Spice- Induced Catatonia

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Topics of Discussion

* Catatonia
  * What do we see?
  * Epidemiology
  * Substypes
  * Treatments
* Synthetic Cannabinoids
  * Why is it so dangerous?
    * Case Study
  * Clinical presentations
  * Epidemiology
  * Minocycline for neuroprotection

What do we see?

Waxy flexibility

Immobility

Refusal to eat or drink

Echopraxia/ echolalia

Deadpan staring

Negativism

Mutism

Impulsivity

Rigidity

Excitability

Deserves 1 to 1 observation

Table 1. Principal Features of Catatonia[1]

Feature	Description
Mutism	Verbal unresponsiveness, not always complete nor always associated with immobility.
Stupor	Altered arousal during which the patient fails to respond directly to queries (similar in presentation to the effects of dissociative anesthesia); when severe, the patient is mute and immobile and does not withdraw from painful stimuli.
Negativism (gegenhalten)	Resistance to the examiner's manipulations, whether light or vigorous, with strength equal to that applied, as if bound to the stimulus of the examiner's actions.
Posturing (catalepsy)	Maintaining postures for long periods. Includes facial postures, such as grimacing or schnauzkrampf (lips in an exaggerated pucker). Body postures, such as psychological pillow (patient lying in bed with his or her head elevated as if on a pillow), lying in a jackknifed position, sitting with upper and lower portions of the body twisted at right angles, holding arms above the head or raised in prayerlike manner, and holding fingers and hands in odd positions; prolonged mundane positions are common examples.
Waxy flexibility	The patient's initial resistance to an induced movement before gradually allowing himself or herself to be postured, similar to bending a candle.
Stereotypy	Non–goal-directed, repetitive motor behavior. The repetition of phrases and sentences in an automatic fashion, similar to a scratched record, termed *verbigeration*, is a verbal stereotypy. The neurologic term for similar speech is *palilalia*, during which the patient repeats the sentence just uttered, usually with increasing speed.
Automatic obedience	Despite instructions to the contrary, the patient permits the examiner's light pressure to move his or her limbs into a new position (posture), which may then be maintained by the patient despite instructions to the contrary.
Ambitendency	The patient appears "stuck" in an indecisive, hesitant movement, resulting from the examiner verbally contradicting his or her own strong nonverbal signal, such as offering his or her hand as if to shake hands while stating, "Don't shake my hand. I don't want you to shake it."
Echophenomena	Includes echolalia, in which the patient repeats the examiner's utterances, and echopraxia, in which the patient spontaneously copies the examiner's movements or is unable to refrain from copying the examiner's test movements, despite instruction to the contrary.
Mannerisms	Odd, purposeful movements, such as holding hands as if they were handguns, saluting passersby, or exaggerations or stilted caricatures of mundane movements; odd speech cadences and feigned accents are other examples.

Epidemiology of Catatonia

* 9%-15% of patients admitted to typical acute care service meet diagnostic criteria for catatonia 1-3
* Underlying causes of Catatonia
  * Affective Disorder: 46%
  * Schizophrenia: 20%
  * Schizoaffective Disorder: 6%
  * Medical/ neurological illnesses: 16%
  * Benzodiazepine withdrawal: 4%

1. Rosebush PI, Hildebrand AM, Furlong BG, Mazurek MF. Catatonic syndrome in a general psychiatric in-patient population: frequency, clinical presentation and response to lorazepam. J Clin Psychiatry. 1990;51:357–362.
2. Bush G, Fink M, Petrides G, Dowling F, Francis A. Catatonia 1. Rating scale and standardized examination. Acta Psychiatr Scand. 1996;93:129–136.
3. Lee JW, Schwartz DL, Hallmayer J. Catatonia in a psychiatric intensive care facility: incidence and response to benzodiazepines. Ann Clin Psychiatry. 2000;12:89–96.
4. Rosebush PI, Mazurek MF. Catatonia: clinical features, differential diagnosis and treatment. In: Jeste DV, Friedman JH, eds. Current Clinical Neurology: Psychiatry for Neurologists. Totowa, NJ: Humana Press Inc; 2006:81–92.
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Subtypes of Catatonia[1]

