Update on Catatonia

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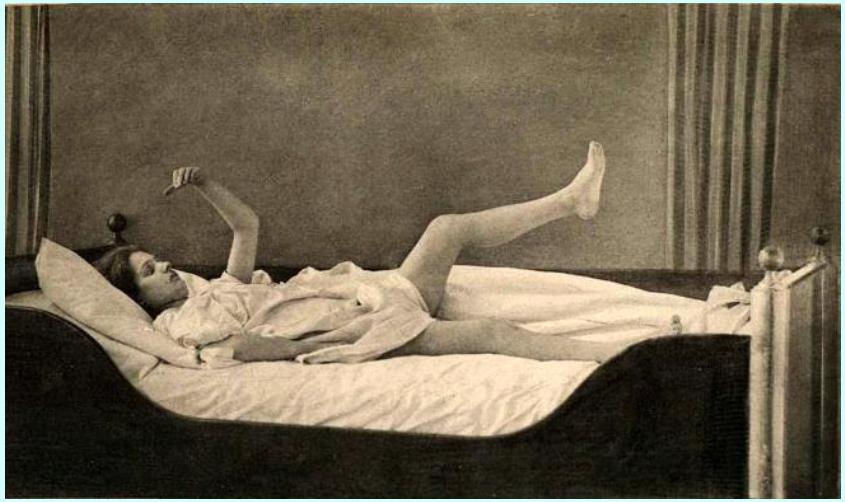
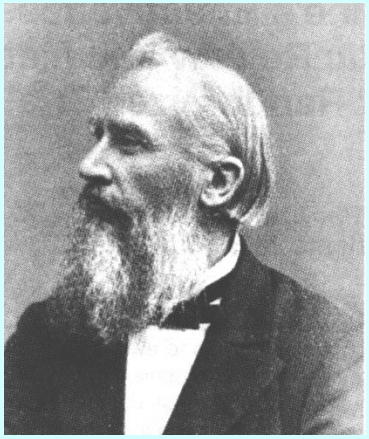
- No disclosures
- No industry or federal support
- Full-time, salaried Penn State employee
- Off-Label use of Rxs for catatonia



www.catatonia.org



“... the patient remains entirely motionless, without speaking and with a rigid, masklike facies, the eyes focused at a distance; he seems devoid of any will to move or react to any stimuli; there may be a fully developed "waxen" flexibility, as in cataleptic states, or only indications of this striking phenomenon.

...the general impression conveyed by such patients is one of profound mental anguish or immobility induced by severe mental shock ...

Once the clinical signs are manifest, they tend to persist, although in some patients they appear for relatively short periods and then tend to recur.

The obvious association of this illness with other signs of disease, and its constant occurrence with certain somatic (particularly muscular) disorders, have been more or less ignored.”

Karl L. Kahlbaum, 1874

'Die Katatonie, oder das Spannungsirresein'

ACTA PSYCHIATRICA
SCANDINAVICA
ISSN 0001-690X

Catatonia. I. Rating scale and standardized examination

Acta Psychiatr Scand 1996: 93: 137–143

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Catatonia. II. Treatment with lorazepam and electroconvulsive therapy

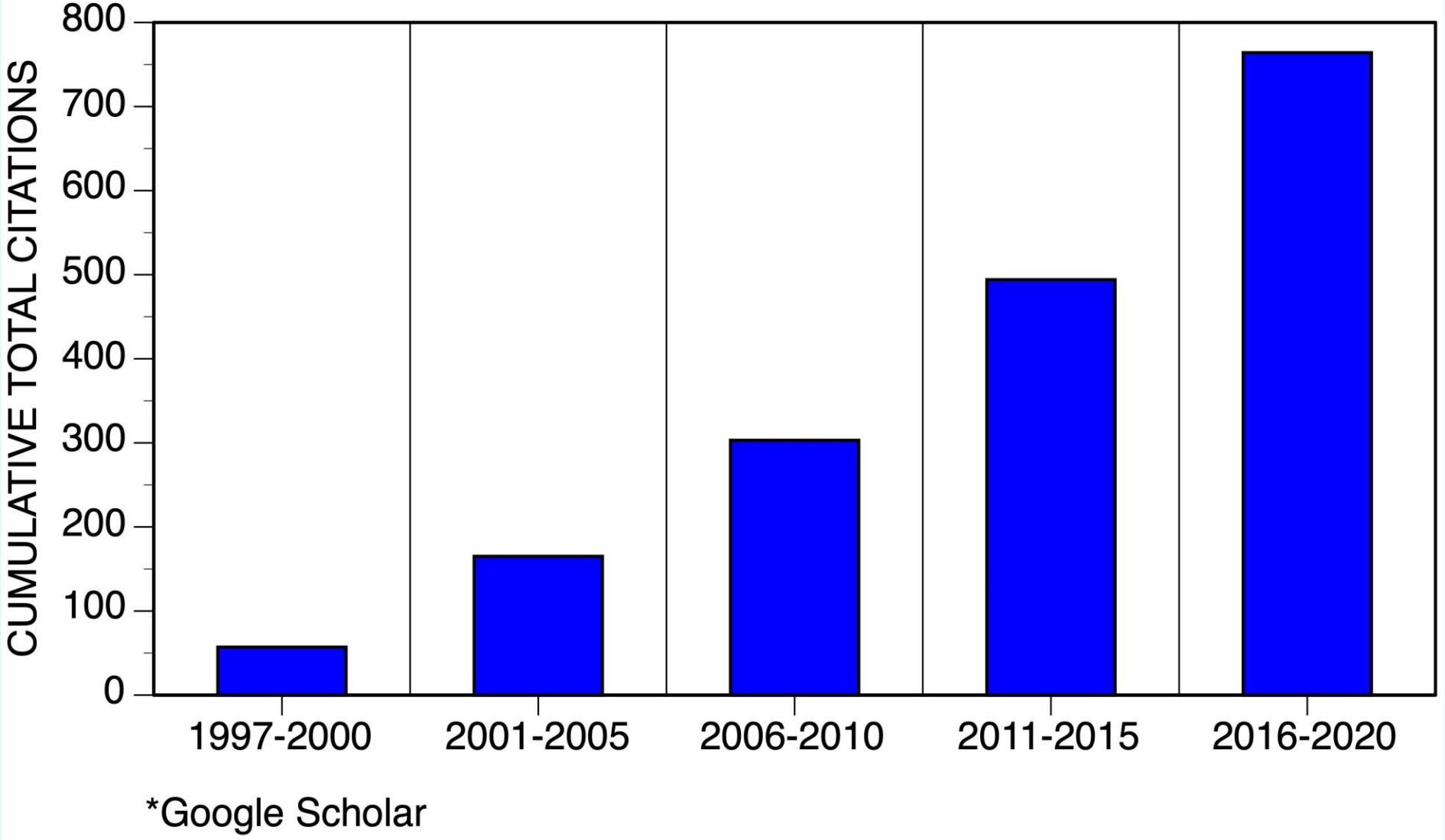
Bush G, Fink M, Petrides G, Dowling F, Francis A. Catatonia. II. Treatment with lorazepam and electroconvulsive therapy.
Acta Psychiatr Scand 1996: 93: 137–143. © Munksgaard 1996.

