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COMPARING STIMULANT EFFECTS IN YOUTH WITH ADHD SYMPTOMS AND EPILEPSY

Joseph Gonzalez-Heydrich, M.D.^a, Olivia Hsin, Ph.D.^a, Sarah Gumlak, S.B.^a, Kara Kimball, M.P.H.^a, Ashley Rober, B.S.^a, Muhammad W. Azeem, M.D.^b, Meredith Hickory, Psy.D.^c, Christine Mrakotsky, Ph.D.^a, Alcy Torres, M.D.^d, Enrico Mezzacappa, M.D.^a, Blaise Bourgeois, M.D.^e, and Joseph Biederman, M.D.^f

^aDepartment of Psychiatry, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA

^bAlbert J. Solnit Children's Center, Middletown, CT, USA

^cPeak Development Associates, Apex, NC, USA

^dDepartment of Neurology, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA

^eDepartment of Epilepsy & Clinical Neurophysiology, Boston Children's Hospital, Harvard Medical School, Boston, MA

^fDepartment of Psychiatry, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Abstract

To retrospectively examine response to stimulant treatment in patients with epilepsy and ADHD symptoms as predicted by seizure freedom for six months, use of methylphenidate (MPH) versus amphetamine (AMP) preparations, and cognitive level, medical records were searched for patients under age 18 with epilepsy and ADHD symptoms treated with MPH or AMP ($n = 36$, age 10.4 ± 3.5 ; 67% male). “Responders” had a CGI-Improvement score of 2 and did not stop medication due to adverse effects. “Worsened” patients discontinued medication due to agitation/emotional lability. Seizure freedom did not predict treatment response. Lower cognitive level was associated with increased rate of worsening ($p=0.048$). No patients who were seizure-free at start of the medication trial experienced an increase in seizures. Of the patients having seizures at the start of trial, one patient on MPH and two on AMP had increased seizures during the trial. Seizures returned to baseline frequency or less after stimulant discontinuation or anticonvulsant adjustment. MPH was associated with a higher response rate, with 12 of 19 given MPH 0.62 ± 0.28 mg/kg/day compared to 4 of 17 given AMP 0.37 ± 0.26 mg/kg/day responding ($p=0.03$).

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Corresponding Author: Joseph Gonzalez-Heydrich, MD, 617-355-6680, Joseph.Gonzalez-Heydrich@childrens.harvard.edu, Boston Children's Hospital, Department of Psychiatry: Fegan 8, 300 Longwood Ave, Boston, MA 02115.

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MPH treatment and higher cognitive level were associated with improved treatment outcome while seizure freedom had no clear effect. Confidence in these findings is limited by the study's small, open label, and uncontrolled nature.

Keywords

Epilepsy; Seizures; ADHD; Stimulant; Methylphenidate; Amphetamine; Pharmacotherapy

1. Introduction

There are relatively few studies of stimulant treatment in youth with co-occurring epilepsy and Attention Deficit Hyperactivity Disorder (ADHD) [1, 2]. This has led clinicians to prescribe standard ADHD medications to these children despite the meager evidence base. This retrospective chart review study examines the treatment outcomes of children with epilepsy who were prescribed either methylphenidate (MPH) or amphetamine (AMP) preparations for symptoms of ADHD.

Compared to the estimated 2–16% of school age children in the general population with ADHD [3, 4], rates of ADHD in children with epilepsy range from 30–40%, making ADHD the most common behavior problem that is associated with pediatric epilepsy [2]. ADHD symptoms have deleterious effects on youth with and without epilepsy. In ADHD patients without epilepsy, studies have found robust and approximately equal response rates to MPH and AMP preparations [5, 6]. However, there are concerns about potential seizure related adverse effects. For example, the Physician's Desk Reference [7] contains warnings not to use methylphenidate in patients with seizures. While these warnings have little empirical support, chart reviews have shown an initial reluctance to diagnose and initiate ADHD treatment in children with epilepsy [8].

