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# Electrographic Features of Catatonia with and without Comorbid Delirium

Running title: EEG in Catatonia and Delirium

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**Abstract** 

Objective: Catatonia is an under-diagnosed disorder characterized by speech and motor

abnormalities. Electroencephalography (EEG) may enhance improve diagnosis, but clinical

and electrographic correlations have not been established. This study describes catatonic

features and EEG findings in a large multi-site retrospective cohort.

Methods: The clinical records of two health systems were searched for patients with EEG

recording and catatonia assessment using the Bush Francis Catatonia Rating Scale (BFCRS)

within 24 hours of each other. Included patients were retrospectively screened for delirium

using chart-based assessment. Augmented Inverse Propensity Weighting (AIPW) was used to

estimate the causal effects of delirium and catatonia on the presence of an abnormal EEG.

Results: 178 patients met inclusion criteria, of whom 144 (81%) had catatonia; among

catatonic patients, 43% also had delirium. EEG abnormalities were present in 46% of patients

with catatonia, including 28% of patients with catatonia without delirium and 69% of patients

with co-occurring catatonia and delirium. There was poor correlation between individual

catatonic signs and EEG abnormalities. In AIPW models, delirium diagnosis was associated

with a higher odds of an abnormal EEG (OR 6.8; 95% CI: 2.8 to 16.1), while a diagnosis of

catatonia was not (OR 1.8; 95% CI: 0.8 to 4.2).

Conclusions: EEG abnormalities are common in individuals with catatonia, but these are

difficult to disentangle from abnormalities resulting from co-occurring delirium. Further

research is needed to define the role of EEG in the assessment of catatonia and delirium.

Keywords: Electroencephalography, catatonia, delirium, cohort studies, diagnosis

Catatonia is a neuropsychiatric disorder which presents with substantial deficits of motor function, affect, and cognitive-behavioral function (1, 2). It can be associated with transition to a severe form, malignant catatonia, which may be fatal (3, 4). Catatonia is diagnosed using physical exam and interview, with the Bush-Francis Catatonia Rating Scale (BFCRS) as the most frequently used assessment tool (5–7). Catatonia was first described in 1874 in patients with mental and physical illnesses (8). Since that time, catatonia has been increasingly identified in a range of conditions (9, 10), with 40% of catatonia hospitalizations resulting from medical or neurologic illness (11). Recognition of catatonia is poor, with one retrospective chart review by expert clinicians finding that only 41% of likely catatonia cases in the general hospital were diagnosed by the treatment team (12). One challenge to the diagnosis of catatonia is that catatonic signs overlap with features of delirium, which is itself a neuropsychiatric disorder characterized by changes in attention, awareness and cognition (13). Under DSM-5-TR criteria catatonia may not be diagnosed in the presence of delirium (14), but prospective assessment indicates that the two conditions commonly co-occur. For instance, a prospective assessment of 378 critically-ill patients who received daily catatonia and delirium assessments found that 22% displayed features of both disorders (15), and among 205 medical inpatients diagnosed with delirium, 30% also had catatonia (16).

While catatonia and delirium share similar clinical features, they display markedly different responses to treatment. Catatonia often responds rapidly to treatment with benzodiazepines (17, 18), with refractory cases of catatonia generally responding rapidly to treatment with electroconvulsive therapy (ECT) (19, 20). While effective in catatonia, benzodiazepines and ECT may worsen delirium (21), and antipsychotics that are often used in the management of delirium are associated with worsening of catatonia and potentially fatal transformation to malignant catatonia (22). As a result, developing improved tools to

characterize catatonia and delirium and to distinguish between the conditions is essential to enhancing diagnostic accuracy and optimizing treatment.

One tool for characterizing neurophysiology is electroencephalography (EEG), which provides a non-invasive, bedside measure of cortical activity (23). Clinically, EEGs are read by electrophysiologists who describe the *visual features* (including background rhythms, sharp waves, and seizures) of a tracing in a clinical report using standardized nomenclature (24), akin to a radiologist's report describing a medical image. EEG findings in catatonia have been reported since 1938 (25), with a 2023 systematic review identifying 355 such studies reporting findings in 707 patients (26). In a meta-analysis of 12 studies totaling 308 patients (largest N=79), an abnormal EEG was found to predict that a medical (rather than psychiatric) condition was present in the individual with catatonia with a sensitivity of 0.82 and specificity of 0.66. These studies were limited by substantial heterogeneity, however, with most studies not reporting on specific EEG abnormalities and none using the most recent terminology to describe EEG features (24, 27). Research on EEG findings in delirium has indicated that slowing of the background is strongly correlated with delirium severity (28, 29), and that slowing is correlated with poor clinical outcomes including longer hospital length of stay and mortality (30).