G. Bush, M. Fink, G. Petrides, F. Dowling, A. Francis

Department of Psychiatry and Behavioral Sciences

BUSH-FRANCIS CATATONIA RATING SCALE

CUMULATIVE TOTAL CITATIONS 1996-2020*



*Google Scholar

Bush-Francis Catatonia Rating Scale (23 Items)

Screening Items (14)	Full Scale Items (9)
Excitement*	Impulsivity
Immobility/Stupor*	Automatic Obedience
Mutism*	Mitgehen
Staring	Gegenhalten
Posturing*/Catalepsy*	Ambitendency
Grimacing*	Grasp Reflex
Echopraxia*/Echolalia*	Perseveration
Stereotypy*	Combativeness
Mannerisms*	Autonomic Abnormality
Verbigeration	
Rigidity	*OBSERVED*
Negativism*	*ELICITED*
Waxy Flexibility*	*EXAMINED*
Withdrawal	

*DSM-5 Catatonic Signs [3/12]

DSM-5 Catatonia Specifier

DSM-5 293.89 --- ICD-10 F06.1

A. The clinical picture is dominated by three (or more) of the following symptoms:

1. Stupor (i.e., no psychomotor activity; not actively relating to environment).
2. Catalepsy (i.e., passive induction of a posture held against gravity).
3. Waxy flexibility (i.e., slight, even resistance to positioning by examiner).
4. Mutism (i.e., no, or very little, verbal response [exclude if known aphasia]).
5. Negativism (i.e., opposition or no response to instructions or external stimuli).
6. Posturing (i.e., spontaneous and active maintenance of a posture against gravity).
7. Mannerism (i.e., odd, circumstantial caricature of normal actions).
8. Stereotypy (i.e., repetitive, abnormally frequent, non-goal-directed movements).
9. Agitation, not influenced by external stimuli.
10. Grimacing.
11. Echolalia (i.e., mimicking another's speech).
12. Echopraxia (i.e., mimicking another's movements).

Procedure:	Examines:
1) Observe patient while trying to engage in conversation.	Activity level Abnormal movements Abnormal speech
2) Examiner scratches head in exaggerated manner	Echopraxia
3) Examine arm for cogwheeling. Attempt to reposture, instructing patient to "keep your arm loose" - moving arm with alternating light/heavy force	Rigidity Negativism Waxy Flexibility Gegenhalten
4) Ask pt to extend right arm; Place one finger beneath hand and try to raise slowly after stating, “Do NOT let me raise your arm"	Mitgehen
5) Extend hand, firmly stating, "Do NOT shake my hand”	Ambitendence
6) Reach into pocket and state, "Stick out your tongue, I want to stick a pin in it.	Automatic Obedience
7.) Check for grasp reflex	Grasp Reflex
8. Check chart for past 24 hr re: PO intake, VS, etc	Autonomic signs
9) Attempt to observe patient indirectly, at least for a brief period each day	

Video Examples of Catatonia

Verlag von Julius Springer Berlin N. Heliogr. Meisenbach Riffarth & Co. Berlin.

TAFEL 32

Narrated Video Examples of Catatonia

Located at:

www.catatonia.org

INCIDENCE OF CATATONIA

Psychiatric Samples

TABLE 1. Prospective Studies of the Incidence of Catatonia

Authors	Year	Patients Screened	Percent With Catatonia Syndrome	Percent With Mutism	Percent With Negativism or Withdrawal
Rosebush et al[1]	1990	140	9	85	78
Ungvari et al[2]	1994	212	8	94	67
Bush et al[3,4]	1996	215	7	86	75
Peralta et al[5]	1997	567	3.5	55	60
Northoff et al[6]	1999	1259	2.7	—	—
Bräunig et al[7]	2000	297	12	54	58
Lee et al[8]	2000	160	15	54	71
Peralta and Cuesta[9]	2001	187	17	84	69
Chalasani et al[10]	2005	208	12	63	50
Peralta et al[11]	2010	200	12	38	54
Mean (SEM)			*9.8 (1.4)*	*68 (6)*	*62 (3)*