There have been few prospective studies on the use of MPH for the treatment of comorbid epilepsy and ADHD. In a double-blind placebo crossover MPH trial, in a study of 10 children with ADHD and well-controlled epilepsy on one antiepileptic drug [9] Feldman and colleagues found that on a 0.3mg/kg/dose of MPH twice per day 70% of participants had improved and none experienced seizures during the trial. Gross-Tsur and colleagues [10] studied 30 children with ADHD and epilepsy in an open-label study with a single-day double-blind crossover portion. After a two-month observation period, a single morning 0.3 mg/kg/day MPH dose was given for 8 weeks. According to parent report, 70% of the children had an improvement in ADHD symptoms. None of the children who had been seizure-free during the observation period experienced seizures during MPH treatment. Five patients with an average of 1.8 seizures/week during the observation period experienced an average of 3 seizures/week during MPH treatment ($p=NS$). Following 57 children with epilepsy on open label MPH for one year, Gucuyener and colleagues found that the average seizure frequency during the year of treatment did not increase [11].

In contrast, Hemmer and colleagues [12] studied 205 children with ADHD who did not have epilepsy but underwent EEG examination prior to starting MPH. Thirty-six patients exhibited epileptiform activity. Three out of these 36 patients had new onset seizures

compared to one of the 169 with a normal EEG. A randomized controlled crossover study of 33 children with ADHD and epilepsy demonstrated good efficacy for an extended release-MPH preparation (OROS-MPH), but found some evidence of increased seizure risk with higher MPH doses [13]. Yoo and colleagues assessed tolerability and effectiveness of MPH with respect to quality of life improvements for patients with ADHD and epilepsy. While quality of life improved, there were two seizures among the 25 patients in this trial, though this study was not designed to address the question of MPH effect on seizure risk. Collectively, these studies suggest that MPH can improve ADHD symptoms in children with epilepsy, though none had enough statistical power to determine conclusively whether MPH is associated with an increase in risk of seizures [14].

Even less research exists to guide treatment with AMP products. There is only one study of AMP preparations used to treat ADHD symptoms in children with epilepsy. Ounsted found that only 10% of patients with epilepsy and impulsive/hyperactive symptoms responded well to dextroamphetamine [15]. There is also a case report of possible seizure in a 9-year-old girl after taking mixed AMP salts [16].

While the above studies provide valuable data on the effect of stimulants in patients with epilepsy, they are difficult to generalize to actual clinical practice where children with epilepsy are often taking multiple antiepileptic drugs, have other comorbid medical conditions, and may require higher doses of stimulant preparations. They also do not address cognitive impairment, which commonly accompanies epilepsy and ADHD. Studies have found a positive, but reduced response to stimulant treatment in children with cognitive impairments [20, 21]. Furthermore, they do not address the significant clinical question as whether to prescribe stimulants in the face of ongoing seizures.

These studies also do not compare the effects of MPH and AMP in patients with epilepsy. Both MPH and AMP competitively bind to the dopamine and norepinephrine transporter, thus blocking the reuptake of dopamine and norepinephrine from the synapse [17]. However, AMP also causes release of catecholamines from intracellular vesicles [18]. In theory, this additional effect of AMP might decrease the ability of presynaptic autoreceptors and other homeostatic mechanisms to dampen the increase in dopamine and norepinephrine at the synapse, thereby reducing its tolerability [18].

This study examined the response to and tolerability of stimulants in youth with co-occurring epilepsy and ADHD symptoms seen in an outpatient clinical program. Seizure status (seizure-free for at least six months versus not), the type of stimulant medication (MPH versus an AMP preparation), and patient cognitive level were hypothesized to predict differential response to stimulant medication.

