



Case Report

Forced normalization's converse as nature's model for use of ECT in the management of psychosis: An observational case series



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ABSTRACT

Though electroconvulsive therapy (ECT) has long been utilized to treat mood disorders, it was originally developed to treat psychosis. Our two case reports demonstrate that for patients who experience the converse of forced normalization, ECT may be a logical therapy for their psychosis. Patient 1, a 14-year-old male, and patient 2, a 27-year-old female, each experienced debilitating psychosis, which largely cleared following one seizure and two events thought to be clinical seizures, respectively. We would argue that ECT, as a medically controlled seizure, continues to be underutilized to treat psychosis, particularly in cases of forced normalization and its converse.

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1. Introduction

In the mid-twentieth century, psychiatry was increasingly utilizing convulsive therapy, using various pharmacologic agents, as a treatment for schizophrenia [1]. The Italian professor of neuropsychiatry Ugo Cerletti and his colleague Lucio Bini developed the idea of using electricity as a substitute for pentyleneetetrazol (Cardiazol) for convulsive therapy [2]. Electroconvulsive therapy soon replaced Cardiazol therapy worldwide primarily because of cost and convenience [3]. Thus, a new treatment for mood disorders was born — a treatment more effective than anything developed before or since [4].

Epilepsy is a neurological disorder characterized by seizures and is associated with sudden changes in electrical activity of the brain. These changes generate movement, as well as alterations of behavior, emotion, and perception. Naturally accrued epileptic activities have been witnessed and recorded for millennia [5].

The psychiatrist Hans Berger developed the EEG in 1929 to diagnose psychiatric illness [6], but it would never fulfill that role. Moreover, there is simply no consensus as to the nature of various EEG patterns in psychiatric illnesses. Complicating matters, patients with status epilepticus may demonstrate various neuropsychological aberrations, such as thought disorders, language impairment, or change in sensorium, accompanied by automatisms [7]. Their behavior may be so bizarre that the condition merits the label ictal psychosis.

The phenomena of psychosis and epilepsy are historically and intrinsically intertwined, as are the professions of neurology and psychiatry. This paper explores the psychiatrically therapeutic potential of the seizure and its relation to the converse of the phenomenon of forced normalization.

2. Patient 1

Patient 1 first presented to our clinic in 2011 at the age of 14, with no formal psychiatric history. He had recently begun to experience demoralizing and disturbing auditory and visual hallucinations, as well as disturbing, obsessive thoughts about harming small children or animals and watching them bleed to death. He also exhibited several obsessive and compulsive symptoms, such as feeling “driven” to create hundreds of Gmail accounts with dark or sexually perverted names and experiencing intrusive thoughts about sexually molesting children. Advancing negative symptoms announced the progression of his disease, as he began to isolate himself in his room and lose his social skills and ability to express empathy.

From 2012 to 2014, the patient's functional status declined; he had two psychiatric hospitalizations, and he experienced failed trials of several antipsychotics and mood stabilizers for psychotic symptoms and selective serotonin reuptake inhibitors for obsessive–compulsive symptoms. The medications were either not sufficiently effective or caused intolerable side effects. In March 2014, aripiprazole was discontinued in favor of olanzapine for refractory psychosis. One month later, at nearly 17 years old, patient 1 experienced his first ever seizure, generalized tonic–clonic in nature. At his next psychiatric appointment, two weeks

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later, he revealed that following the seizure, his hallucinations, which had progressed over the past few years to daily occurrences, had ceased completely. His negative symptoms had also diminished, and he presented as bright and cheerful, with dramatically increased prosocial behavior. His grades and functional status improved. In June 2014, he experienced two more seizures, and a sleep-deprived EEG suggested a genetic generalized epilepsy, so levetiracetam was initiated for seizure prophylaxis.

Then, in January 2015, he began reporting self-injurious cutting behavior, as well as the return of auditory and visual hallucinations and negative symptoms, all of which were less severe than the symptoms experienced prior to his initial seizure. However, over the next year, these symptoms continued to improve.

3. Patient 2

Patient 2 was first admitted to the psychiatric inpatient unit at age 27. She was adopted, so much of her early history was unclear, but she had a complicated perinatal course (in utero exposure to substances of abuse, born prematurely, diagnosed with toxoplasmosis at birth) and was soon diagnosed with spastic cerebral palsy. She had a history of febrile seizures in the first year of life, as well as three witnessed convulsive seizures at ages 6, 10, and 22. After the seizure at 22 years old, she was diagnosed with a seizure disorder and started on levetiracetam for seizure prophylaxis. Starting at age 20, she also experienced several episodes of violent, bizarre behavior with psychosis, some of which resulted in psychiatric hospitalizations.