Francis et al. 2010

Lorazepam Treatment of Catatonia

Protocol

IV Challenge 1 mg q5 min w/ratings

Daily lorazepam at 4-8 mg/d up to 5d total

PO, IM, IV Routes

Daily BFCRS ratings

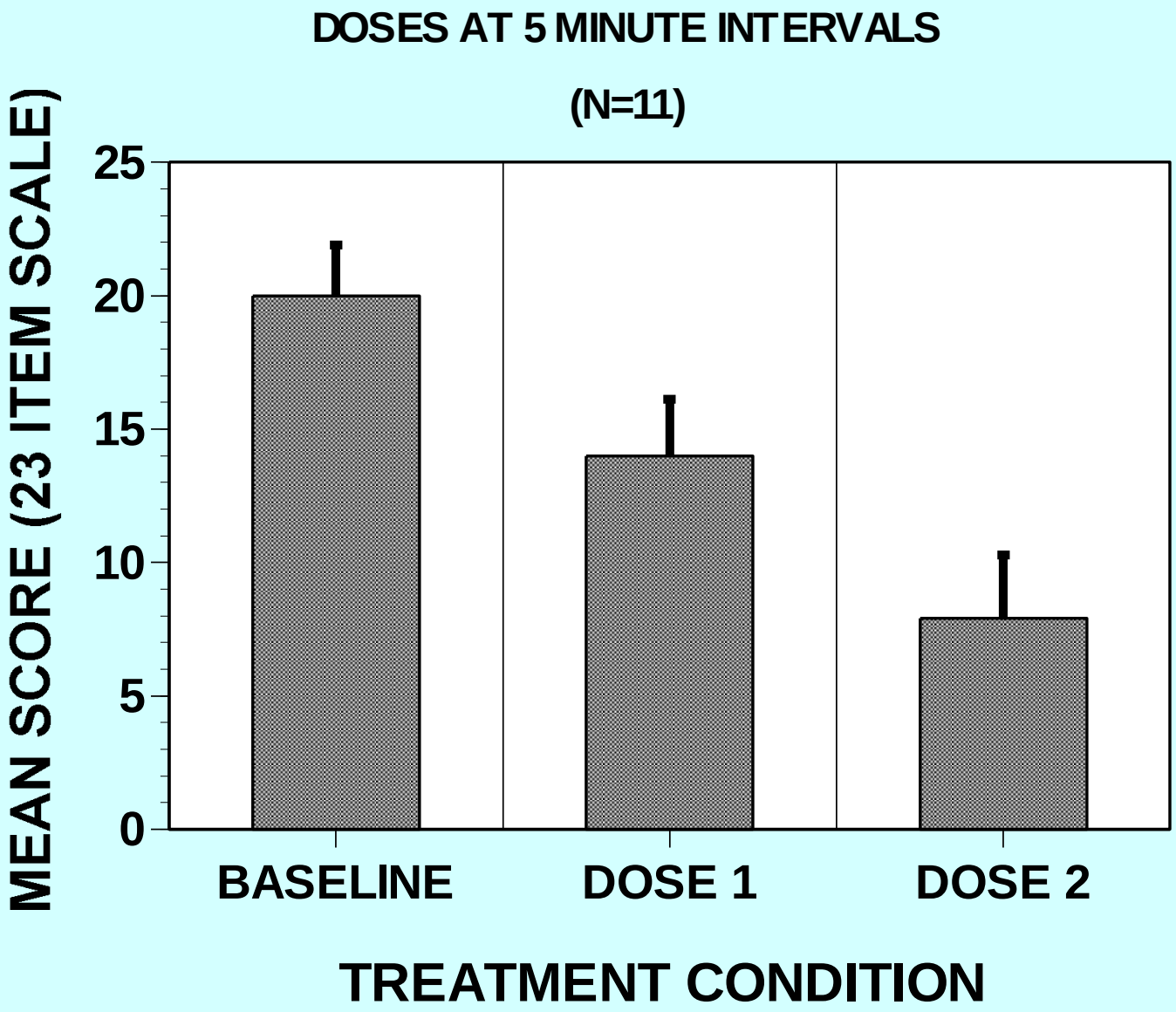
Success

<2 signs

Failure

>2 signs; agitation not controlled; worsening clinical status

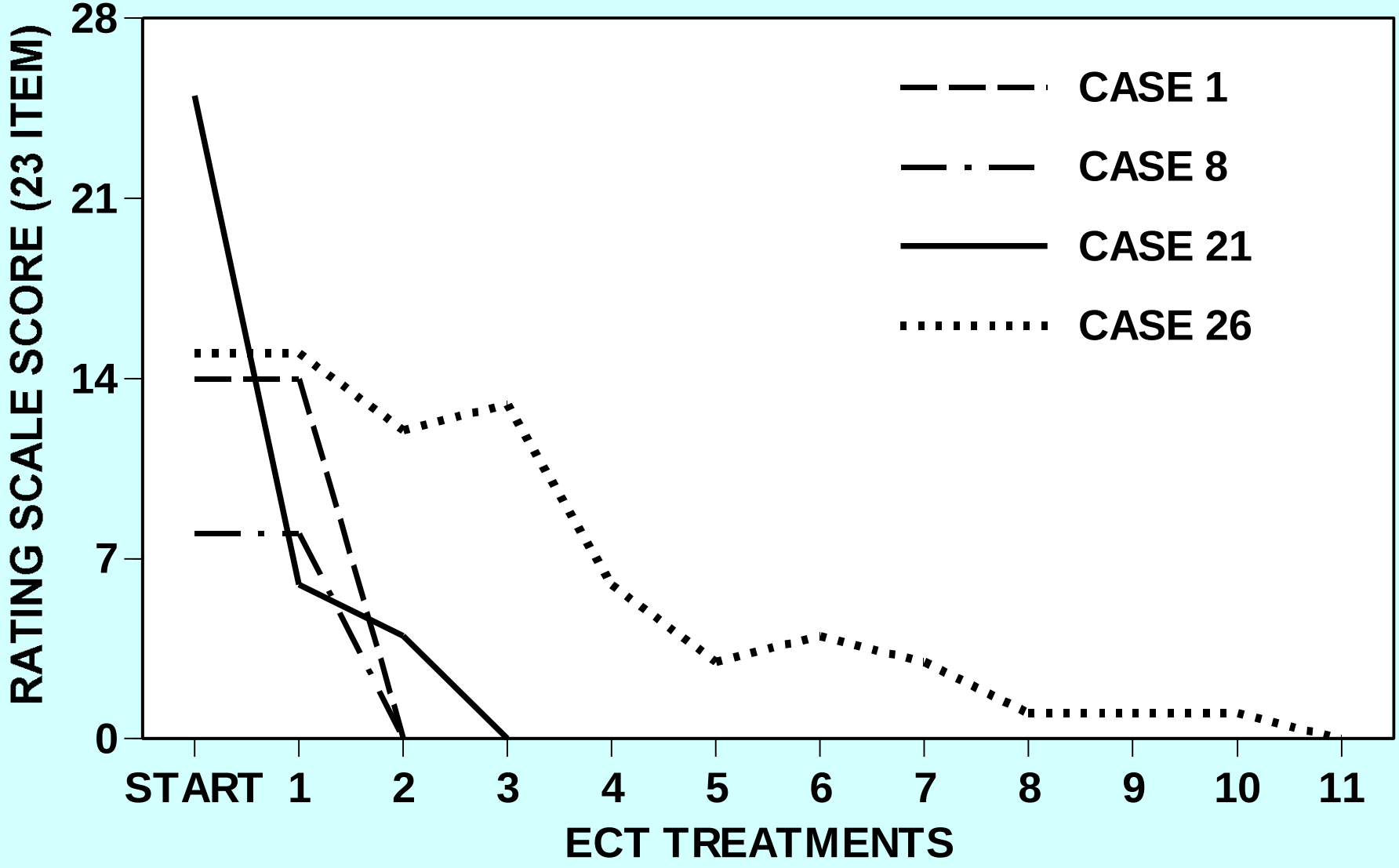
FIGURE 4. TREATMENT OF CATATONIA WITH INTRAVENOUS LORAZEPAM



Clinical Characteristics: Responders vs. Non-Responders

Characteristic	Lorazepam Responders N = 16	Lorazepam Failures N = 5	P
Age	33.1 ± 12.2	25.6 ± 5.8	N.S.
Catatonia Score (BFCRS)	17.7 ± 6.8	17.4 ± 3.5	N.S.
Gender (F/Total)	11/16	3/5	N.S.
Organic Mental Disorders[a]	3/16	0/5	N.S.
Mania (296.4x)	4/16	3/5	N.S.
Duration of catatonia (days) prior to entering treatment	3.8 ± 3.5	11.0 ± 12.1	<0.05[b]
Percent drop in BFCRS score (day 0 to day 1 of treatment)	88.3% $\pm$ 22.5	24.8% $\pm$ 27.6	<0.001[c]
Average daily dose of lorazepam (mg/d/patient)	3.0 $\pm$ 1.6	5.5 $\pm$ 2.0	<0.01[d]

FIGURE 6. TIME COURSE OF ECT RESPONSE



Treatments for Catatonia

- “No” placebo response
- Barbiturates: amobarbital
- Convulsive therapy: camphor, electroconvulsive
- Neuroleptics: risk of exacerbation NMS (?10 %)
- Miscellaneous agents: (anticonvulsants anticholinergics lithium)
- Benzodiazepines: lorazepam etc.
- Other GABA-a agonists: zolpidem
- NMDA? Amantadine, memantine
- Atypical antipsychotics: ???

Complications of Catatonia

- Aspiration pneumonia
- Renal Failure
- Cardiac arrest
- Seizures
- Sepsis
- Pulmonary embolism
- Pulmonary edema
- Rhabdomyolysis
- Respiratory failure

[Addonizio et al 1987; Dickey 1991; and Ebadi et al 1980]

Clinical questions in catatonia

Validity as a syndrome
Prevalence and phenomenology
