Dystonia

Excerpt from www.dystonia-foundation.org:

What is Dystonia?

Dystonia is a movement disorder that causes the muscles to contract and spasm involuntarily. The neurological mechanism that makes muscles relax when they are not in use does not function properly. Opposing muscles often contract simultaneously as if they are 'competing' for control of a body part. The involuntary muscle contractions force the body into repetitive and often twisting movements as well as awkward, irregular postures. There are multiple forms of dystonia, and dozens of diseases and conditions include dystonia as a major symptom.

Dystonia may affect a single body area or be generalized throughout multiple muscle groups. Dystonia affects men, women, and children of all ages and backgrounds. Estimates suggest that no fewer than 300,000 people in North America are affected. Dystonia causes varying degrees of disability and pain, from mild to severe. There is presently no cure, but multiple treatment options exist and scientists around the world are actively pursuing research toward new therapies.

Although there are multiple forms of dystonia and the symptoms of these forms may outwardly appear quite different, the element that all forms share is the repetitive, patterned, and often twisting involuntary muscle contractions.

Dystonia is a chronic disorder, but the vast majority of dystonias do not impact cognition, intelligence, or shorten a person's life span. The main exception to this is dystonia that occurs as symptom of another disease or condition that can cause such complications.

Eur J Pharmacol. 2002 Nov 15;454(2-3):145-51.

Effects of pharmacological manipulations of cannabinoid receptors on severity of dystonia in a genetic model of paroxysmal dyskinesia.

Richter A, Löscher W.
Source

Institute of Pharmacology and Toxicology, School of Veterinary Medicine, FU Berlin, Koserstrasse 20, 14195 Berlin, Germany. angelika.richter@tiho-hannover.de

Abstract

Previous studies have shown beneficial effects of the cannabinoid CB(1)/CB(2) receptor agonist (R)-4,5-dihydro-2-methyl-4-(4-morpholinylmethyl)-1-(1-naphthalenylcarbonyl)-6H-pyrrolo [3,2,1-ij]quinolin-6-one mesylate (WIN 55,212-2) in dt(sz) mutant hamsters, a model of idiopathic paroxysmal dystonia (dyskinesia). To examine the pathophysiological significance of the cannabinergic system in the dystonic syndrome, the effect of the cannabinoid CB(1) receptor antagonist N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-3-pyrazole-carboxamide (SR 141716A) on severity of dystonia was investigated in dt(sz) mutants which exhibit episodes of dystonic and choreoathetotic disturbances in response to mild stress. SR 141716A (5 and 10 mg/kg i.p.) failed to exert any effects on the severity of dystonia. While the antidystonic efficacy of WIN 55,212-2 (5 mg/kg i.p.) was confirmed, cannabidiol (which has low affinity to cannabinoid receptors) tended to delay the progression of dystonia only at a high dose (150 mg/kg i.p.). The antidystonic and cataleptic effects of WIN 55,212-2 (5 mg/kg i.p.) were completely antagonized by pretreatment with SR 141716A at doses of 2.5 mg/kg (catalepsy) and 10 mg/kg (antidystonic efficacy). These data indicate that the antidystonic efficacy of WIN 55,212-2 is selectively mediated via CB(1) receptors. The lack of prodystonic effects of SR 141716A together with only moderate antidystonic effects of WIN 55,212-2 suggests that reduced activation of cannabinoid CB(1) receptors by endocannabinoids is not critically involved in the dystonic syndrome. In view of previous pathophysiological findings in mutant hamsters, the antidystonic efficacy of WIN 55,212-2 can be explained by modulation of different neurotransmitter systems within the basal ganglia.

PMID: 12421641 [PubMed - indexed for MEDLINE]

Open label evaluation of cannabidiol in dystonic movement disorders.

