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Acute Phase Treatment Outcomes of Electroconvulsive Therapy in Adolescents and Young Adults

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Abstract

Objective: Electroconvulsive therapy (ECT) is a highly efficacious, well-tolerated treatment in adults. Little is known, however, about its effectiveness in adolescents and young adults. Our objective is to assess clinical outcomes after acute phase ECT in adolescents and young adults, and determine whether screening positive or negative for a substance use disorder (SUD) is associated with differences in treatment outcomes.

Methods: Study sample consisted of all patients 16–25 years old who received ECT May 2011-August 2016, and who completed self-reported SUD screens and the Behavior and Symptom Identification Scale-24 (BASIS-24) initially and completed the BASIS-24 again after the fifth ECT treatment. For five BASIS-24 domains, longitudinal changes in mean domain scores were assessed; mean changes by SUD screening status were also examined using linear mixed models.

Results: 190 adolescents and young adults, with mean age 21.0±2.6 years, met inclusion criteria. ECT was associated with significant clinical improvement (score decreases) in all five BASIS-24 domains during the acute phase treatment ($p<0.001$). Sixty-four percent (122/190) screened positive for SUD. Compared to adolescents and young adults screening negative for SUD, those screening positive for co-occurring SUD had greater improvement in depression/functioning (−0.37±0.14, $p=0.009$), interpersonal relationships (−0.27±0.13, $p=0.045$), and emotional lability (−0.27±0.14, $p=0.044$) domains after the fifth ECT treatment.

Conclusions: ECT in adolescents and young adults was associated with significantly improved clinical outcomes during acute phase treatment. Adolescents and young adults screening positive for SUD had better acute phase ECT outcomes in self-reported depression/functioning, interpersonal relationships, and emotional lability than those screening negative. More research is needed to clarify adolescents and young adult patient characteristics that may be associated with differential ECT outcomes.

Keywords

electroconvulsive therapy; adolescents; young adults; substance use; mood disorders; psychosis

In adults, electroconvulsive therapy (ECT) is a highly efficacious, well-tolerated treatment for major depressive disorder, depression with psychotic features, and schizophrenia[1–4]. Clinical features in adults associated with better treatment response include depression with

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psychotic features, shorter duration of the mood episode, lack of comorbid personality disorder, and older age with catatonic symptoms[3]. ECT has also been shown to be effective therapy for older, medically complex patients with psychiatric illness who may be resistant to other treatments[5,6].

Younger adults (i.e., ages 18–45) who received ECT for treatment resistant depression have comparable outcomes to middle age and older adults with respect to response to ECT and tolerability of ECT[7]. In children ages 7–22, ECT has been reported to result in responses rates of up to 88% in heterogeneous samples with small sample sizes (i.e., 8–42 patients) and can be indicated for treatment of severe mood disorders, treatment resistant mood disorders, neuroleptic malignant syndrome, and catatonia[8,9].

The transition from adolescence to young adulthood is rife with adjustments and challenges as adolescents strive to become independent, develop their own identity, and adjust to a new phase of life. During this stage in development, the brain is not yet biologically mature, particularly in the frontal cortex where maturation continues into the early 20s affecting executive functioning, decision making, and response inhibition[10]. An increasing appreciation of this developmental biology and transitions in social role functions has recently led some to suggest adolescence should be defined as continuing through age 24[11]. Given their unique set of developmental challenges and distinct stage of brain development, the discrete population in the age range of about 16 to 25 years have sometimes been called transitional age youth[12]. Over two million adolescents and young adults in the U.S. are estimated to have a serious mental illness, approximately 6.5% of non-institutionalized young adults in that age range[13]. Also, among adolescents and young adults with serious mental illness, co-occurring substance use disorders (SUD) are common, with a prevalence of up to 35%[14,15].While there is strong evidence supporting the efficacy of ECT in adults, little is known about its efficacy or effectiveness in adolescents and young adults, and the evidence is limited to a few case reports with small sample sizes (e.g., 3 – 42 patients)[9,16–18]. In addition, to our knowledge, though substance use is common in this population, up to 37% in one sample with severe mood disorders who were referred for ECT[9], no prior research examines the association of substance use on outcomes of ECT in adolescents and young adults. In this study, we examined the clinical and demographic characteristics of adolescents and young adult patients receiving ECT and the clinical outcomes associated with ECT treatment on the largest adolescents and young adult sample reported to date. We also studied whether screening positive or negative for a substance use disorder (SUD) was associated with differences in treatment outcome. We hypothesized that adolescents and young adults who received ECT would improve clinically after an initial course of acute phase ECT. We hypothesized that adolescents and young adults who screened positive for SUD might not show as much improvement associated with ECT compared to those who screened negative for SUD.