Patient AC had been at her baseline health and functioning – living with her parents, working part-time as a librarian, and able to drive a car – until three days prior to the current presentation, during which time she had gotten very little sleep, had become inconsistent with taking her prescribed levetiracetam, and had demonstrated increasingly odd affect and behavior. She presented to the emergency department (ED) with disorientation, confusion, tearfulness, decreased alertness, decreased attention, decreased concentration, disorganized and slowed thought process, delusional thought, and auditory and visual hallucinations. Her levetiracetam level was subtherapeutic. She was transferred to the inpatient psychiatric unit for further psychiatric evaluation and treatment.

On the evening of presentation and admission, AC had a witnessed, tonic-clonic seizure, with left-gaze deviation, cyanosis, and oxygen saturations in the low 90s. She was sent to the ED for stabilization and medical clearance and returned to the psychiatric unit early the following morning. Medical evaluation for altered mental status, including complete blood count with differential, basic metabolic panel, urinalysis, vitamin B12, thyroid-stimulating hormone, human immunodeficiency virus screen, serology for syphilis and Lyme disease, ceruloplasmin, erythrocyte sedimentation rate, and antinuclear antibody, was unremarkable.

Upon her return to the psychiatric unit, olanzapine was initiated for psychotic symptoms because of the medication's efficacy during AC's past psychotic episodes and her past adverse reactions to trials of risperidone and aripiprazole. Over the following three days, AC's thought blocking decreased, and lucid thought increased. Then, her psychotic symptoms worsened again for two days until she experienced a seizure-like event, involving facial flushing and purposeless movements of the bilateral upper extremities. The event lasted a few minutes, with associated tachycardia, hypertension, and amnesia without loss of consciousness and terminated likely because of the administration of PRN olanzapine and lorazepam. Later that afternoon, her mental status began to improve – she was oriented to person, place, and time, with increasingly lucid thought processes – and her aggressive behavior diminished.

She was transferred to the general inpatient neurology service to undergo continuous video-EEG monitoring, in order to better characterize her seizure-like events and their possible relation to her psychotic symptoms. During this time, she reported five pushbutton “seizure”

events, two of which were associated with anxiety and mild tachycardia, but none of which were associated with an abnormal EEG correlate or clinical seizure activity. The EEG study was interpreted as inconclusive, and she was discharged with no further changes to her medication regimen of olanzapine, levetiracetam, and clobazam established in the psychiatric unit.

4. Discussion

The antagonism between epilepsy and episodes of psychiatric disorders, especially episodic psychosis, occurring as alternating pathologies, has long been observed in patients with epilepsy, especially as the efficacy of antiepileptic drugs (AEDs) has improved over the past few decades [8]. Forced normalization, first described by Landolt in 1953 [9], is a phenomenon in which, during the occurrence of psychotic states, the EEG normalizes or improves, as compared with previous or subsequent EEG findings. Many, but not all, of Landolt's cases were provoked by administration of a new AED to a patient with epilepsy [9–11]. Tellenbach called the clinical phenomenon of reciprocal epilepsy and psychosis “alternative psychosis”, which refers to psychosis coinciding with the resolution or improvement of clinical seizures and so does not rely on EEG findings, as Landolt's term does [12]. In 1999, Krishnamoorthy and Trimble proposed diagnostic criteria for forced normalization (Fig. 1, [13]). The pathophysiology behind forced normalization is not fully understood, though several theories have been proposed [13–17].

We would argue that both of the cases we present demonstrate the converse of forced normalization or, more accurately, alternative psychosis, as will be explained in the next paragraph. Though there are many reports in the literature of forced normalization (e.g., [17,18]) or other psychoses in patients with epilepsy, such as interictal psychosis, postictal psychosis, or chronic comorbid psychosis (e.g., [19]), we have had difficulty finding reports in the literature involving the improvement or resolution of psychosis with the onset of seizure activity, though they may exist.

Both patient 1 and patient 2 experienced psychosis that resolved or improved following the onset of clinical seizures. For patient 1, the onset of epilepsy coincided with almost complete resolution of three years of debilitating psychosis. Patient 2's psychotic symptoms largely and rapidly cleared following her seizure the first night of her hospital admission and again following the seizure-like event several days into her hospitalization. Of note, the initiation of olanzapine coincided with her improvement in mental status following the first seizure, potentially raising the difficulty of disentangling seizure effect from medication

Primary (essential) criteria

1. Established diagnosis of epilepsy based on clinical history, EEG and imaging.
2. Presence of a behavioral disturbance of acute/subacute onset characterized by one or more of the following:

Psychosis with thought disorder, delusions, hallucinations.
Significant mood change, hypomania/mania or depression.
Anxiety with depersonalization, derealization.
Hysteria: motor, sensory, abasia.

3A. Reduction in the total number of spikes counted in a 60-min awake EEG recording with a 16-channel machine, using standard 10-20 electrode placement, by over 50% compared to a similar recording performed during a normal state of behavior.

OR

3B. Report of complete cessation of seizures for at least 1 week, corroborated by a relative or carer.