Consroe P, Sandyk R, Snider SR

International Journal of Neuroscience 1986;30(4):277-282

Major outcome(s): 20-50% improvement of dystonia; deterioration of tremor and hypokinesia in 2 patients with Parkinson's disease

Indication	Dystonia; Parkinson's disease
Medication	Cannabidiol
Route(s)	Oral
Dose(s)	100-600 mg per day
Duration (days)	42
Participants	5 patients with dystonia
Design	Open study

Abstract

Cannabidiol (CBD), a nonpsychoactive cannabinoid of Cannabis, was given to 5 patients with dystonic movement disorders in a preliminary open pilot study. Oral doses of CBD rising from 100 to 600 mg/day over a 6 week period were administered along with standard medication. Dose-related improvement in dystonia was observed in all patients and ranged from 20 to 50%. Side-effects of CBD were mild and included hypotension, dry mouth, psychomotor slowing, lightheadedness, and sedation. In 2 patients with coexisting Parkinsonian features, CBD at doses over 300 mg/day exacerbated the hypokinesia and resting tremor. CBD appears to have antidystonic and Parkinsonism-aggravating effects in humans.

Tardive Dystonia and the Use of Cannabis.

Beckmann Y, Seçil Y, Güngör B, Yiğit T.

Turk Psikiyatri Derg 2010;21(1):90-91.

Major outcome(s)	Significant improvement by cannabis and dronabinol.
Indication	Dystonia
Medication	Cannabis;Delta-9-THC
Route(s)	Inhalation;Oral
Participants	1 patient with tardive dyskinesia due to the use of neurolep
Design	Uncontrolled case report
Type of publication	Medical journal

No abstract.

A 48-year-old man diagnosed with paranoid schizophrenia presented to our department complaining of neck discomfort and involuntary movements in the orofacial region. He reported that his first complaint was difficulty in his relationship with his wife when he was 28 years old and then hearing voices was added. Since his complaints increased into the next 2 years he was taken into a psychiatric hospital and diagnosed with paranoid schizophrenia. He had used one 200-mg zuclopenthixol depot injection per month, and biperiden 6 mg and sulpride 100 mg daily for 1 year. At the end of the 8-month treatment with these drugs, he presented with involuntary movements of the orofacial region, with difficulty swallowing and chewing. At the same time, he developed involuntary sustained contraction of the neck muscles. These involuntary movements exacerbated over the next months until his speech became dysarthric and his neck became severely disabled. Five months after the initiation of his symptoms he began smoking cannabis 3 or 4 times a week for 2 years and observed that his involuntary movements significantly decreased. For this reason, he continued smoking cannabis to self-treat his symptoms until he was arrested due to smuggling. He stopped smoking cannabis and his symptoms then exacerbated and became fixed during the 7 months he was in prison. The administration of the same antipsychotic drugs was continued in prison.

On admission to our clinic the general physical examination was normal. Neurological examination showed an alert patient with dysarthric speech. His head was turned to the left and upwards due to the sustained contraction of his neck muscles. There were continuous oro-bucco-linguo-masticatory dyskinesias as well. The neurological examination was normal, except for fixed dystonic posturing in the neck muscles and orofacial dyskinesia. Family history of movement disorders and psychiatric disease was negative. Cranial and cervical magnetic resonance imaging, electroencephalogram, full blood count, serum chemistry, thyroid tests, serum ceruloplasmin level, and 24-h urinary copper excretion were all normal. Genetic testing for Huntington's disease was negative. Acanthocytes were not observed in the peripheral blood smear. The patient's Extrapyramidal Symptom Rating Scale (ESRS) score was 31 (1).