To advance EEG as a potential diagnostic tool in catatonia, this study examines EEG features in a large multi-site retrospective cohort of patients with contemporaneous catatonia clinical exam and EEG. Its aims were to describe EEG abnormalities in patients with catatonia and to assess the relationship between a diagnosis of catatonia, a diagnosis of delirium, and an abnormal EEG.

#### Methods

Sample

The electronic health records of two large health systems (one in the Northeastern United States and one in the Southern United States) were queried for patients with a discharge diagnosis of catatonia and an EEG recording during the corresponding clinical encounter. Records were searched for one health system for the period of January 2007 to October 2023, and for the second health system from July 2021 through October 2023. Clinical records were manually reviewed to identify patients with an EEG recording and clinical exam for catatonia using the full BFCRS documented within 24 hours of each other. Patient demographics, diagnoses, discharge disposition, and hospital length of stay were extracted from the clinical record. Patients were considered to have a primary psychiatric cause of their catatonia if the first-listed diagnosis on the hospital discharge summary was a psychiatric diagnosis, while they were considered to have a primary medical diagnosis if the the first-listed diagnosis on the hospital discharge summary was not a psychiatric diagnosis. This study was approved by the Institutional Review Board of each health system with a waiver of informed consent from participants.

### **EEG Recordings**

Clinical EEGs were recorded using the standard international 10–20 electrode placement by qualified EEG technicians. As part of routine clinical practice, all EEG recordings were interpreted by physician electroencephalographers before reports were finalized and published in the electronic medical record. Clinical EEG reports were then manually reviewed to identify the presence of various findings as described in the 2021 American Clinical Neurophysiology Society Critical Care EEG terminology (24). These included posterior dominant rhythm, theta slowing (generalized or focal), delta slowing (generalized or focal), generalized rhythmic delta activity, lateralized rhythmic delta activity, sporadic discharges, periodic discharges (generalized or lateralized), low-voltage/generalized

attenuation, brief potentially ictal rhythmic discharges (BIRDs), and seizures (focal or generalized).

#### Clinical Assessment

Catatonia was assessed using the BFCRS (5). For this scale, the first 14 items were defined as the Bush Francis Catatonia Screening Instrument (BFCSI), whereas overall catatonia severity was measured using the full 23-item BFCRS. As the psychometric properties of BFCRS scoring have not been established, all items of the BFCRS were treated as binary variables (present or absent). Patients were defined as having catatonia if they had 4 or more catatonic signs on the BFCSI, consistent with prior research studies in the general hospital setting (31). This threshold was chosen to enhance the specificity of catatonia diagnosis in patients in the general hospital as the original BFCSI was created in the psychiatric inpatient setting, where other conditions that may overlap in clinical features with catatonia (for instance, non-convulsive status epilepticus, serotonin syndrome, or neuroleptic malignant syndrome) are expected to be less common. As structured delirium assessments were not performed along with catatonia assessment, each patient was retrospectively screened for delirium using a standardized and validated methodology based on chart review (the CHART-DEL tool, with a sensitivity of 74% and specificity of 83% compared to prospective delirium assessment) (32). This tool has not, however, been specifically validated in the cohort of individuals with comorbid neuropsychiatric dysfunction such as catatonia.

# Statistical Analysis

Demographics, catatonia scores, and EEG features are presented using descriptive statistics. The correlation between individual catatonia signs and EEG features are described using Pearson correlation, with analysis done using Python (Version 3.13). For the primary statistical analysis, Augmented Inverse Propensity Weighting (AIPW) was used to estimate

the causal effects of delirium and catatonia on the presence of an abnormal EEG. This method utilizes doubly robust estimation which combines outcome regression with weighting by the propensity score to provide an effect estimator that is robust to misspecification of either the outcome model or the propensity model (33). Delirium (yes/no) and catatonia (yes/no) were used as binary exposure variables in separate AIPW models, each with the presence of an abnormal EEG (yes/no) as the outcome and age, sex, study site, and primary diagnosis (medical vs. psychiatric) as covariates. AIPW models utilized 10-fold cross validation. Calculations were performed using the AIPW package (v0.6.3.2) (34) in R Statistical Software (v4.3.3; R Core Team 2021).