Materials and Methods

Population and Setting

This was a retrospective observational study of adolescent and young adult patients, between ages 16 and 25 years old, who received ECT during the study period May 2011 through

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August 2016 at a freestanding psychiatric hospital. All research conducted for this study was approved by the hospital organization's Institutional Review Board. As part of routine care, the hospital Psychiatric Neurotherapeutics Program, which includes inpatient and outpatient ECT, participates in the hospital's electronic patient reported outcomes measurement program, the Clinical Measurement Initiative (CMI). In the CMI, patients who receive ECT complete clinical measures that include a screen for alcohol and drug use (AUDIT-C[19] and a single item drug screen derived from the Drug Abuse Screening Test (DAST)-10[20,21]), and the Behavior and Symptom Identification Scale-24 (BASIS-24)[22] at baseline before the first ECT treatment. Repeat assessments using the BASIS-24 occur after the fifth ECT treatment. All measures were patient self-reported alone or with assistance by nursing staff if needed.

Patients are referred to this ECT clinic from the hospital's inpatient services, residential programs, and partial hospital programs, as well as from the local community, the state, and around the country. State regulations guide treatment for patients under age 16, but not for older adolescents and young adults. All patients who are referred for ECT receive a consultation from one of the ECT providers to determine appropriateness of this treatment. The indications for ECT are typically severity of illness and/or treatment resistance/intolerance. Patients participate in a thorough informed consent process and cannot be treated against their will without a court order or guardianship in place. Prior to treatment, all patients receive medical clearance from the hospital internists consisting of bloodwork which includes but is not limited to complete blood count, comprehensive metabolic profile, thyroid stimulating hormone, and pregnancy test, as well as a pre-treatment electrocardiogram. Further workup is done as requested by the internist or by the anesthesiologist when they evaluate the patient prior to treatment.

All patients received ECT using a Mecta Spectrum 5000Q (Tualatin, OR). Seizure threshold is determined on treatment one by dose titration, and subsequent treatments are done at six time seizure threshold starting on treatment two. Dosage may be increased if seizures are felt to be inadequate in morphology or if the patient is not progressing clinically. Most patients are started with ultrabrief pulse, right unilateral and continue with this modality through at least the first five treatments. If no improvement is seen after this period, patients generally receive higher power ultrabrief pulse unilateral treatment or are switched to brief pulse unilateral or bilateral depending on illness severity and patient preference after full discussion of risks and benefits. Occasionally patients may be started with bilateral or brief pulse unilateral if there is an acute need for a faster response such as in the case of catatonia, psychosis, severe suicidality, or in the case of a history of response in the past to one of these modalities. Generally, methohexital is used as the anesthetic agent, but this can be replaced by etomidate or ketamine if seizures are inadequate, which is unusual in this population. Succinylcholine is used as the muscle relaxant and a small dose of propofol is typically used post-treatment to help prevent post-treatment agitation.

Acute phase of ECT treatment usually consists of six to twelve ECT treatments, typically occurring within a three to four week period (i.e., three treatments per week). In this study, we examined mid-acute phase ECT treatment outcomes, which we defined as evaluating clinical outcomes after the fifth ECT treatment. We chose this time-frame because the adult ECT research finds that younger age is associated with earlier response[23], that most patients

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respond to ECT within five treatments[24], and that early response is associated with sustained response and remission[24,25]. We excluded patients for whom we had incomplete data, that is, those who did not complete all of the CMI assessments: 1) SUD screening assessment at baseline, 2) BASIS-24 on admission, or 3) BASIS-24 after the fifth ECT treatment.