* Retarded Catatonia
* Excited Catatonia
* Malignant Catatonia
  * Life threatening
  * Confused with NMS
    * Indistinguishable in 20% of cases [2]
  * Misdiagnosis of delirium → Antipsychotic use → WORSENS catatonia[3]

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2. Mann SC, Caroff SN, Bleier HR, Welz WK, Kling MA, Hayashida M: Lethal catatonia. Am J Psychiatry 1986; 143:1374–1381
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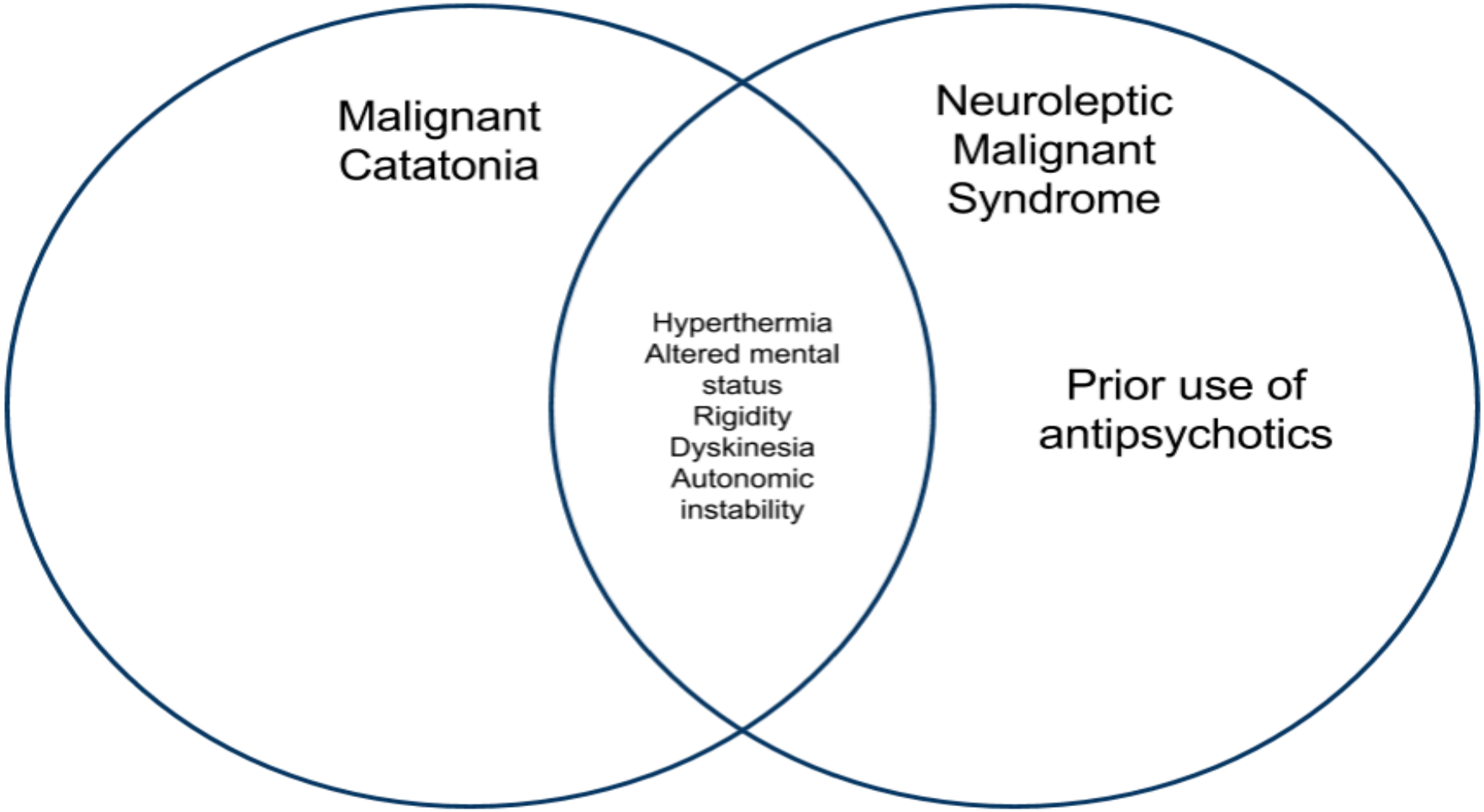
NMS vs. Malignant Catatonia