Treatment response
Subtypes: excited-retarded, acute-chronic, primary-secondary, benign-malignant
Discrimination from other motor syndromes
NMS as Toxic Malignant Catatonia
Delirium with Catatonic Features

Delirium With Catatonic Features

A New Subtype?

by Andrew Francis, MD, PhD
and Antonio Lopez-Canino, MD

Delirium has been recognized and described since antiquity. It is a brain disturbance manifested by a syndrome of diverse neuropsychiatric symptoms. Various terms have been used for delirium, such as acute brain disorder, metabolic encephalopathy, organic brain syndrome, and ICU psychosis. The *DSM-IV* model views delirium as an acute reversible neuropsychiatric syndrome caused by

active, hyperactive, and mixed subtypes based on the salient activity pattern.[3] Numerous studies over the past 20 years have attempted to define these motor subtypes of delirium. These studies show various rates of the hypoactive, mixed, and hyperactive forms using differing criteria and definitions. Some studies have found that these subtypes predict etiology, clinical course, morbidity, presence of psychosis, and other factors.

Other studies of delirium have

nin) in patients with hypoactive delirium.[5] Levels of 6-SMT were markedly elevated in patients with hypoactive delirium, and were reduced during recovery. Patients with the hyperactive subtype of delirium showed an opposite pattern, with initially low levels that increased with recovery.

In addition to etiology and clinical features, the motor subtype of delirium may affect treatment response. This view is supported by an open prospective study of delirium treat-

*Francis A., Lopez-Canino A. *Delirium with Catatonic Features: A New Subtype?* Psychiatric Times 26: 32-36, 2009.