2. Methods

2.1. Participants

Between 11/1998 and 11/2002, the electronic medical records system (EMRS) of the Boston Children's Hospital's Psychopharmacology Clinic [19] was searched for patients <18 years with a diagnosis of epilepsy who had past or current treatment with MPH or AMP

preparations. Most patients were referred from the clinician treating their epilepsy to the outpatient psychopharmacology clinic specifically for treatment of their ADHD symptoms. Epilepsy was defined using International League Against Epilepsy (ILAE) criteria [22] as a history of repeated, afebrile, unprovoked seizures, or a single seizure that lasted longer than 15 minutes before starting antiepileptic treatment or the presence of electroencephalographic (EEG) findings clearly implicating an epilepsy diagnosis [23]. Patients with febrile seizures, seizures occurring only during an acute illness with known metabolic dysfunction, or isolated seizures were excluded. This study was approved by the Hospital's Committee on Clinical Investigation and conducted in accordance with institutional guidelines.

2.2. Procedures

During patient visits, the treating child psychiatrist or nurse practitioner enters information prospectively into the EMRS which includes entries for all the axes of the DSM-IV, Clinical Global Impression (CGI) [24] scores, and narrative fields for psychiatric history, medical history, laboratory evaluations, psychiatric history, and demographic information [19]. Information was based on treating clinicians' interviews with the patient and family during the visits. Missing data and some neurological information were abstracted from the patient's medical charts at the hospital.

2.3. Patient characteristics

The following information from the EMRS and medical charts were obtained: demographic information, psychological information such as clinical psychiatric diagnoses, and neurological information such as seizure types, description of earlier EEGs, and characterization of abnormal EEG localization. As this was a retrospective chart review, the clinical psychiatric diagnoses recorded were those given by the treating clinician and were not based on structured interviews. For patients given a clinical diagnosis of ADHD, information in the medical record was insufficient to reliably categorize the ADHD into its subtypes.

Patients had all begun stimulant treatment in the clinic. "Baseline visit" was defined as the last visit for which patient data were available before beginning stimulant medication. "Last visit" was the last visit during which the patient was still taking stimulant medication or, if the patient discontinued the stimulant between visits, the visit immediately after discontinuation. The last visit was examined for the effects of the stimulant and the length of treatment, as well as dosages of stimulants and concurrent medications.

2.3.1. Seizure frequency—Seizure frequency for the 6 months before beginning stimulant treatment, during the trial and at its end was determined by patients and/or parents reports on the number of seizures experienced during a given period of time. Despite limitations [25, 26], use of a seizure count was considered appropriate in this population because patients with pediatric epilepsy and their parents have considerable experience in recognizing seizures, increasing the likelihood that their reports would be accurate [27].

2.3.2. Seizure Status—Patients were considered "Seizure-Free" if they had been seizure-free for at least six months prior to starting the stimulant, while patients were categorized as

“Not-Seizure-Free” if they had had at least one seizure in the six months prior to starting the stimulant. The six-month time frame was deemed more reliable than a shorter time frame given the frequency of patient visits noted in the medical records.

2.3.3. Type of Stimulant—Patients were grouped into those who received MPH or AMP preparations. Six participants had trials with both MPH and AMP preparations, and in these instances only the first trial was analyzed. The differences among the two groups regarding psychiatric clinical diagnosis, seizure types, concurrent medications, and clinical effect and tolerability of stimulants were compared.

2.3.4. Cognitive Level—The medical records for each patient were examined by a postdoctoral fellow in neuropsychology and information on IQ was then reviewed with an attending neuropsychologist. Patients were put into categories based on intelligent quotients (IQ) as determined by information in their medical records: profound Intellectual Disability (ID) (IQ<20–25), severe ID (IQ 25–40), moderate ID (40–55), mild ID (55–70), Borderline ID (71–80), Low Average (81–91), Average (92–108), High Average (109–118), Superior (119–134), and Very Superior ability (135+).

2.3.5. EEG Information—EEG information was abstracted from the treating neurologist’s notes in the medical charts to determine whether type and location of seizures might be associated with different outcomes. To ensure that differences in trial outcomes were not biased by people who had already failed other stimulant trials, we treated the number of previous stimulant trials that patients had undergone as a potential continuous independent variable as well.