Diagnosis

* Lorazepam Challenge Test
  * 1 or 2mg of Lorazepam IV → 5 minutes, may repeat 1 more time
  * IM route → 15 min
  * PO route → 30 min

Treatments of Catatonia

* $GABA_A$ Agonists
  * Benzodiazepines
    * Remission rates reported to be as high as **70–80%** 1-7
    * **8 to 24 mg per day** are common and are tolerated without ensuing sedation, especially when instituted using daily incremental dosages 8
  * Zolpidem
    * **7.5 to 40 mg per day** without noticeable adverse effects 9,10
* NMDA Antagonist [11]
  * Amantadine
    * **100–500 mg TID**
  * Memantine
    * **5–20 mg/day**

1. Rosebush PI, Mazurek MF. Catatonia and its treatment. Schizophr Bull (2010) 36 (2):239–42.
2. Lee JW, Schwartz DL, Hallmayer J. Catatonia in a psychiatric intensive care facility: incidence and response to benzodiazepines. Ann Clin Psychiatry (2000) 12 (2):89–96.
3. Rosebush PI, Hildebrand AM, Furlong BG, Mazurek MF. Catatonic syndrome in a general psychiatric inpatient population: frequency, clinical presentation, and response to lorazepam. J Clin Psychiatry (1990) 51 (9):357–62. 83.
4. Rosebush PI, Hildebrand AM, Mazurek MF. The treatment of catatonia: benzodiazepines of ECT? Am J Psychiatry (1992) 149 (9):1279–80. 84.
5. Hawkins JM, Archer KJ, Strakowski SM, Keck PE. Somatic treatment of catatonia. Int J Psychiatry Med (1995) 25 (4):345–69. .
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Treatments of Catatonia

* ECT[1]

Table 1 | ECT in catatonia: retrospective chart reviews.

Author(s), year	ECT EP/Schedule	Mood (%)/psychotic disorder (%)	N responders/*N* total	Responders (%)
Morrison (134)	NA/NA	0/100	40/75	53
Pataki (28)	BT/NA	56/44	6/9	67
McCall (135)	BT/NA	75/12	7/8	88
Rohland (33)	BT/3*W	59/23	26/28	93
van Waarde (47)	BT (93%)/daily [first week (56%)]	48/44	16/27	59
England (63)	BT/NA	NA	10/12	83
Raveendranathan (136)	BT/3*W	41/30	56/63	89

EP, electrode position; BT, bitemporal; N, number; NA, not available.