Table

Possible correspondence between hypoactive delirium and catatonia

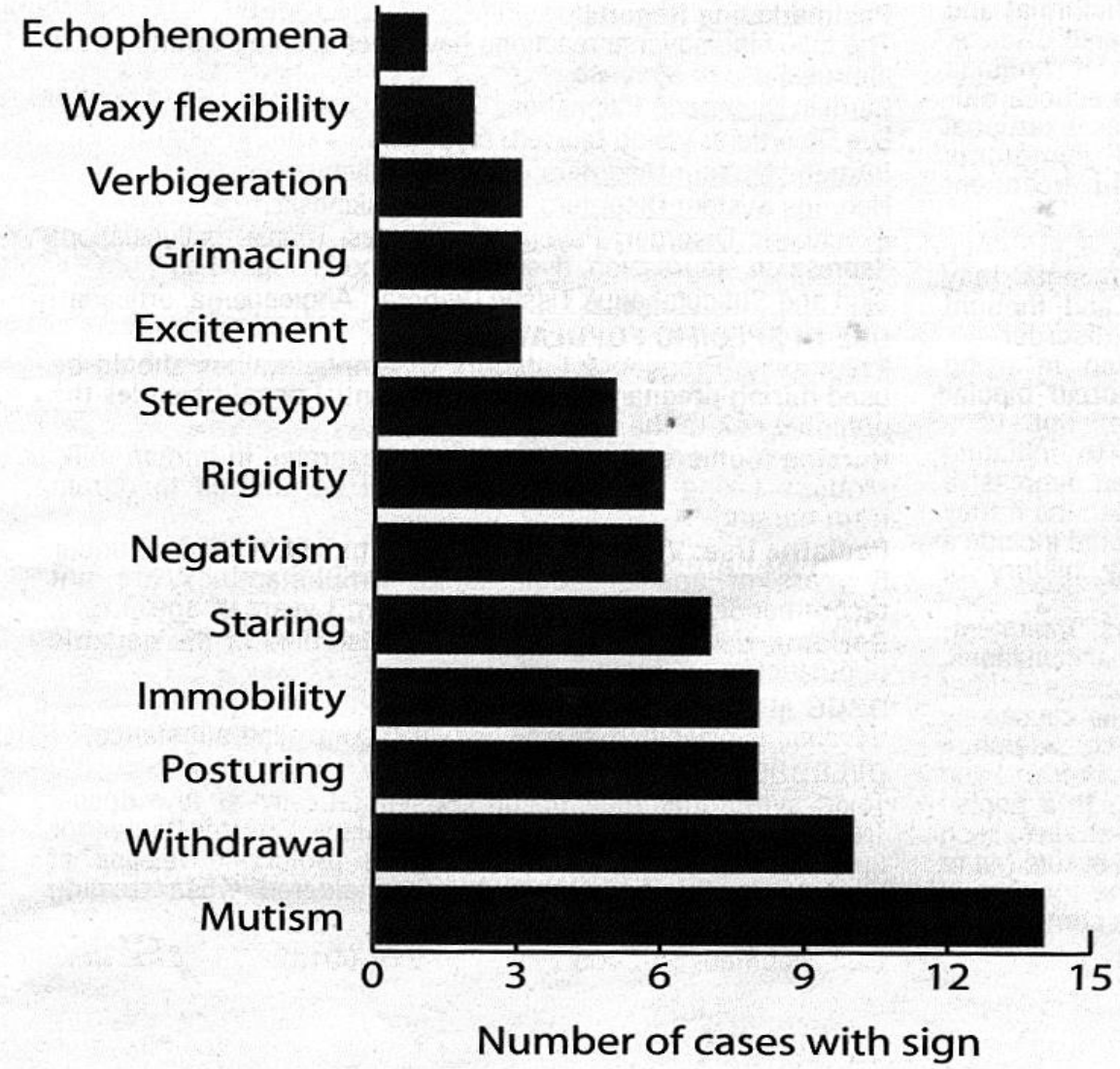
Source	"Hypoactive" item or description	Possible catatonic sign from BFCRS
Confusion assessment method[20]	Decreased level of motor activity, such as sluggishness, staring into space, staying in one position, moving very slowly	Immobility/stupor, staring, posturing
Empirical study of delirium subtypes[21]	Unawareness, decreased alertness, sparse or slow speech, lethargy, slowed movements, staring, apathy	Immobility/stupor, mutism, staring, withdrawal
Memorial Delirium Assessment Scale[22]	Reduced or slowed movements, rarely moves or speaks, is catatonic	Immobility/stupor, mutism, withdrawal
Delirium Rating Scale-Revised-98[18]	Reduced frequency, spontaneity, or speed of motor movements (mild, moderate, severe)	Immobility/stupor, mutism, posturing, withdrawal
Factor analysis[3]	Decreased amount of activity, decreased speed of actions, reduced awareness of surroundings, decreased amount of speech, decreased speed of speech, listlessness, and reduced alertness and/or withdrawal	Immobility/stupor, withdrawal, mutism

BFCRS, Bush-Francis Catatonia Rating Scale.

*Francis A., Lopez-Canino A. *Delirium with Catatonic Features: A New Subtype?* Psychiatric Times 26: 32-36, 2009.

Figure 2

Frequency of catatonic signs in 16 patients with concurrent delirium and catatonia



DSM-5	DSM-IV
A. Disturbance in *attention* (i.e., reduced ability to direct, focus, sustain, and shift attention) and awareness (reduced *orientation to the environment*).	A. Disturbance of consciousness (i.e. reduced clarity of awareness of the environment) with reduced ability to focus, sustain or shift attention.
B. The disturbance develops over a short period of time (usually hours to a few days), *represents an acute change from baseline attention and awareness*, and tends to fluctuate in severity during the course of a day.	B. A change in cognition or the development of a perceptual disturbance that is not better accounted for by a pre-existing, established or evolving dementia.
C. An additional disturbance in cognition (e.g.memory deficit, disorientation, language, visuospatial ability, or perception).	C. The disturbance develops over a short period of time (usually hours to days) and tends to fluctuate during the course of the day
D. The disturbances in Criteria A and C are not better explained by a pre-existing, established or evolving neurocognitive disorder and *do not occur in the context of a severely reduced level of arousal such as coma.*	D. There is evidence from the history, physical examination or laboratory findings that the disturbance is caused by the direct physiological consequences of a general medical condition.
E. There is evidence from the history, physical examination or laboratory findings that the disturbance is *a direct* physiological consequence of another medical condition, *substance intoxication or withdrawal (i.e. due to a drug of abuse or to a medication), or exposure to a toxin, or is due to multiple etiologies.*	

Prospective Study: Catatonia in Delirium

(Grover et al., Psychiatr Clin Neurosci, 2014)

- Teaching hospital, India
- N=205 consecutive C/L referrals
- Delirium: DRS-98R
- Catatonia: Bush-Francis [2/14], DSM5 [3/12]
- Catatonia: 32% B-F, 13% DSM5
- +Correlation: DRS-98R and BFCRS
- +Correlation: Hypoactive Delirium

Crit Care Med. 2017 Nov; 45(11): 1837–1844.

PMID: 28841632

doi: 10.1097/CCM.0000000000002642

Delirium and Catatonia in Critically Ill Patients: the DeCat prospective cohort investigation

Jo E. Wilson, MD MPH,[1,7] Richard Carlson, MD,[1] Maria C. Duggan, MD MPH,[2,7] Pratik Pandharipande, MD MSCI,[5] Timothy D. Girard, MD MSCI,[6] Li Wang, MS,[4] Jennifer L. Thompson, MPH,[4] Rameela Chandrasekhar, PhD,[4] Andrew Francis, MD PhD,[8] Stephen E. Nicolson, MD,[9] Robert S. Dittus, MD MPH,[3,7] Stephan Heckers, MD MSc,[1] E. Wesley Ely, MD MPH,[3,7] and for the Delirium and Catatonia (DeCat) Prospective Cohort Investigation