2.3.6. Illness Severity—The CGI-Severity (CGI-S) scores entered by the clinician prescribing the stimulant at baseline and last visit were examined to estimate the severity of the psychiatric illness prior to starting and while being treated with stimulant medication. The CGI-S is a 7-point scale used by clinicians to indicate severity of a patient’s symptoms with 1 indicating “normal” and 7 “extremely ill” (NIMH, 1985).

2.3.7. Change in illness—The CGI-Improvement (CGI-I) score entered by the treating clinician at the last visit was used to estimate improvement or worsening of psychiatric symptoms compared to baseline. The CGI-I is a scale used by clinicians to rate clinical improvement since baseline. The scale runs from 1 to 7, with 1 indicating that the patient is “very much improved” and 7 indicating that the patient is “very much worse” [21].

2.3.8. Result of trial—Patients were classified as “Responders” if they did not stop stimulant medication due to adverse effects and had a CGI-I score of 1 or 2 (psychiatric symptoms very much or much improved) at the last available visit. This dependent variable was dummy-coded to indicate whether a patient was a responder or not.. “Worsened” patients discontinued medication due to agitation or emotional lability; these patients are a subset of the patients who discontinued due to adverse effects. This dependent variable was also dummy-coded to indicate whether or not patients worsened. Other adverse effects that lead to discontinuation, such as tics, appetite suppression, and insomnia, were tracked.

2.4. Analyses

The differences between the Seizure-Free group versus the Not-Seizure-Free group were compared regarding psychiatric diagnosis, seizure types, concurrent medications, and effectiveness and tolerability of stimulants.

T-tests were used to identify differences between groups on continuous variables. Wilcoxon signed rank test was used to identify differences in median CGI scores between start and end of trial, and differences in CGI scores between groups. Chi-square was used to determine if there were differences in rates of diagnoses between groups (e.g., learning disorders in seizure-free versus not-seizure-free groups). Multiple hierarchical regression was used to examine the association between potential predictors and final CGI-severity score, controlling for covariates.

Logistic regression models identified significant predictors of being a “Responder” or “Worsened”. Although seizure status, stimulant type (MPH or AMP), and cognitive level were the main variables we believed would be significant predictors, we also included the following independent variables into the logistic regression model using stepwise selection technique initially: age, sex, previous stimulant trial result, number of previous stimulant trials, and seizure type. Significant predictors from the stepwise selection technique in Statistical Analysis Software (SAS® 8.0 and 9.0) were kept in the final model. Forward selection was used in the final model and run in SPSS 14.0 to determine percentage of variance explained by predictors.

3. Results

There were 36 patients with epilepsy (mean age 10.4 ± 3.5 ; 67% male), of which 19 were treated with MPH (average dose 0.62 ± 0.28 mg/kg/day) and 17 were treated with AMP (average dose 0.37 ± 0.26 mg/kg/day). Descriptive information on patient demographic and treatment characteristics are presented in Table 1.

3.1. Seizure-Free versus Not-Seizure-Free Patients

In the six months preceding the start of stimulant treatment, there were 17 (47%) Seizure-Free and 19 (53%) Not-Seizure-Free patients. In the latter group, the patients experienced 1–75 seizures per month. The treating clinician did not assign a diagnosis of ADHD for all of the patients in the study. One out of 17 of the Seizure-Free and 5 out of 19 Not-Seizure-Free patients were not assigned a clinical psychiatric diagnosis of ADHD ($p=NS$). These two groups did not differ significantly in terms of age, sex, types of seizure, number of prior psychotropic trials, or rates of comorbid clinical psychiatric diagnoses. The mean number of concomitant antiepileptic medications at the start and end of trial was higher in the Not-Seizure-Free group ($t(34)=4.003$, $p<0.000$; $t(34)=4.590$, $p<0.000$, respectively). The proportion of patients who were prescribed MPH versus AMP preparations was not significantly different between the groups.