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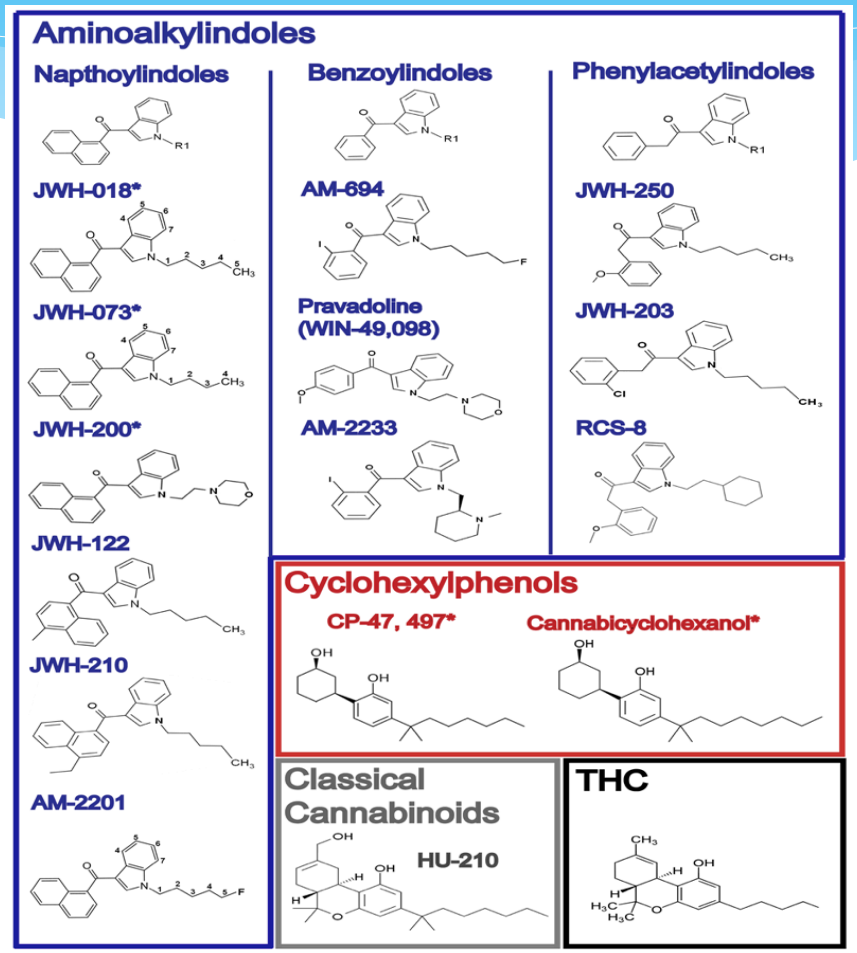
Synthetic Cannabinoid

* "K2," "spice," "crazy monkey," "chill out," "spice diamond," "spice gold," and "chill X"
* Potencies ranging from **2 to 800 times greater than delta-9 tetrahydrocannabinol**[1]
* **JWH** synthesized by **Dr. John W. Huffman** in 1994[2]
* **Class I** controlled substance in the U.S[2]



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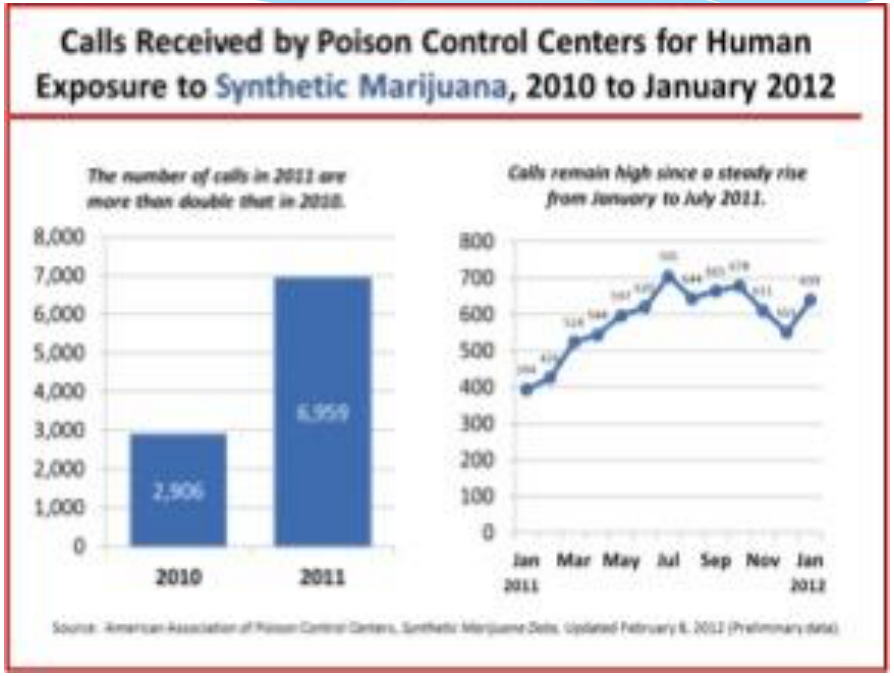
2. Huffman, J.W., Dai, D., Martin, B.R., Compton, D.R., 1994. Design, synthesis, and pharmacology of cannabimimetic indoles. Biomed. Chem. 4, 563–566.
3. Drug Enforcement Administration, Department of Justice. Schedules of controlled substances: temporary placement of four synthetic cannabinoids into Schedule I. Final order. Fed Regist 2014; 79:7577.