Outcomes

The BASIS-24 is a self-report measure validated in diagnostically diverse psychiatric samples. It has six domains: depression/functioning, interpersonal relationships, psychosis, emotional lability, self-harm, and substance abuse. Items and domain means are scored from 0–4, with 0 representing “no difficulty”, 2 representing “moderate difficulty” and 4 representing “extreme difficultly”. We did not include the BASIS-24 substance abuse domain as an outcome because, unlike the other BASIS24 domains, changes in SUD outcomes associated with ECT are less relevant in a predominantly inpatient setting and over a short duration of treatment (i.e., early acute phase, approximately two weeks).

Explanatory Variables

We defined age as age at admission, sex as male or female, and race/ethnicity as white, black, latino/a, or other/unknown. We defined screening positive for SUD as a positive screen for either the AUDIT-C or the single-item drug screen[19,21]. Baseline data on demographic characteristics (age, sex, race/ethnicity, educational attainment), clinical characteristics (screening positive for SUD, admission non-SUD BASIS-24 domain scores), and a subjective rating of physical health from the BASIS-24 demographic questions were also obtained from the demographic portion of the BASIS-24. From the hospital’s electronic health record and an internal database maintained by the ECT service, the following information was extracted: clinical diagnoses, patient location when ECT was initiated, ECT pulse-width and placement, and total number of ECT treatments.

Statistical Analysis

We calculated univariate statistics (e.g., means/standard deviation, percent) of the patient demographic and clinical characteristics, and ECT parameters, at baseline. We also compared these characteristics to the excluded population (i.e., adolescents and young adults who received ECT but who had incomplete information at baseline or the interim CMI assessment after treatment five) to examine if the excluded population differed from our study population in these observable characteristics.

Analyses were then conducted in the study population, to assess change from baseline to the mid-acute phase (i.e., after the fifth ECT treatment) follow-up assessment in the five BASIS-24 domains using linear mixed models that included the effect of time to estimate the mean change and incorporated repeated measures of the BASIS-24 domains on each subject. To determine whether changes in the BASIS-24 domains were associated with screening positive for an alcohol or drug use disorder, a binary indicator for screening positive for a SUD was added to the linear mixed models that included the effects of time; in addition, the inclusion of an interaction between time and the binary indicator provided a formal

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comparison of whether the pattern of changes in the means of the BASIS-24 domains differed by those who screened positive for SUD versus those who screened negative.

All statistical analyses were conducted using SAS, version 9.4.

Results

The total number of adolescents and young adult patients who received ECT during the study period was N=292. Among these, N=102 (34.9%) were excluded from the analysis due to missing information, that is, they were missing either the initial (baseline) CMI assessment or the repeat BASIS-24 after the fifth ECT treatment. Thus, our study population consisted of the remaining N=190. During the study period, approximately 2,890 inpatients at our institution aged 16–25 years were treated, with approximately 6% treated with ECT. The study population and those excluded from analysis did not differ in a statistically significant way with regard to age, sex, race, and level of care where receiving ECT (i.e., inpatient, residential or ambulatory care) (data not shown). However, they did differ in terms of diagnosis, with patients diagnosed with depressive disorders less likely to be in the excluded population, while those with bipolar disorder or primary psychotic disorder were more likely (p=0.002). Those who were excluded from the study were also more likely to start with bilateral ECT rather than unilateral ECT ($p < 0.001$). The differences in diagnosis and ECT placement and pulse parameters suggest that the included sample had less severe illness compared to those who were excluded. Because incomplete information about SUD screening and BASIS-24 on admission was part of the exclusion criteria, data on these two variables were available for only approximately two thirds of the excluded sample. When compared to the included sample, there were no significant differences in rates of positive SUD screens and in mean BASIS-24 scores in any of the subdomains.