At the end of the trial, the mean and median CGI-S scores for the Seizure-Free versus Not-Seizure-Free groups were not significantly different. There was also no significant difference in the percentage of responders who were Seizure-Free (53%) and Not-Seizure-

Free (37%) or in the percentage of Seizure-Free patients (17%) and Not-Seizure-Free patients (37%) who worsened.

3.2. MPH versus AMP Treated Patients

Results of MPH and AMP groups are summarized in Table 2. The MPH and AMP groups did not differ significantly in terms of age, seizure status, types of seizure, number of concurrent antiepileptic or psychotropic medications at the start and end of trials, cognitive levels, number of prior psychotropic trials, mean CGI-S score at baseline, or in the rates of comorbid clinical psychiatric diagnoses. There was a significant difference between the groups in terms of gender; 16/19 patients in the MPH group were male whereas 8/17 patients in the AMP group were female ($\chi^2(1)=5.573$, $p=0.018$). There were more patients in the MPH group (11/19) than the AMP group (4/13) who were diagnosed with a learning disorder ($\chi^2(1)=5.573$, $p=0.018$).

The MPH group had a significant change in CGI-S scores ($t(18)=4.359$, $p<0.001$) for means; $Z=-3.094$, $p=0.002$ for medians), whereas there was no significant difference for the AMP group. At the end of trial, the MPH participants were rated as having less severe symptoms than AMP participants. While there was no significant difference between the CGI-S scores of MPH and AMP groups at the start of trial, there was a significant difference at the end of trial between the MPH group (mean = 3.79, median = 4, range = 2–6) and AMP group (mean = 4.65, median = 5, range = 3–6), ($t(34)=-2.606$, $p=0.014$ for means; $-Z=2.418$, $p=0.016$ for medians). There were more responders in the MPH group (12/19) than in the AMP group (4/17) ($\chi^2(1)=5.707$, $p=0.017$).

3.3. Cognitive Level

Half the patients (18/36, 50%) had IQs falling in the intellectually disabled (ID) range. Table 3 shows the distribution of patients' cognitive level. In hierarchical multiple regression, patients' cognitive level was not significant for independently predicting CGI-severity score at the end of trial after controlling for the type of stimulant prescribed. However, in examining whether patients were responders, there was a slight trend for cognitive level to be associated with chance of responding ($p=.133$), with higher cognitive level being associated with better chance of being a responder.

3.4. Response to Stimulants

Seizure status (Seizure-Free or Not-Seizure-Free) was not significant in predicting response. There was no significant difference in responder rates between Seizure-Free patients (53%) and Not-Seizure-Free patients (37%).

We used a model with the CGI-S at end of trial as the dependent variable (i.e., examining purely the symptom severity without taking into account whether the patient discontinued medication despite decrease of symptoms), baseline CGI-S as the first step, seizure status as the second step, cognitive level as the third step, and stimulant level as the fourth step. Hierarchical multiple regression indicated that this model was significant ($F(3,38)=3.127$, $p=0.037$). Models without stimulant type were insignificant as summarized in Table 2. The final regression equation was $\text{CGI-S}' = 2.25 + 0.37 (\text{baseline CGI-S}) - 0.33 (\text{Seizure Status})$

– 0.02 (Cognitive Level) +.88 (Stimulant Type). This model explains 29.4% of the variance. However, stimulant type was the only variable that independently and significantly predicted CGI-S score ($p = 0.009$), with MPH treatment being associated with less severe symptoms at the end of the trial and accounting for 16.3% of the variance in CGI-S scores.

There were a significantly higher percentage of responders to MPH (63%) than to AMP (24%). There was no significant difference in percentage of seizure-free patients in AMP and MPH groups, nor were there significant differences in age or cognitive level. Using logistic regression to examine odds ratios for being a responder, MPH was associated with a 5.57 greater chance of treatment response than AMP preparation ($\chi^2(1)=5.903$, $p=0.015$). There was a trend for cognitive level to predict whether a patient was a responder ($p=0.13$). Age, type of seizure, and previous stimulant trial results were not associated with differences in chances of being a responder to medication.