Psychiatric examination revealed blunted affect, anxious mood, coherent speech, and mildly increased talkativeness. His hygiene was poor and he had sporadic loosening of associations. Anorexia and insomnia were described. The patient reported that he had auditory hallucinations, delusions of persecution, reference, and grandeur, and thought withdrawal, and reported he was capable of thought broadcasting. The patient and his family reported that he had experienced auditory and visual hallucinations, bizarre delusions, and delusions of persecution, reference, and grandeur since he was 28 years old. He had not had any manic episodes. He was diagnosed with schizophrenia, as he was unable to perform his job or engage in social activities, and because his psychotic symptoms, such as hallucinations and delusions, were constant since he stopped smoking cannabis. Subsequently, the patient was diagnosed with antipsychotic-induced tardive

oro-bucco-linguo-masticatory dyskinesia and tardive neck dystonia. At that time, olanzapine was started (up to 20 mg d?1) over a period of 4 weeks, during which time his orofacial dyskinesia began to gradually abate. Two months after the initiation of olanzapine the patient continued to experience remarkable improvement in his orofacial dyskinesia and his psychiatric symptoms were controlled, but tardive dystonia in his neck remained unchanged. Subsequently, diazepam (10 mg d?1 PO) for 1 month did not improve the patient's tardive dystonia, nor did the addition of baclofen (up to 30 mg d?1) for 2 months decreased his dystonic symptoms. Consequently, botulinum toxin was injected into the bilateral trapezius and splenium capitis muscles, but the symptoms of tardive dystonia did not diminish. As botulinum toxin therapy failed to provide long-lasting improvement of his dystonic symptoms, sormodren (up to 8 mg d?1) was administered. At the start of the 6th month of our follow-up (with respect to olanzapine start date), the patient had a trial of treatments sequentially by about monthly intervals (sormodren, 8 mg d?1; gabapentin, 1200 mg d?1), but again there was no clinical change in his tardive dystonia, although he was free of orofacial dyskinesia while on olanzapine.

The mechanisms of tardive dyskinesia and dystonia remain poorly understood; numerous theories have been proposed, including dopamine receptor supersensitivity, catecholamine hyperactivity, and lack of g-aminobutyric acid (GABA). Presynaptic dopamine receptor blockage in the substantia nigra and ventral tegmentum by serotoninergic neurons, secondary oxidative stress, and neuron death are among the other hypotheses (Yetimalar et al., 2007).

The endocannabinoid system plays a role in the control of movement. As numerous cannabinoid CB1 and CB2, and vanilloid VR1 receptors are located in the areas that are key to movement, such as the basal ganglia and cerebellum, adds support to this hypothesis. Some studies have reported that plant-derived synthetic and endogenous cannabinoid agonists have powerful actions, mostly inhibitory effects on motor activity in humans and laboratory animals (Richter, 1994; Müller-Vahl, 1999; Fernández-Ruiz, 2005). In addition, changes in CB1 receptors in different neurodegenerative diseases were observed in postmortem studies, and symptoms were reduced in Parkinson's disease, Huntington's disease, and Tourette's syndrome after the administration of cannabinoids. Anecdotal reports have suggested that cannabis might alleviate symptoms in a variety of neurological conditions, including dystonia. High levels of cannabinoid receptor bindings are found presynaptically in the globus pallidus and substantia nigra pars reticulata. It has been proposed that cannabinoid receptor stimulation enhances GABA transmission and reduces overactivity of the globus pallidus, thereby reducing dystonic symptoms (Fox, 2002; Sagredo, 2007). An open trial that included 5 patients with dystonia due to a variety of causes reported that symptoms improved with oral synthetic cannabinoid receptor agonist use (Consroe et al., 1986).

Tardive dystonia in our patient did not improve following several drug regimens. Our patient's involuntary movements decreased significantly while he smoked cannabis for 2 years. Although we did not have the opportunity to administer and observe the effects an oral cannabinoid agonist while treating this patient, as cannabinoid agonists are not available in Turkey, we think that cannabinoid agonists might be an appropriate choice in the treatment of intractable tardive dystonia.

In summary, we report a patient that developed tardive dystonia secondary to antipsychotic use that was not successfully treated with several therapy regimens; however the patient remained free of the symptoms of tardive dystonia for the 2 years he smoked cannabis. In addition, we performed a comprehensive review of the literature regarding the use of cannabinoids to control dyskinesia.