In the study population, the mean age was 21.0 years, 16 patients were under age 18, and 51.6% were female (Table 1). Sixty-four percent (N=122) screened positive for a substance use disorder. There was a variety of psychiatric diagnoses among the population of patients who received ECT, the most prevalent being depressive disorders (62.1%) and psychotic disorders (16.5%). The majority (67.9%) of patients initiated their ECT course while inpatient. Baseline BASIS-24 scores ranged from a mean (standard deviation) of 0.61 (0.89) for psychosis and 2.69 (0.88) for depression/functioning.

ECT was associated with significant clinical improvement in all five BASIS-24 domains in mid-acute phase treatment. Mean domain decreases (i.e., improvements) were found in depression/functioning (-0.84 ± 0.070, $p<0.001$; $t=-12.05$, $df=189$), interpersonal relationships (-0.36 ± 0.064, $p<0.001$; $t=-5.59$, $df=189$), self-harm (-0.65 ± 0.071, $p<0.001$; $t=-9.05$, $df=189$), emotional lability (-0.35 ± 0.067, $p<0.001$; $t=-5.25$, $df=189$), and psychosis (-0.17 ± 0.049, $p<0.001$; $t=-3.58$, $df=189$) (Table 2).

Compared to screening negative for a SUD, screening positive for a SUD was associated with greater self-reported mid-acute phase clinical improvement in several BASIS-24 domains: depression/functioning (−0.99 vs. −0.62, p=0.009; t=−2.63, df=188), interpersonal

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relationships (−0.47 vs. −0.20, p=0.045; t=−2.02, df=188), and emotional lability (−0.46 vs. −0.19, p=0.044; t=−2.03, df=188) (Table 3).

Discussion

To our knowledge, this is the largest case series of ECT in adolescents and young adults published to date. Our data show that acute phase treatment in transitional age youth who have varied psychiatric disorders was associated with significant improvement, as demonstrated by patient self-reported outcomes in the BASIS-24. This is consistent with prior literature from smaller case series in adolescents and young adults with psychotic disorders, depression, and catatonia[17,26].

Additionally, we found that screening positive for co-occurring SUD was common in our sample (60%), and associated with greater improvement in acute phase ECT outcomes in BASIS-24 subdomains of self-reported depression/functioning, interpersonal relationships, and emotional lability, compared to screening negative.

Possibly, our finding of improved outcomes in adolescents and young adults who screened positive for SUD is an artifact of abstinence from substance use during ECT treatment, rather than a direct effect of ECT on these clinical domains. Inpatients would not have access to alcohol or drugs during ECT treatment and outpatients at our institution are asked to cease the use of all substances during their ECT treatment course. In particular, opioid and cocaine use are a contraindication to ECT. Patients who cannot abstain from medical or other marijuana are asked to minimize their use to avoid difficulty evaluating efficacy/side effects of ECT. Anecdotally, we have observed that marijuana use during ECT tends to aggravate memory issues, both anterograde and retrograde. Alcohol use can affect seizure threshold and misuse can affect the safety of the anesthesia. In addition, adolescents and young adults may have lower seizure thresholds given their age and thus are at additional risk of prolonged seizures with alcohol use[9]. Also possible is that ECT itself (independent of reduced substance use/abstinence) may improve outcomes among adolescents or young adults, as it has been associated with activation of the dopamine system and enhanced modulation of dopamine transmission[27]. Alteration of the dopaminergic system is also implicated in substance use disorders, which may explain why those who screened positive for substance use disorders had significantly greater improvement from ECT. Further research will be needed to better clarify this relationship and how the dopaminergic system may be altered in those with substance use disorders. Though our finding differs from reports in the literature of adult patients where co-occurring SUD in general is associated with worse clinical outcomes for patients with psychiatric illness[28], an emerging ECT literature in adults has examined the association between SUD and ECT response and has found mixed results. Aksay and colleagues found that co-occurring substance use disorders was a predictor of worse clinical response to ECT[29], whereas Moss and Vaidya found that a history of co-occurring alcohol use disorders was a positive predictor of response to ECT[30]. More research is needed to clarify the role substance use plays in the recovery of adolescents and young adults who receive ECT and determine whether confounding factors may have influenced our results.