Supportive criteria

Recent change (within 30 days) of pharmacotherapeutic regimen.
Report of similar episodes of seizure cessation and behavioral disturbance in the past, from close relative or carer, or general practitioner, or documentation of this in hospital records with or without EEG evidence. This may or may not be linked with an anticonvulsant drug.

To make the diagnosis:

Primary criteria 1, 2, and 3A.

OR

Primary criteria 1, 2, and 3B and one supportive criterion.

Fig. 1. Proposed criteria for forced normalization.

effect; however, no medication changes cooccurred with her improvement following the second event. If forced normalization and alternative psychosis propose that psychosis coincides with reduction or elimination of epileptiform EEG activity or seizures, respectively, then it is logical that both of our patients experienced the converse — resolution of psychosis with the onset of clinical seizure activity. It is worth noting that, though we have used the phrase “converse” or “opposite of forced normalization” throughout this case series for concision and clarity, neither case, at this point in time, includes adequate information to assert the opposite of the improvement in EEG activity required by forced normalization — patient 1 lacks a normal or improved EEG for comparison with his EEG showing epileptiform activity, while the case of patient 2 lacks any evidence of epileptiform activity on EEG. It is unknown why patient 2’s EEG study showed no epileptiform activity, but it is possible that she may have been experiencing psychogenic nonepileptic seizures or frontal lobe seizures without ictal EEG correlates, either of which would produce a nonepileptiform EEG. In addition, she had no clinical seizure activity during the continuous video-EEG monitoring, so the study could not examine whether such activity, such as the two events during the inpatient hospitalization, would produce epileptiform EEG changes.

Cases of the converse of forced normalization or alternative psychosis, such as those of patient 1 and patient 2, seem to suggest that epileptiform or seizure activity may have a protective effect against psychosis in patients with epilepsy. Yet, we have known for a long time that seizures are not harmless because of dangers during the event, such as falls; the risk for conversion to status epilepticus; and long-term structural and functional effects on the brain [20]. Electroconvulsive therapy would serve as a medically induced, medically controlled seizure that could be used to treat psychosis, interestingly analogous to its initial use decades ago.

Forced normalization or alternative psychosis is an important risk to consider when starting a patient with epilepsy on an AED, just as it is crucial to recognize the development of the opposite phenomenon in a psychiatric patient with new-onset seizures. Both neurologists and psychiatrists should recognize and manage both conditions, often in conjunction with one another. Electroconvulsive therapy can be used to treat the psychosis component of forced normalization [4], and we would expect that it could also be used in cases of the opposite condition, in which certain patients may require continued “maintenance seizures” to prevent the return of psychosis. For instance, AC required two seizure-like events for a lasting improvement to her psychosis. It is possible that patients with this condition vary in the number and frequency of seizures required for continued control of psychotic symptoms.

In 2001, the American Psychiatric Association (APA) endorsed the efficacy of ECT for psychosis, typically as an adjunct to antipsychotic medications, and particularly in acute schizophrenia, medication-refractory chronic schizophrenia, schizophreniform disorder, and schizoaffective disorder [4]. We would argue that ECT continues to be underutilized to treat psychosis of various etiologies, particularly in cases of forced normalization or its opposite. In addition, newer neuromodulation techniques with milder side effect profiles, such as repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS), also merit further exploration as adjunctive treatments in psychosis, as research today is sparse but possibly encouraging [21].

5. Conclusion

At the time of this report, in February 2016, patient 1 is an 18-year-old male with diagnoses of schizophrenia, obsessive-compulsive disorder, and genetic generalized epilepsy. His mood is stable, and though some obsessive thinking remains, he denies hallucinations, suicidal ideation, and homicidal ideation. Sleep and appetite are adequate, weight is stable, and he denies medication side effects. He continues to see a

neurologist and a psychiatrist for medication management and ongoing psychotherapy. His medication regimen remains unchanged.

Patient 2 is currently a 28-year-old female with diagnoses of spastic cerebral palsy, psychosis NOS, and seizure disorder NOS. At her neurology appointment in January 2016, she denies having had any seizures since discharge from the psychiatric inpatient unit in October 2015. She has been attending group therapy, and her dose of olanzapine has been increased, while her doses of AEDs have remained the same. She has resumed her work as a part-time librarian, and her family reports that patient 2’s mood and personality are back to baseline.

If patient 1 or 2’s psychotic symptoms were to worsen again, ECT could be considered as a treatment modality, based upon the presumed interaction between psychotic symptoms and seizures in the past in each case and its consistency with the theory of the opposite of alternative psychosis.

As scientists, we observe and then we modify our observations into reproducible treatments intended to benefit our patients. The brain is a perplexing, systemically convoluted pathway of neurons coupled with glorious ground effect. It is a mixture of biology, spirituality, and experience at which practitioners marvel from afar and in which they intervene with only the greatest of respect.

Conflict of interest

There is no conflict of interest.

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