The Effect of Electroconvulsive Therapy (ECT) on Neuropsychological Functioning in Adolescents who suffer from Major Depressive Disorder

by

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Author Note

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Abstract

The primary aim of this study was to determine whether adolescents who undergo electroconvulsive therapy (ECT) for severe depression show neuropsychological deficits either before treatment or after. A chart review of 15 patients (8 females, 7 males; mean age=15.1 years \pm 2.7) who had data available for both pre- and post-treatment evaluation sessions was conducted. Domain scores for measures of intellectual functioning, academic achievement, verbal and visual memory, as well as executive functioning were computed when possible. We also retained scores for measures that were administered to all subjects. Baseline findings were examined for the number of test performances that fell 1.5 standard deviations below the normative mean. To examine significant change post-treatment, we computed matched-pair ttests for domain scores and individual measures. At baseline our results showed that only one measure fell below 1.5 standard deviations from the normative mean (i.e., visual motor speed). Matched-pair t-tests showed fine motor speed showed statistically significant gains between preand post-treatment evaluations. In contrast, visual motor speed (i.e., Trails B) declined. Baseline performances in our sample of patients showed that depressed patients exhibited relatively weaker performances in visual motor speed skills. Patients' performance post-ECT improved across most domains, particularly memory. Although memory complaints are typical in this group, the results show that patient's neuropsychological functioning appears to improve except for processing speed. These results should be regarded as preliminary, due to the small sample size.

Keywords: Depression, Adolescents, ECT, Neuropsychology

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Major depressive disorder (MDD; commonly known as "depression") is a mental illness that causes feelings of helplessness, loneliness, and sadness. This disorder leads to emotional and physical problems; depressive symptoms significantly interfere with an individual's day-to-day activities. In addition to feeling helpless, sad and lonely, depression may also produce marked changes in sleep habits and appetite, workplace and school difficulties, as well as suicidal ideation (Bylund, 2007). According to Kessler et al., (2003), major depression is the most common of all psychiatric disorders. In addition, the National Institute of Mental Health states that MDD occurs in 6.7% of the U.S. adult population; 2.0% of diagnosed cases are classified as having severe depression (Kessler, 2005). The World Health Organization estimates that, at the current rate of around 14 million adults per year in the U.S. (Kessler, 1994), depression will be the second most common disability after heart disease by the year 2020 (Michaud, 2001).

Depression not only affects adults but is also common in children and with up to 38% of children experiencing at least one depressive symptom in their life (Lewinsohn, 1998). Point prevalence estimates of depression in children and adolescents ranges between 2 and 5% with estimates varying by age (Birmaher et al., 1996, Byland & Reed, 2007; Lewinsohn, Rohde, & Seeley, 1998). Among adolescents, the point prevalence of depression ranges between 4-8% and steadily rises to 25% among older adolescents (Kessler et al., 2001). Factors that influence risk of depression in adolescents include socioeconomic status (particularly poverty), stressful life events, early abuse and neglect, and interpersonal problems (Hill et al., 2004; Shanahan, Copeland et al., 2011). In addition, negative cognitive style has also been shown to contribute to the development of depression (Lewinsohn, Rohde, & Seeley, 1998).

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Studies examining the neuroanatomical correlates of depression are increasing. Adult depression for example has been shown to be related to limbic, frontal, and subcortical regions (Langenecker, Lee, & Bieliauskas, 2009). Neuroanatomic studies of depression in children and adolescents are quite rare. However, those studies that have examined children and adolescents have reported similar alterations in subcortical, limbic, and frontal regions. For example, Frodl et al. (2004) examined hippocampal volume in two groups of never depressed and depressed adolescents at intake and 1 year later. No significant differences were found in hippocampal structures of either group at baseline but these authors did find that hippocampal structure volume at follow up was associated with the level of depression reported. Volumetric studies of adolescent depression have also shown significant reductions in prefrontal white matter volumes, as well as whole brain volumes (Hamilton et al., 2012). With regard to the amygdala, a limbic structure associated with mood, children and adolescents with MDD have shown variable volumetric differences with the consensus being that with initial onset of a first depressive episode, amygdala volumes increase in size reflecting hyper activation, but then over the duration of the illness, volumes decrease (Hulvershorn, 2011).

Although symptoms for both adult and adolescent depression are similar, the largest difference is the way adolescents react to treatments for depression. There are two main types of treatments that have been shown to be effective in treating depression in young adults: firstly, *psychotherapy* including cognitive behavioral therapy and secondly, *pharmacotherapy* (i.e., medications; Cheung et al., 2007). Despite studies showing good effects for either therapy or pharmacotherapy in adolescent depression, not all adolescents respond to either treatment modality (Cheung et al., 2007). In such cases, patients may be considered for non-conventional forms of treatment, such as Electroconvulsive Therapy (ECT).