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There are some limitations worth noting in this study. First, our study was conducted at a single site and, rather than report on a psychiatric sample described by structured diagnostic interviews, we instead used a self-report symptom tool (the BASIS-24). However, the BASIS-24 is a well-validated tool to measure psychiatric symptom severity that has been validated in heterogeneous psychiatric diagnostic populations. Further, our baseline BASIS-24 domain means are similar in severity to means in a national sample of patients hospitalized for psychiatric disorders[22], thus demonstrating the generalizability of our sample from a national inpatient sample. Therefore, while we are not able to report our study results based on structured diagnostic research interviews, our results do reflect symptom outcomes in a usual care sample which better reflects the heterogeneity of adolescents and young adults who receive ECT. Additionally, we examined outcomes at mid-acute phase (i.e., after five treatments, approximately two weeks), which is shorter than the typical clinical duration of acute phase ECT. However, the adult ECT research finds that younger age is associated with earlier response[23], most patients respond to ECT within five treatments[24], and early response is associated with sustained response and remission[24,25]. In adolescents, a longer course of ECT may be required before a response is clinically apparent[31], therefore, while we expect that our results are a conservative estimate of clinical outcomes, measuring ECT response within five treatments is a clinically meaningful outcome. Third, the substance use measure included was a screen, not a diagnostic tool, assessing for problematic alcohol or drug use in the past thirty days and did not quantify substances of use or quantity of use. In addition, thirty-five percent of the adolescents and young adults who received ECT during the study period were excluded from our sample because they either did not have complete baseline information/assessments in the CMI, or did not complete a repeat assessment after the fifth treatment. We found that the patients who were excluded were similar in several observable demographic and clinical characteristics, but differed based on two characteristics consistent with illness severity diagnosis (i.e., individuals with bipolar disorder and psychotic disorders) and ECT placement and pulse parameters. These differences may be largely explained by the fact that patients were excluded based on missing data from computerized patient self-reported assessments, which may be more difficult for patients who are severely ill to complete due to symptoms including anxiety, agitation or psychosis. Our exclusion criteria were incomplete information about SUD screening status and BASIS-24 on admission or discharge; therefore due to data missingness, we were unable to provide definitive comparisons of the excluded versus included population on these characteristics. Thus, there is the possibility of a selection bias between those who were excluded due to incomplete assessments compared to those included in the study sample. Future study is needed to understand if there are differential clinical effects of ECT based on patient diagnosis and/or illness severity. Another limitation to note is that our study did not include a non-intervention control group and therefore we cannot rule out that the patients might have improved (or improved similarly) absent the ECT intervention. That said, typically ECT is prescribed after several rounds of ineffective prior treatment and/or in treatment-resistant individuals, making a “placebo effect” in these ECT-treated adolescents and young adults less likely. Also, we note that our assessment of the association between clinical improvement and screening positive for co-occurring SUD was not subject to this limitation.

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This study provides new and important information about a large sample of adolescents and young adults with severe mental illness who receive ECT in a large hospital-based usual-care sample. ECT was associated with clinical improvement. Furthermore, adolescents and young adults who screened positive for a SUD had greater improvement in clinical outcomes, compared to those who screened negative. More research is needed to clarify further which adolescents and young adult patients characteristics may be associated with differential ECT outcomes, and whether the differential improvement in certain domains for patients who screen positive for co-occurring SUD may be due to confounding factors (including, temporary abstinence from substances during treatment).

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Table 1.

Baseline patient characteristics for adolescents and young adults who had initial administrations of BASIS-24, substance use screening, and BASIS-24 after the fifth ECT.