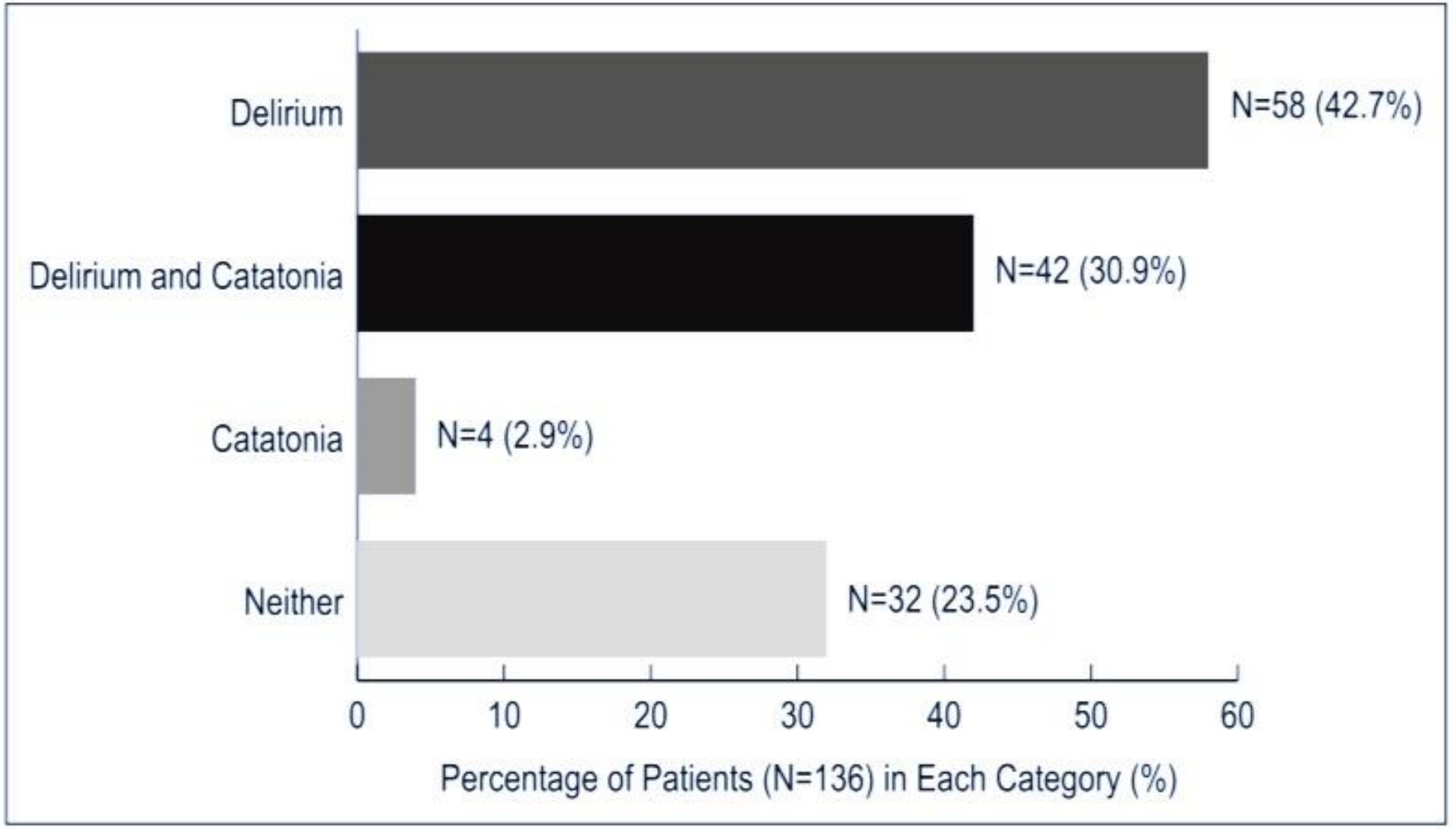


Figure 1. Distribution of delirium and/or catatonia. Bar graph showing distribution of delirium and/or catatonia over the entire ICU stay by individual patients ($n = 136$ patients). This figure demonstrates that 31% of patients met criteria for both delirium and catatonia during their ICU or hospital stay, which goes against current *Diagnostic Statistical Manual* (*DSM*) *5* catatonia nosology precluding diagnosis of catatonia due to another medical condition when delirium is present. †Delirium was diagnosed using Confusion Assessment Method for the ICU. *Catatonia was diagnosed using greater than or equal to three *DSM 5* criterion A items.