#### Results

# Patient Demographics

In total, 178 patients met inclusion criteria by having an EEG and documented BFCRS within 24 hours of each other. Of these, 34 (19%) had a BFCSI < 4 and were defined as non-catatonic, while 144 (81%) had a BFCSI ≥ 4, consistent with the presence of catatonia. 72 patients (42%) had delirium based on CHART-DEL criteria including 10 individuals without catatonia (29% of non-catatonic patients) and 62 with catatonia (43% of catatonic patients). Demographic information for individuals without catatonia, those with catatonia without co-occurring delirium, and those with both catatonia and delirium are listed in Table 1. Demographics of non-catatonic patients with and without delirium are given in Table S1.

# Diagnoses

Across the entire cohort, 103 (58%) had a primary discharge diagnosis that was psychiatric in nature, while 75 (42%) had a primary discharge diagnosis that was medical. Of the 144 patients with catatonia, 85 (59%) had a primary psychiatric diagnosis and 59 (41%)

had a primary medical diagnosis. For those patients with catatonia, among psychiatric diagnoses, the most common diagnoses were catatonic schizophrenia, bipolar disorder, and unspecified catatonia. The most common medical diagnoses were unspecified altered mental status, infection, and encephalopathy/delirium. A list of discharge diagnoses for patients with catatonia is given in Table S2.

# Catatonic Signs

Among individuals with catatonia, staring was the most common catatonic sign, present in 79% of patients, followed by mutism (74%) and immobility (62%). The least frequent signs were mannerisms (13%), mitgehen (12%), and combativeness (7%). The proportion of patients displaying each sign of the BFCRS is shown in Figure S1.

#### **EEG Features**

In total, 77 (43%) of the 178-patient cohort had an abnormal EEG, including 23 (28%) of the 82 patients with catatonia without delirium and 43 (69%) of the 62 patients with both catatonia and delirium (46% of catatonia patients overall). Specific EEG abnormalities based on the number of BFCRS features displayed and delirium status are shown in Figure 1. Among EEG abnormalities, generalized slowing was most frequently observed, with low voltage and sporadic discharges being the next most common features. The proportion of patients with catatonia and a primary medical diagnosis having an abnormal EEG was 61% (36 of 59) compared to 35% (30 of 85) of patients with catatonia and a primary psychiatric diagnosis having an abnormal EEG. The presence of an abnormal EEG in this sample has a sensitivity of 0.61 and a specificity of 0.65 for predicting a medical diagnosis, with an area under the receiver operating curve (AUROC) of 0.63.

The correlation between specific BFCRS signs and EEG features was weak (Figure 2). The strongest positive correlation between BFCRS signs and an abnormal EEG were for

withdrawal (Pearson correlation = 0.13; 95% CI: -0.01, 0.28) and mutism (Pearson correlation = 0.10; 95% CI: -0.04, 0.25), while automatic obedience (Pearson correlation = -0.16; 95% CI: -0.31, -0.02) and perseveration (Pearson correlation = -0.11; 95% CI: -0.25, 0.04) had the strongest negative correlation with the presence an abnormal EEG.

In order to estimate the causal effects of delirium and catatonia on the presence of an abnormal EEG, AIPW delirium (yes/no) and catatonia (yes/no) were used as binary exposure variables in separate AIPW models with the presence of an abnormal EEG (yes/no) as the outcome and age, sex, study site, and primary diagnosis (medical vs. psychiatric) as covariates. A diagnosis of delirium was associated with a higher odds of an abnormal EEG (OR 6.8; 95% CI: 2.8 to 16.1), while a diagnosis of catatonia was not associated with a higher odds of an abnormal EEG (OR 1.8; 95% CI: 0.8 to 4.2).

### **Discussion**

This multi-site cohort study of general hospital inpatients with EEG recording and catatonia clinical exam within 24 hours represents the largest study of visually-described EEG findings in catatonia published to date. In this cohort, 46% of patients with catatonia had EEG abnormalities. Among catatonic patients 43% had evidence of delirium on retrospective chart review, and EEG abnormalities were more common in catatonic patients with delirium than those without (69% vs. 28%). There was only weak correlation between individual BFCRS signs and specific EEG abnormalities.