Synthetic Cannabinoid

* **Epidemiology**
  * First reported in U.S in 2008[1]
  * As many as **11 percent of high school seniors** in the United States reported using synthetic cannabinoids in 2012.[2]



1. Understanding the Spice Phenomenon. European Monitoring Centre for Drugs and Drug Addiction. http://www.emcdda.europa.eu/attachements.cfm/att_80086_EN_Spice%20Thematic%20paper%20—%20final%20version.pdf (Accessed on July 01, 2014).
2. Monitoring the Future Survey, National Institute on Drug Abuse. http://www.monitoringthefuture.org/data/data.html (Accessed on July 01, 2014).

Affinity of Cannabinoids present in Spice for CB1 and CB2 receptors

Compound	Type	CB1 Ki (nM)	CB2 Ki (nM)
Delta-9-THC	Classic Cannabinoid	41	36 ± 10
HU-210	Classic Cannabinoid	0.061	0.17
AM-694	Benzoylindone	0.08	1.4
RCS-4 *	Benzoylindone	unknown	unknown
WIN-48,098	Benzoylindone	3155	unknown
CP-47,497	Cyclohexylphenol	2.2 ± 0.5	none detected
JWH-018	Naphtoylindole	9 ± 5	2.9 ± 2.7
JWH-019	Naphtoylindole	9.8 ± 2	5.55 ± 2
JWH-073	Naphtoylindole	8.9 ± 1.8	38 ± 24
JWH-081	Naphtoylindole	1.2	12.4 ± 2.3
JWH-122	Naphtoylindole	0.7 ± 0.5	1.2 ± 1.2
JWH-210	Naphtoylindole	0.5	0.7
AM-2201	Naphtoylindole	1	2.6
JWH-203	Phenylacetylindole	8 ± 1	7 ± 1.3
JWH-250	Phenylacetylindole	11 ± 2	33 ± 2
RCS-8 **	Phenylacetylindole	unknown	unknown

(Aung et al. 2000; D'Ambra et al

an et al. 2005b; Melvin et al.

1993)

* JWH-018 analog;

** JWH-250 analog

Case Study

GF, a 22 yr. old Hispanic male with history of schizoaffective disorder, bipolar type, generally well controlled with therapeutic levels of lithium and Clozaril presented to our Emergency Department in August of 2014 with severe acute psychosis. Patient admitted to smoking synthetic cannabinoid prior to admission. He was unpredictable, violent, and sexually inappropriate. He assaulted peers and staff. On multiple occasions he exposed himself to female staff. He required complete assistance with basic needs such as showering and feeding