	Study Population (N=190)
Age (mean ± SD)	21.03 ± 2.58
	N(%)
Female	98 (51.57)
Race/Ethnicity[1]	
White	161 (84.73)
Black	4 (2.10)
Asian	18 (9.47)
Latino/a	10 (5.26)
Education	
Some high school	26 (13.68)
High school graduate/GED	31 (16.31)
Some college	110 (57.89)
4-year college graduate	17 (8.94)
Post-college education	5 (2.63)
N Missing	1
Physical Health Rating	
Very poor	3 (1.57)
Poor	20 (10.52)
Good	97 (51.05)
Very good	51 (26.84)
Excellent	18 (9.47)
N Missing	1
Screened positive for Substance Use Disorder	122 (64.21)
N Missing	0
Location where patient received initial ECT	
Inpatient	129 (67.89)
Residential	16 (8.42)
Outpatient	45 (23.68)
N Missing	0
ECT Placement[2]	
Unilateral	179 (94.2)
Bilateral	7 (3.7)
N Missing	4 (2.1)
ECT Parameters[2]	
Brief	15 (7.9)
Ultrabrief	171 (90.0)
N Missing	4 (2.1)

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	Study Population (N=190)
Clinical Diagnosis	
Bipolar disorder, without psychosis	19 (10.11)
Bipolar disorder, with psychotic features	8 (4.26)
Depressive disorder, without psychosis	118 (62.11)
Depressive disorder, with psychotic features	10 (5.32)
Primary psychotic disorder	31 (16.49)
Other	1 (0.53)
Unknown	3 (1.60)
Baseline BASIS-24 Scores[3] (mean (SD))	
Depression/Functioning	2.69 (0.88)
Interpersonal Relationships	1.78 (0.73)
Psychosis	0.61 (0.89)
Self-harm	1.68 (1.21)
Emotional Lability	1.70 (1.06)

[1] Categories are not mutually exclusive

[2] Parameters given for initial ECT treatment

[3] BASIS-24 scores: 0 = none, 1 = a little, 2 = moderate, 3 = quite a bit, 4 = extreme difficulty

BASIS-24: Behavior and Symptom Identification Scale-24; ECT: electroconvulsive therapy; SD: Standard Deviation; GED: general equivalency diploma;

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Table 2.

Change in mean BASIS-24 score from baseline to the fifth ECT treatment for adolescents and young adults (N=190 patients) with complete data at baseline and follow-up.

	Baseline BASIS-24 Score*	BASIS-24 Score* After Fifth ECT	p-value
Depression/Functioning	2.69 (0.88)	1.89 (0.95)	<0.001
Interpersonal Relationships	1.78 (0.73)	1.44 (0.70)	<0.001
Psychosis	0.61 (0.89)	0.45 (0.80)	<0.001
Self-harm	1.68 (1.21)	1.07 (1.11)	<0.001
Emotional Lability	1.70 (1.06)	1.37 (0.97)	<0.001

* 0 = none, 1 = a little, 2 = moderate, 3 = quite a bit, 4 = extreme difficulty; BASIS-24: Behavior and Symptom Identification Scale-24; ECT: electroconvulsive therapy;

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Table 3.

Comparison of change in mean BASIS-24 scores between patients who screened positive for substance use disorders (SUD) (N=120) and patients who did not (N=70) for adolescents and young adults with complete data at baseline and follow-up.

	Score change based on SUD screening status*			
	SUD Screen Positive	**SUD Screen Negative**	**Difference**	**p-value**
Depression/Functioning	−0.99	−0.62	−0.37	0.009
Interpersonal Relationships	−0.47	−0.20	−0.27	0.045
Self-harm	−0.65	−0.63	−0.02	0.90
Emotional Lability	−0.46	−0.19	−0.27	0.044
Psychosis	−0.20	−0.13	−0.07	0.46

* 0 = none, 1 = a little, 2 = moderate, 3 = quite a bit, 4 = extreme difficulty; BASIS-24: Behavior and Symptom Identification Scale-24; ECT: electroconvulsive therapy;