The substantial comorbidity between catatonia and delirium observed in this sample is consistent with prior single-center studies (15, 16). While DSM-5-TR rules prohibit the diagnosis of catatonia in the setting of delirium, these results suggest that the two disorders frequently co-occur and that patients with both disorders may differ clinically from those with either disorder alone. Further prospective research is needed to better characterize the

extent of catatonia and delirium overlap, and to determine whether optimal treatment for catatonia should differ depending on the presence of delirium comorbidity. For instance, while a small case series of patients with both catatonia, delirium, and features of generalized periodic discharges on EEG showed improvement in catatonia with treatment with benzodiazepines, it is unclear if this is true for all patients with comorbid catatonia and delirium or if in such patients benzodiazepine administration is relatively contraindicated as these agents may worsen delirium.

Prior meta-analysis suggests that the presence of EEG abnormalities in catatonia is sensitive and specific for predicting a medical diagnosis underlying catatonia, with an AUROC of 0.83 demonstrating relatively high discrimination (26). The largest included study, however, had 79 patients and was published in 1970 with little detail regarding specific EEG abnormalities. In this sample, while abnormal EEGs were more common in patients with a medical diagnosis compared to a psychiatric diagnosis, the presence of an abnormal EEG in this sample has a sensitivity of 0.61 and a specificity of 0.65 for predicting a medical diagnosis, with an AUROC of 0.63. It is possible this discrepancy reflects differences in the ways in which diagnoses was defined: in the meta-analysis, any diagnosis that was considered to underlie catatonia was included and—in cases of comorbidity—a medical disorder overrode a psychiatric disorder, whereas the current study relied on the primary discharge diagnosis, which could be psychiatric, even if other medical conditions had occurred during the hospitalization. It is also possible that delirium mediates the association between medical conditions and an abnormal EEG.

In AIPW models to estimate the causal effects of delirium and catatonia on the presence of an abnormal EEG, a diagnosis of delirium was associated with a higher odds of an abnormal EEG. This is consistent with extensive prior literature documenting EEG abnormalities, particularly background slowing, in patients with delirium (30, 35–37). In

contrast, a catatonia diagnosis was not associated with a higher odds of an abnormal EEG. This suggests that future studies exploring EEG findings in catatonia should also consider conditions such as delirium that may co-occur with catatonia as abnormalities observed may be better attributed to those conditions rather than catatonia alone. Ultimately, one of the most important measures of the utility of a diagnostic tool depends on its ability to predict treatment response, so future studies should investigate whether treatment response in catatonia depends on EEG findings. Furthermore, while the BFCRS is in common use, no studies have correlated increasing severity on this score with clinical outcomes including hospital length of stay or mortality (38), and so the optimal measurement of catatonia, particularly in the general hospital setting, should remain an area of active research.

Strengths of this study include a large sample size, multicenter nature, the use of standardized nomenclature for reporting EEG features, and assessment for both delirium and catatonia at the time of EEG recording. As a retrospective study, there are inherent limitations that derive from the methodology of sample generation. Chiefly, to be included in the sample patients must have had a documented catatonia assessment using the BFCRS. This is not performed systematically in either health system, and thus if the treating providers did not assess for catatonia or did not document such an assessment the patient could be erroneously recorded as a non-case. Furthermore, a cutoff of 4 BFCSI signs was chosen to define catatonia in this sample to emphasize specificity in the diagnosis, however optimal cutoffs for catatonia diagnosis in the general hospital setting have not been rigorously established and different diagnostic cutoff values may yield differing results. Additionally, delirium assessment was determined by retrospective chart review. While this CHART-DEL method has demonstrated high sensitivity and specificity in prior studies, it has not been studied specifically in the population of patients with comorbid neuropsychiatric dysfunction such as catatonia, and so it may misattribute clinical signs to delirium that may more appropriately be