Retrospective Study: Catatonia in Med-Surg
N=54, DSM-5 Catatonia

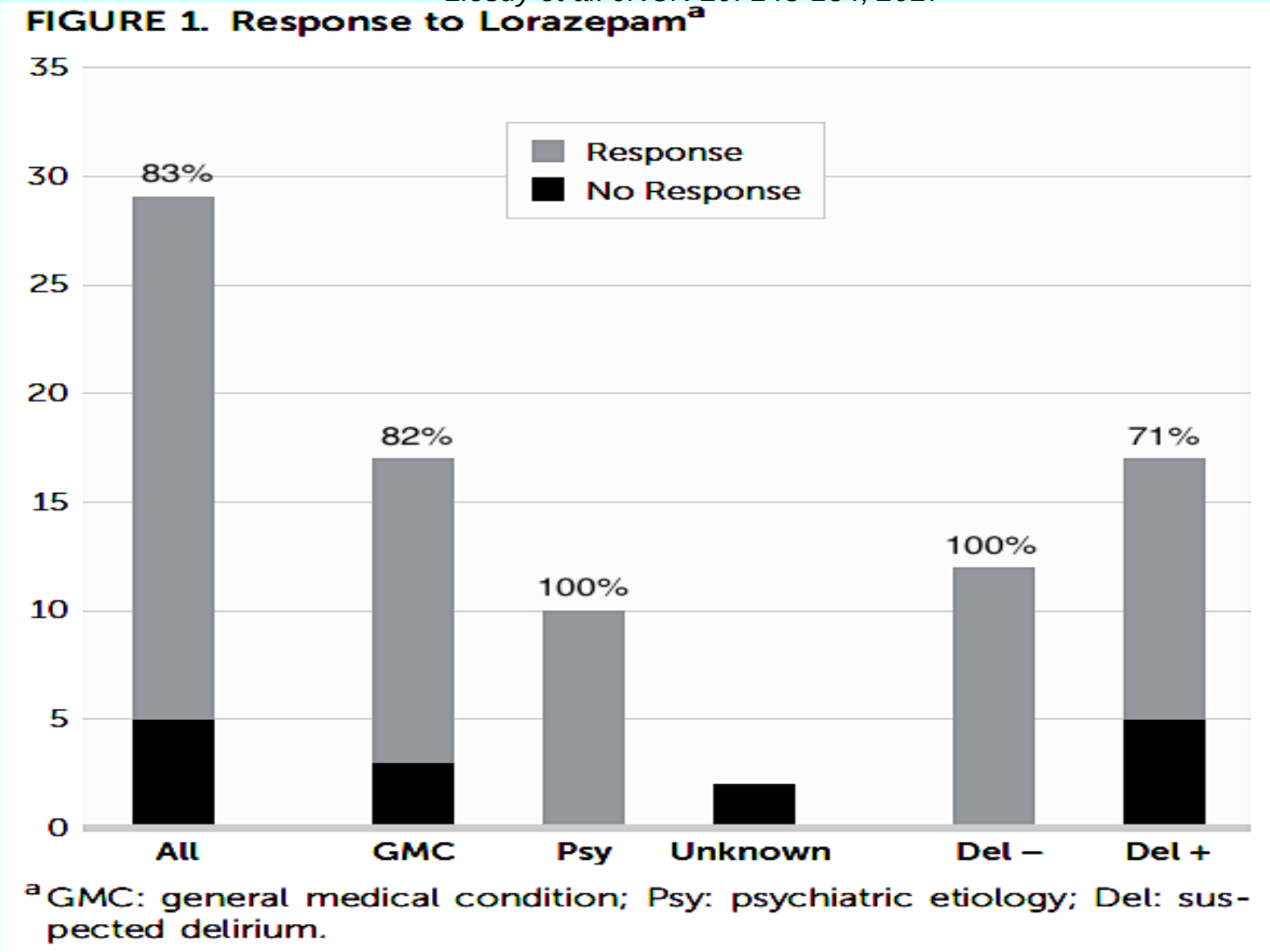
Llesuy et al. JNCN 29: 148-154, 2017

TABLE 1. Clinical Cohort Features and Catatonia Symptoms

Variable	Cases	
Cohort features	N=54	
	Mean	SD
Age (years)	49.6	17.71
	N	%
Female	36	66.67
Past psychiatric history	31	42.59
Family psychiatric history[a]	18[a]	41.86[a]
Suspected delirium	29	53.70
First known episode of catatonia	49	90.74
Dopamine D2 receptor antagonist exposure	32	59.26

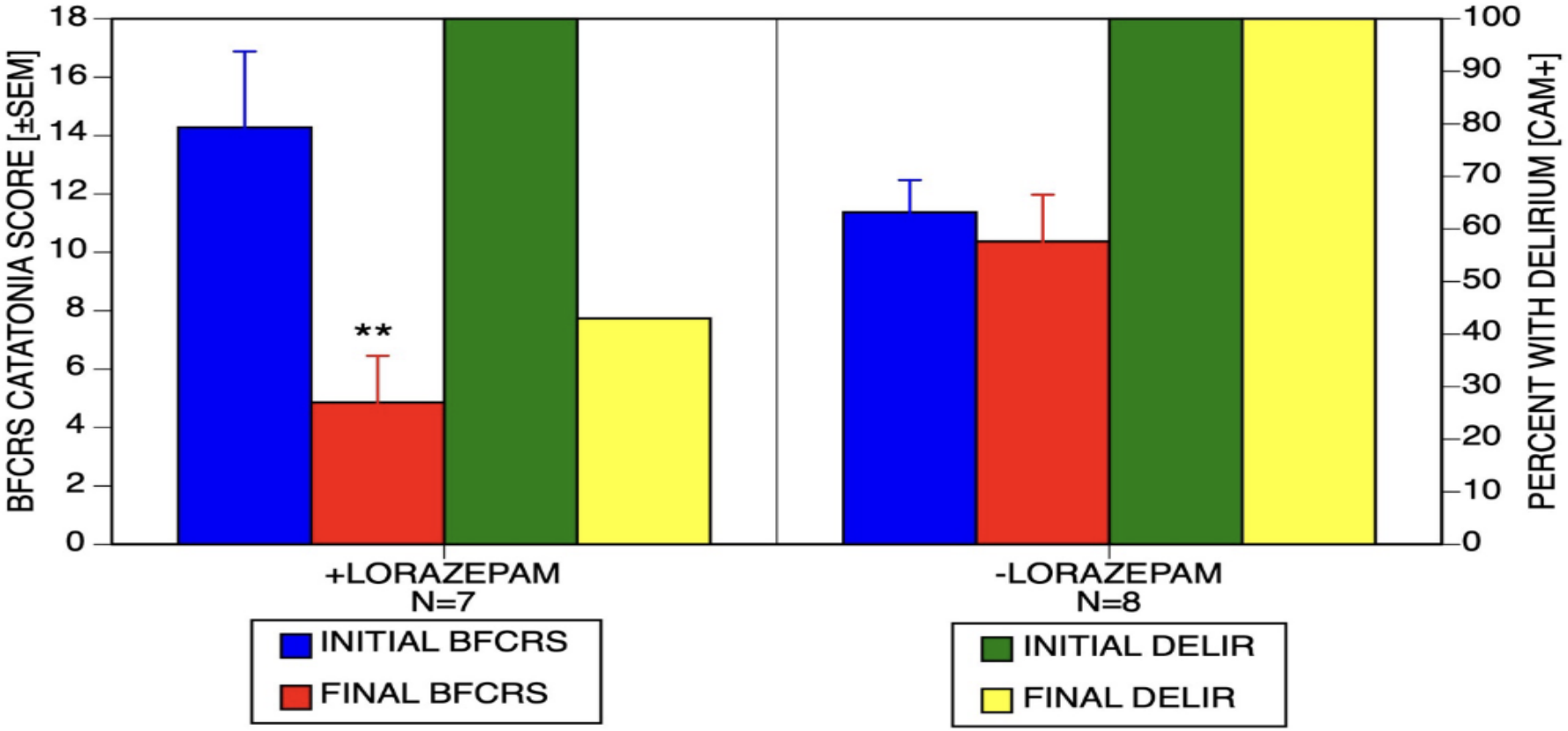
Retrospective Study: Catatonia in Med-Surg
N=54, DSM-5 Catatonia

Llesuy et al. JNCN 29: 148-154, 2017



LORAZEPAM TREATMENT OF CATATONIA IN DELIRIUM
BASELINE CHARACTERISTICS OF SAMPLE

	LORAZEPAM RX	NO LORAZEPAM RX	P
N	7	8	
AGE [±SEM]	77.8±3.3	81.5±2.8	NS
GENDER	4/7F	5/8F	NS
DELIRIUM	7/7	8/8	NS
INITIAL BFCRS [±SEM]	14.3±3.3	11.4±1.1	NS



