed through the beck depression inventory (BDI), the state-trait anxiety inventory (STAI Y-1, STAI Y-2) and the Rao's Brief Repeatable Battery (BRB) which evaluates cognitive domains most frequently impaired in MS. Demographic characteristics of the patients are reported in Table 1. Patients underwent cognitive and psychological evaluation before taking the medication (T0) and after 3-month self-titration with Sativex (T1). The test scores were weighted by age and education level of every single patient and the differences at T0 and T1 were compared by Wilcoxon Signed-Rank Test with statistical significance threshold at p < 0.05.

Age (yrs)	
Mean (SD)	51,9 (6,00)
Median (min-max)	50 (41-59)
Gender	
Male	4
Female	4
DISABILITY	
EDSS score	
Mean(SD)	5,3 (2,7)
Median (min-max)	5,5 (3,0-8,5

Table 1.



## RESULIS

Four BRB's tests (SRT-LTS, SRTC-LTR, PASAT2, SPARTD), BDI and STAI Y-2 showed a statistical significant change (p < 0.05) from T0 to T1, all of them remarking an improvement of the patient's conditions (Table 2).

The most significant improvements were found in STAI Y-2 (p = 0.0107), and in the tests assessing verbal memory (SRT-LTS, p = 0.0140 and SRT-CLTR, p = 0.0173).

Parameters	т0	T1	p value
SRT-LTS	20.7 ± 11.1	30.6 ± 15.4	p=0.0140
SRTC-LTR	12.2 ± 11.6	26.7 ± 15.2	p=0.0173
PASAT2	23.5 ± 14.4	28.1 ± 18.9	p=0.0218
SPARTD	3.8 ± 1.1	6.8 ± 2.3	p=0.0273
BDI	14 ± 8	7,7 ± 5	p=0.0296
STAI-Y 2	49.1 ± 3.9	42.9 ± 4.5	p=0.0107

Table 2.

## CONCLUSIONS

According to the test results, Sativex seemed to have a positive effect on some of the examined cognitive domains, anxiety and depression according to the tests results. The low number of patients enrolled requires a cautious consideration of the results which should only be used as a suggestion to further develop a similar study on a larger amount of patients

### Jenniches I, Ternes S, Albayram O, Otte DM, Bach K, Bindila L, Michel K, Lutz B, Bilkei-Gorzo A, Zimmer A. Anxiety, Stress, and Fear Response in Mice with Reduced Endocannabinoid Levels. Biol Psychiatry. 2015 Apr 14. . Whiting PF, Wolff RF, Deshpande S, Di Nisio M, Duffy S, Hernandez AV, Keurentjes JC, Lang S, Misso K, Ryder S, Schmidlkofer S, Westwood M, Kleijnen J. Cannabinoids for Medical Use: A Systematic Review and Meta-

#### analysis. JAMA. 2015 Jun 23-30;313(24):2456-73

Russo M, Rifici C, Sessa E, D'Aleo G, Bramanti P, Calabrò RS. Sativex-inducedneurobehavioral effects: causal or concausal? A practical advice! Daru. 2015 Apr 17;23:25.