3.5. Tolerability

Patients' discontinuation of medication due to worsening agitation or emotional lability was predicted by lower cognitive level ($p=0.048$) and not by medication type or seizure status. There was no significant difference in the rates that patients discontinued stimulant treatment due to adverse events between the Seizure-Free group (35%) and Not-Seizure-Free group (53%). In the Not-Seizure-Free group, 3 out of 19 patients had a worsening of seizures while on a stimulant. One patient stayed on AMP and had her anticonvulsants adjusted; she later became seizure free while she was still taking AMP. Two of the patients discontinued the stimulant due to increase in seizures: one was on MPH and the other on AMP. Both returned to their baseline seizure frequency after discontinuing the stimulant.

4. Discussion

This retrospective study of youth with comorbid epilepsy and ADHD found that, contrary to expectations, being seizure free did not predict response to stimulant treatment. Lower cognitive level was associated with increased risk of worsening and adverse events. MPH preparations were associated with an increased rate of treatment response; however, since there was no randomization to MPH versus AMP, this should be interpreted with caution. This study is unique in the literature about youth with co-occurring epilepsy and ADHD symptoms given its examination of seizure status, stimulant type, and cognitive level as predictors of response in the context of actual clinical practice.

Our study did not find an association between seizure type and response. The literature on the association between seizure type and behavioral problems is inconsistent and mixed. Dunn and Austin [28] found that seizure type has been inconsistent for predicting pediatric behavioral problems. In contrast, Austin and colleagues have also found more behavioral problems in children with generalized seizures than in children with partial seizures in one study [29] and no difference in behavior problems dependent on seizure type in another study [30].

4.1. Seizure Status

The findings suggest that youth with active seizures may benefit from a stimulant medication trial. Patients who had experienced seizures in the six months prior to start of their stimulant trial did not significantly alter the probability of being a responder to a stimulant medication and/or of discontinuing medication due to worsened agitation or mood lability. Although the difference did not reach statistical significance, it is worth noting that there was a higher percentage of not-seizure-free patients than seizure-free ones who discontinued medication due to adverse events. Three of the patients with seizures in the six months prior to the stimulant trial had increased seizure frequency while on stimulant medication, though this may have been due to underlying variability in their seizure frequencies. A placebo controlled trial in youth with frequent seizures is needed to determine whether MPH or AMP preparations increase seizure risk in a substantial proportion of these children.

It is encouraging to see that a fair percentage of patients in both seizure-free and not-seizure-free groups were responders to stimulant medication, and that all three patients who had increases in seizures were able to have their seizure frequency return to baseline or below after an adjustment of anticonvulsants or removal of stimulant medication.

4.2. Stimulant Type

The percentage (63%) of MPH responders was similar to the response rate in the studies of Feldman and colleagues [9] and Gross-Tsur and colleagues [10]. The much lower rate of response to AMP preparations (24%) was similar to Ounsted and colleagues [15] who found a 10% AMP response. While AMP treatment needs to be further studied, the available data suggests MPH as opposed to AMP preparations, are the better initial stimulant treatment in these children.

4.3. Cognitive Level

The results suggest patients with epilepsy and ADHD with lower cognitive levels are more likely to experience adverse and worsening symptoms while on stimulant medication, yet many of these children did tolerate and respond to stimulants. Thus, with careful monitoring, a stimulant trial can be undertaken in these children..

4.4. Limitations of the Study

This study is limited by its retrospective nature, lack of randomization between MPH and AMP treatment, small sample size, and non-blinded status of the clinicians recording outcomes as part of their routine clinical treatment of these patients. Another potentially confounding variable is that many patients were receiving concurrent medications and psychosocial interventions, which might have contributed to suspected improvement. Larger prospective randomized studies comparing response to MPH, AMP, and placebo treatment will be necessary to answer definitively how stimulant type, seizure-free status, and cognitive level affect rate of response and adverse effects in children with ADHD plus epilepsy. Also, with the information available in the medical record we were unable to reliably categorize the participants into ADHD subtypes. As the inattentive form of ADHD

is much more common in children with epilepsy, this categorization would be clinically useful in future studies [31].