attributed to catatonia. Moreover, EEGs are not obtained for all suspected cases of catatonia, and so this sample may be skewed towards patients with ambiguous presentations or cooccurring medical or neurologic conditions prompting EEG evaluation, and so these patients may not be reflective of all individuals with catatonia. Moreover, nearly all EEGs in this sample were obtained in the general hospital setting, and so generalizability of these findings to catatonic outpatients or those hospitalized in freestanding psychiatric facilities is uncertain. Additionally, findings in this study of two academic health systems may not directly translate to other treatment settings or populations of different sociodemographics. Furthermore, catatonic symptoms are known to fluctuate during a course of illness, and while EEG and BFCRS were assessed within 24 hours of each other it is unclear if the documented catatonic features were the same, or different, at the time of EEG. Moreover, the CHART-DEL method does not permit analysis of individual signs of delirium or of overall delirium severity, and so future studies should perform validated delirium severity scores at the same time as catatonia rating and EEG recording. Finally, this study focuses on visually-described features of EEG, and is unable to assess for features of EEG that may only be apparent using signal processing of the raw EEG tracing.

### **Conclusions**

In conclusion, in this large multi-site cohort of general hospital inpatients with EEG recording and catatonia clinical exam within 24 hours of each other, visually-described EEG abnormalities were common. Delirium was found in a large fraction of patients with catatonia. In AIPW models, catatonia was not associated with EEG abnormalities, but delirium was, and the presence of an abnormal EEG had low sensitivity and specificity for predicting a medical vs. psychiatric diagnosis associated with catatonia. There was poor correlation between individual catatonic signs and EEG features. Further research is needed to define the role of EEG in the assessment of catatonia with and without comorbid delirium.

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# **Figure Legends**

Figure 1: presence of EEG visual features by increasing number of observed BFCSI signs. Each EEG feature is represented by a row and each patient is a single column. Patients without delirium are represented by white boxes where a feature is absent and black boxes where a feature is present. Patients with delirium are represented by pale blue boxes where a feature is absent and bright blue boxes where a feature is present. BIRD= brief potentially ictal rhythmic discharges; EEG = electroencephalogram; GPD=generalized periodic discharges; LPD=lateralized periodic discharges; PDR=posterior dominant rhythm;  $\delta$ =delta;  $\theta$ =theta.

Figure 2: Pearson correlation between BFCRS signs and EEG features. BFCRS = Bush-Francis Catatonia Rating Scale; BIRD= brief potentially ictal rhythmic discharges; EEG = electroencephalogram; GPD=generalized periodic discharges; LPD=lateralized periodic discharges; PDR=posterior dominant rhythm;  $\delta$ =delta;  $\theta$ =theta.

	No Catatonia		Catatonia, no delirium		Catatonia with delirium	
	N	%	N	%	N	%
N	34		82		62	
Male Sex	19	56%	48	56%	22	36%
$Age\ (yrs;\ mean \pm SD)$	$43.1 \pm 22.9$		$37.2 \pm 20.5$		$47.4 \pm 26.4$	
Race						
White	21	62%	44	54%	44	71%
Black	9	27%	25	31%	12	19%
Asian	1	3%	5	6.%	4	7%
Other	2	6%	8	10%	1	2%
Hispanic (yes)	3	9%	5	6%	1	2%
Study Site						
1	4	12%	14	17%	16	26%
2	30	88%	68	83%	46	74%
Primary Diagnosis						
Psychiatric	18	53%	60	73%	25	40%
Medical	16	47%	22	27%	37	60%
EEG Type						
Spot	30	88%	68	83%	48	77%
LTM	4	12%	14	17%	14	23%
Delirium (yes)	10	29%	0	0%	62	100%
BFCSI Features (mean $\pm$ SD)	$2.3 \pm 0.8$		$5.7 \pm 1.3$		$5.9 \pm 1.9$	
$BFCRS$ Features (mean $\pm$ SD)	$3.9 \pm 1.4$		$7.5 \pm 2.3$		$8.3 \pm 3.0$	
Hospital Day of EEG (mean ± SD)	$6.7 \pm 6.8$		3.9 ± 4.4		$5.3 \pm 6.4$	
Hospital Length of Stay (mean ± SD)	$17.5 \pm 15.5$		$14.9 \pm 13.8$		$22.1 \pm 19.8$	

Table 1: demographics of patients without catatonia (<4 BFCSI features), those with catatonia without co-occurring delirium (using CHART-DEL), and those with both catatonia and delirium. Given small sample sizes, for privacy reason "other" race includes pacific islander, native America, and two or more races.