Table 1. Intervention Timeline for patient GF				
	Abnormal findings	Locations	Interventions	Clinical presentation
Admission		Admit to mental health hospital	Lithium 450mg PO BID, Clozapine 200mg PO daily	Patient is frequently physically aggressive towards staff members and peers. He requires frequent isolation, intramuscular injections, restraints, and one to one observations. He consistently exhibits bizarre behaviors such as punching the wall, laughing inappropriately, grunting, making threats to hurt others, and undressing self on the unit. Patient is unable to perform any activities of daily living and requires maximal assistance in areas such as showering, eating, and clothing. As a result, he experiences significant weight loss. He also demonstrates neurological symptoms such as urinary and bowel incontinence.
Week 6	CPK = 342, unstable vital signs	Admit to mental health after NMS is ruled out in ED	Haloperidol 10mg PO TID, Valproic acid 500mg PO BID	
Week 10	CPK = 800-900, unstable vital signs	Admit to mental health after NMS is ruled out in ED	Lithium 450mg PO BID, Clozapine titration from 12.5mg, Gabapentin 100mg PO TID, Clonazepam 1mg PO TID	
Week 13	CPK = 2104, Altered mental status	Admit to ICCU	Clozapine 150mg PO BID, Valproic acid 750mg IV BID, Dexmedetomidine 0.2mcg/kg/hour	
Week 15	Enlarging subarachnoid cyst	Transfer to Neuropsychiatric Center	Clozapine 150mg PO BID	
Week 18	Grand mal seizure	Admit to mental health	Clozapine titrate from 25mg PO daily, Lithium 300mg PO BID, Phenobarbital 64mg PO BID	

Week 20		Transfer to Neurosurgical Center	Removal of Subarachnoid cyst	Patient responds to assessments with "no." Patient is visible on the unit, and socializes with others. Patient makes his needs known. Patient is cooperative and compliant with medications and assessments. Patient continues making bizarre, nonsensical statements.
Week 22			Olanzapine 10mg PO BID, Phenobarbital 64mg PO BID, Lithium 450mg PO BID	
Week 25			Clozapine 150mg PO BID, Valium 7.5mg PO TID, Lithium 1050mg PO BID, Trazodone 150mg PO at bedtime, Carbamazepine 300mg PO TID, Minocycline 100mg PO BID, Memantine 10mg PO BID, Phenobarbital 129.6mg PO BID	

Clinical Manifestations: Psychiatric

Vearrier and Oster-houdt, 2010[22]	1	JWH-018 "Pure" product purchased online	One "bong hit"	Case report	17 F	Agitation; visual hallucinations; anxiety; tachycardia (pulse 120), mild blood pressure increase (135/85); occasional muscle fasciculations; hypokalemia (2.9 mEq/L). Given lorazepam and effects
Zimmerman et al., 2009[18]	1	Spice Gold (JWH-018, CP 47,497)	3 g/day (chronic use)	Case report	20 M with untreated ADHD	DSM-IV/ICD-10 dependence with tolerance and withdrawal that started on Day 2 of abstinence with: cognitive impairment; craving; diaphoresis; nausea; diarrhea; tremor; headache; internal unrest; insomnia; nightmares; depressed mood; palpitations; mild sustained hypertension and tachycardia (blood pressure 140/85–90 and pulse 95–100).

Neuroprotective Treatment

* Minocycline
  * Crosses blood brain barrier
  * Provides neuroprotection to excitotoxic insults

Table 2. Summary of Human Trials of Minocycline Treatment for Neurological Diseases

Disease	Dosage, mg/d	Route	Duration	Effect	Source
Acute stroke	200	Oral	5 d	Lower NIHSS, lower mRS, increased BI	Lampl et al[29]
Spinal cord injury	400 or 800	Intravenous	7 d	Improved ASIA, FIM, SCIM	Casha et al[30]
Multiple sclerosis	200, with glatiramer acetate	Oral	9 mo	Reduced gadolinium-enhancing lesions	Metz et al[31]
Parkinson disease	200	Oral	18 mo	Passed the safety and efficacy trial	NINDS-NET-PD Investigators[32]
Huntington disease	200	Oral	24 mo	Ameliorated psychiatric symptoms	Bonelli et al[33]
Huntington disease	200	Oral	6 mo	No significant differences in UHDRS, AIMS, and MMSE	Thomas et al[34]
ALS	200	Oral	9 mo	Declined ALSFRS-R	Gordon et al[35]

1. Plane, Jennifer M., et al. "Prospects for minocycline neuroprotection." *Archives of neurology* 67.12 (2010): 1442-1448.

Recommendations

* GC-MS
  * Urgency for diagnosis
* ECT
  * Resistant catatonia

Questions

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