Conclusions

- Catatonia is a distinct syndrome, associated with morbidity if severe/untreated
- Often responds to Tx if Dx'ed
- Catatonia and Delirium May Co-Exist
- ?Treatment Implications
- ?Consider lorazepam trial
- ?Avoid neuroleptics
- Other agents? Memantine?

www.catatonia.org

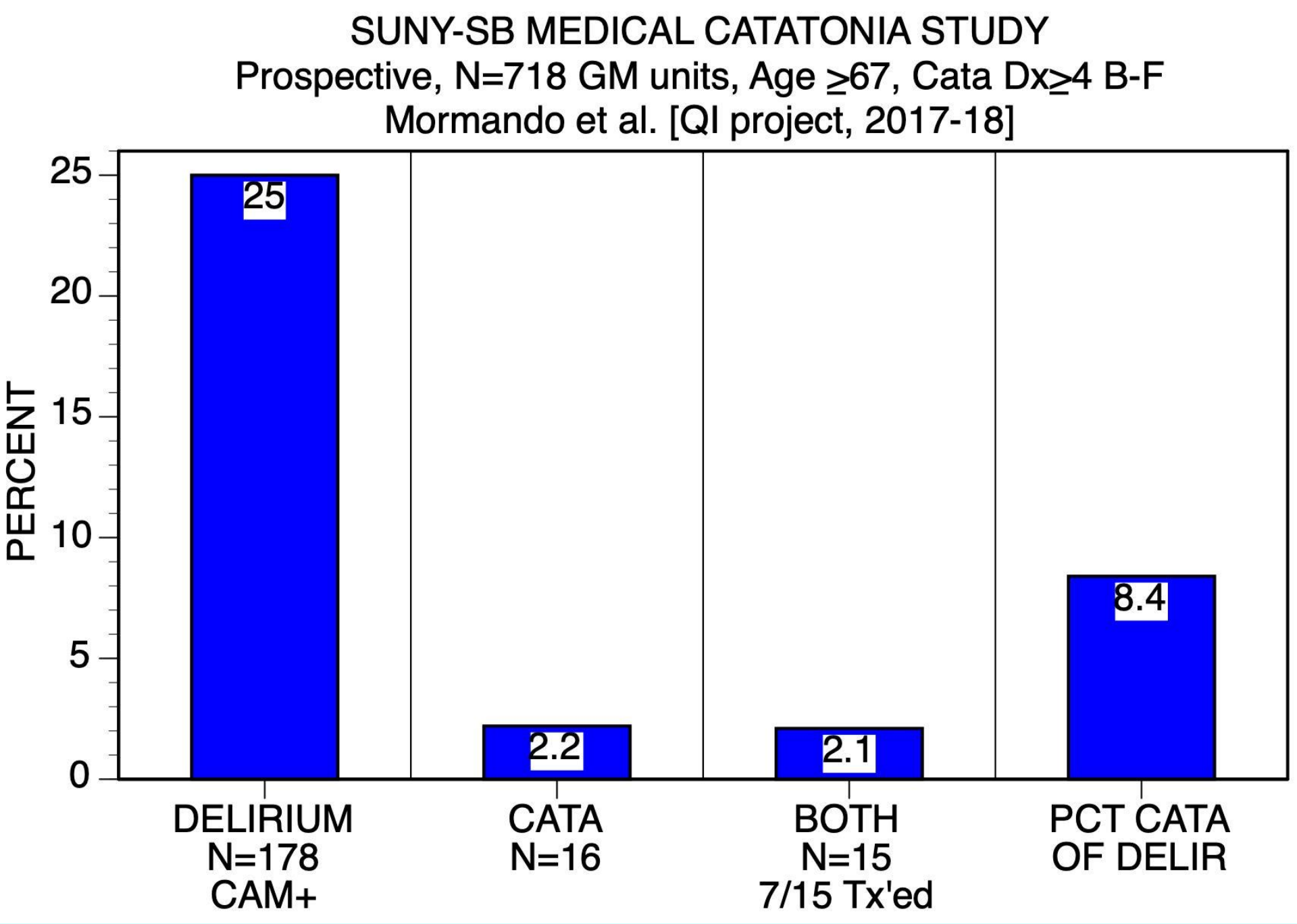
Biology of Catatonia

- Variety of brain lesions, frontal lobe
- 15q15 Linkage for periodic catatonia
- ↑urinary monoamine metabolites
- ↑Incr pHVA, esp in LZ responders
- ↓ GABA-A binding in R Fr/Par Ctx
- +/- ↑CPK, ?linked to autonomic sx?
- F-MRI: ↑ Activity L frontal and SMA

Psychological Theory of Catatonia

"Scared Stiff: Catatonia as an Evolutionary-Based Fear Response" Moskowitz (2004)

- This is a theoretical paper linking the anxiety/fear as "causative" for catatonia.
- Thesis: Catatonia is 'relic' of ancient defensive strategy in early humans [freezing to escape predator's attention]
- Support: Animal analogues exist; Anxiety/Fear common in catatonia; Rx's include BZDP and barbiturates that relieve anxiety
- Problems: 1-Freezing transient, flight/fight ensues if predator closes in, Catatonia may be chronic & fatal; 2-Catatonia Rx dose>>Anxiolytic dose; 3-ECT best Catatonia Tx but not useful for anxiety; 4-Fallacy of assigning one item of syndrome as cause of entire syndrome


SUNY-SB MEDICAL CATATONIA STUDY
Prospective, N=718 GM units, Age ≥67, Cata Dx≥4 B-F
Mormando et al. [QI project, 2017-18]
PERCENT
25
20
15
10
5
0
25
2.2
2.1
8.4
DELIRIUM
N=178
CAM+
CATA
N=16
BOTH
N=15
7/15 Tx'ed
PCT CATA
OF DELIR

Psychosomatics 2020:■:■–■

Case Report

Can Memantine Improve Catatonia and Co-occurring Cognitive Dysfunction? A Case Report and Brief Literature Review

Julie Graziane, M.D., Erin Davidowicz, M.D., Andrew Francis, Ph.D., M.D.

Catatonia + Delirium National Data
TriNetX Database
N=213,000,000+

Delirium ICD-F05
N=734,004

Confusion ICD-R41.0
N=1,757,176

Confusion OR Delirium
N=2,329,869

PLUS [±1d] Catatonia ICD-F06.1
N=1,531