4.5. Implications of the study

This study provides support for the premise that current seizures are not reason enough to avoid stimulants in patients with comorbid epilepsy and ADHD, provided that children are carefully monitored. Youth with lower cognitive functioning require especially careful monitoring, and their families must be informed of potentially increased risk for worsening of symptoms. This study highlights the need for prospective, randomized, and controlled studies in children with comorbid epilepsy and ADHD large enough to compare the effects of seizure frequency and type, cognitive level and the use of MPH versus AMP in order to guide treatment.

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Research Highlights

- Seizures in the six months prior to start of a stimulant trial did not significantly alter the probability of a good clinical response to the stimulant in children with epilepsy.
- Lower cognitive level was associated with a higher probability of worsened agitation and/or emotional lability on the stimulant in children with epilepsy.
- No patients who were seizure-free at start of the stimulant trial experienced an increase in seizures in this sample of children with epilepsy.

Table 1

Patient Demographic and Treatment Characteristics of Youth (n=36) with Co-Occurring Epilepsy and ADHD

	Seizure Free	Not Seizure Free	Total
Number of Patients	17	19	36
Gender (Percent Male)	71%	63%	67%
Age	12.3 ± 6.9	10.1 ± 3.8	11.2 ± 5.4
Diagnosis (patients may have more than one diagnosis)			
ADHD	94%	74%	84%
Intermittent Explosive Disorder	6%	37%	22%
Bipolar Disorder NOS	24%	11%	16%
Anxiety Disorder	24%	21%	22%
Depressive Disorder	18%	21%	19%
Learning Disorder	47%	68%	57%
Pervasive Developmental Disorder	12%	11%	11%
Intellectual Disability	41%	58%	50%
Psychotic Disorder	0%	5%	3%
Seizure Type (patients may have only 1 seizure type)			
Generalized	61%	79%	70%
Localization Related	33%	21%	27%
Undetermined	6%	0%	3%
Prior Psychotropic Trials	2.8 ± 2.6	2.8 ± 1.8	2.8 ± 2.1
Concurrent AED Start *	0.47 ± 0.61	1.30 ± 0.64	0.93 ± 0.75
Concurrent AED End *	0.47 ± 0.61	1.35 ± 0.71	0.95 ± 0.78

* p<0.05 Significant difference between the Seizure-Free and Not-Seizure-Free groups.

Table 2

Comparison of Results between Amphetamine and Methylphenidate in Youth (n=36) With Co-Occurring Epilepsy and ADHD

	Amphetamine	Methylphenidate
Number of Patients	17	19
Average Dose	0.37 ± 0.26 mg/kg/day	0.62 ± 0.28 mg/kg/day
CGI Severity Start	4.71 ± 0.92; Median: 5	4.79 ± 0.86; Median: 5
CGI Severity End	4.65 ± 0.93; Median: 5	3.79 ± 1.03; Median: 4 ^{**}
CGI Improvement	3.41 ± 1.73; Median: 3	2.47 ± 1.74; Median: 2 [*]
Responders %	24%	63% ^{**}
Worsened %	41%	27%
Discontinuation due to AE	53%	37%

*
p=0.05,

**
p=0.02

Table 3

Cognitive level in Youth (n=36) with Co-Occurring Epilepsy and ADHD

	Frequency	Percent
Severe ID (IQ 25–40)	2	5.6
Moderate ID (40–55)	8	22.2
Mild ID (55–65/70)	8	22.2
Borderline ID (71–80)	5	13.9
Low average IQ (81–91)	10	27.8
Average IQ (92–108)	2	5.6
High average IQ (109–118)	1	2.8
Total	36	100