Cannabidiol in dystonic movement disorders.

Sandyk R, Snider SR, Consroe P, Elias SM.

Psychiatry Res. 1986 Jul;18(3):291.

Cannabidiol (CBD) reduced dystonic movements

Indication	Dystonia
Medication	Cannabidiol
Route(s)	Oral
Dose(s)	200 mg
Participants	2 case reports
Design	Uncontrolled case report
Type of publication	Medical journal

Abstract

Letter to the editors:Evidence has recently accumulated to suggest that cannabidiol (CBD), a nonpsychoactive cannabinoid of marijuana, may be useful in the management of hyperkinetic movement disorders (Snider and Consroe, 1984, 1985). We have therefore tested the efficacy of CBD in two patients with dystonic movement disorders.A 65-year-old woman had idiopathic spasmodic torticollis of 2 years' duration. Her condition was characterized by a lateral pulling of her neck to the right, which occurred at a frequency of 8-12/minute. In addition, she had essential-type tremor affecting both hands, which was only partially relieved with atenolol (50mg/day). CBD (200mg, orally) produced an amelioration of the dystonic movements within 3 hours of the lateral neck movements to 2-4/minute. The patient's improvement was confirmed by an evaluation of two independent neurologists.A 31-year-old man had generalized torsion dystonia (dystonia musculorum deformans) of 20 years' duration. He had obtained mild benefit from high doses (25-45 mg/day) of trihexyphenidyl, but was confirmed to a wheelchair. CBD (200 mg, orally) produced an amelioration of his symptoms (especially of his more severely affected right leg) within two hours of administration. Following CBD administration, he was able to walk without support, an effect that lasted about 24 hours. In both cases, CBD produced no adverse effects.Cannabidiol (CBD) has been shown to have significant muscle relaxant effects and to reduce muscular spasms in humans (Petro, 1980). In rodents, CBD has been reported to reduce cholinergic transmission (Revuelta et al., 1978) and to increase turnover of gamma-aminobutyric acid (Revuelta et al., 1979). Acute administration of delta-tetradydrocannabinol to rats greatly potentiated the hypokinetic effect of reserpine (Moss et al., 1984), suggesting that this compound may have antidyskinetic properties in humans and that further studies of CBD in other hyperkinetic movement disorders in humans and warranted.

Treatment of Meige's syndrome with cannabidiol.

Snider S.R, Consroe P.

Neurology 1984;34(Suppl):147.

Major outcome(s)	50% improvement in spasm severity and frequency
Indication	Dystonia
Medication	Cannabidiol
Route(s)	Oral
Participants	A 42 year old Meige syndrome patient
Design	Uncontrolled case report
Type of publication	Medical journal

Abstract

Cannabidiol (CBD) is the major nonpsychoactive cannabinoid in marijuana. The anticonvulsant properties of CBD were demonstrated in humans 5 years ago. Based on anecdotal reports of improvement of generalized dystonia with marijuana smoking, we decided to try CBD in a patient with severe cranial dystonia (Meige syndrome). The patient, a 42-year-old man, first developed mild blepharospasm 9 years ago. The abnormal movements gradually spread to the oromandibular and neck muscles and worsened to the point that the patient was unable to drive. Many drugs were tried, with disappointing results. CBD was initiated at 100 mg/day, in divided doses, and slowly increased over several weeks to 400 mg/day. Other drugs were kept the same. Spasm frequency, counted twice daily by a relative while the patient was either talking or driving, gradually decreased from 20 to 30 per min before CBD to 7 or 15 per min at a dosage of 400 mg/day. Examinations at weekly intervals using a standard rating scale confirmed at least 50 % improvement in spasm severity and frequency. Withdrawal of CBD for 24 hours resulted in reappearance of severe spasm at 25 to 30 per min. Side effects included dry mouth, transient morning headache, and slight sedation.