According to Lisanby (2007), ECT involves an electrical shock to the head, which induces seizures. ECT has been documented to minimize depressive symptoms, but it also appears to have benefits for neurobiological functioning. In terms of depression, the Consortium for Research in ECT (CORE) reported a remission rate of 75% for 217 patients who had completed a short course of ECT, with 65% of these patients achieving remission through the fourth week of ECT (Husain et al., 2004). In addition, the United Kingdom ECT Review Group conducted a meta-analysis on ECT therapy in comparison to pharmacotherapy and found that out of 18 trials involving 1,144 patients, a pooled effect size of 0.80 was found, which corresponds to a "large" effect in reduction of symptoms (UK ECT Review Group, 2003). Furthermore, a meta-analysis found that antidepressant medications alone proved to be less effective than ECT with that study concluding that ECT showed more positive results than combination pharmacotherapy (Parker et al., 1992).

Although ECT is effective in the treatment of depression in adult patients, Freeman and Cheshire (1986) reported that ECT "has a negative image in the media" (p. 8). In a recent study by Lauber et al., (2004) it is stated that "based on outdated myths about the procedures and side effects, ECT is often depicted in the media as an inhumane or even sadistic form of treatment" (p. 205). Other psychologists and psychiatrists also perceive that "the anti-psychiatric movement is perpetuating this negative attitude [towards ECT], which is affecting the lay public and professionals" alike (Chanpattana et al., 2001, p. 100; Gass, 1998). Thus, there is a disconnect between research findings and media portrayals, which probably leads to the misconceptions about how ECT can be a beneficial treatment for serious mental health disorders in adults. In children and adolescents, very few studies have been conducted examining the efficacy of ECT. This may reflect negative attitudes that many physicians and clinicians continue to hold (Bertagnoli & Borchardt, 1990; Parmar 1993). Parmar and colleagues (1993) found that child

psychiatrists demonstrated a "general reluctance towards physical treatments for depression as opposed to medications within this age group," even though these psychiatrists were "equally as likely to prescribe medication to these children as they would to adults suffering from depression" (p. 12). One likely reason that psychiatrists are hesitant to use ECT is the lack of knowledge and possibly limited scientific research examining the use of ECT in adolescent mental disorders. One study reported that only 1.5% of patients aged 11-20 were treated with ECT in 1980 (Thompson & Blaine, 1987). The lack of research focused on adolescents is most likely why this specific treatment is under-utilized in this age group (Ghaziuddin et al., 1996).

The primary use of ECT in adolescents is to alleviate and treat the symptoms for severe mood disorders, including depression. A study conducted by Rey and Walter (1997) showed that out of 154 patients, approximately 67% showed improvement in major depressive symptoms after undergoing ECT treatments. However, it is noteworthy that the participants in the Rey and Walter study were severely depressed and therefore conclusions about the efficacy of ECT in patients with less severe symptoms is limited (Prudic et al., 1996). However, Rey and Walter (1997) conclude that in adolescents who may be non-responsive to conventionally "safe" treatments, ECT may be the most effective treatment approach.

One of the main criticisms of ECT in any population has been the reported disturbance in cognitive functioning (Ingram, Saling, & Schweitzer, 2008). Several studies have reported that ECT appears to predominantly affect memory. Research has documented that many patients who have undergone ECT "experience difficulties in acquiring and retaining new information, known as anterograde amnesia as well as the ability to recall past events and information learned before ECT, known as retrograde amnesia" (Ingram et al., 2008, p. 4). With respect to anterograde amnesia, studies have shown that there are significant memory disturbances the first few days following ECT (Steif, Sackeim, & Portnoy, 1986). For example, Lerer et al. (1995) reported that

patients performed worse on memory tasks 1 month after ECT compared to their pre-ECT assessments. However, Steif et al. (1986) found that just four days after the patients completed their last ECT session, acquiring and retaining information returned to baseline levels. In addition, a follow-up study conducted by Sackeim et al. (1993) two months after treatment found *improvement* in patients' memory function exceeding the scores received at baseline prior to receiving ECT.

Factors that may contribute to differences in these study outcomes include ECT administration differences. Specifically, ECT administered through bilateral electrode placement (BL) as opposed to right unilateral placement (RUL) appears to confer greater memory impact (Sackeim, Prudic, & Devanand, 2000). Another difference may be how memory is measured in these studies. For example, patients have complained that they are unable to recall important events in their life, dubbed autobiographical memory (Sackeim, Prudic, & Devanand, 2000). However, as reported by Ingram et al. (2008), "retrograde or autobiographical memory is inherently difficult to measure in a standardized way because it must assess memory for information and events that are highly unique to [each] individual" (p. 5). More specifically, this kind of memory is difficult to assess objectively because typically there is no verification of an individual's unique recall.

Although Consoli, De Carvalho, and Cohen (2013) conclude that ECT treatment is associated with decreased general intellect, slower information processing speed/reaction time, decreased attention, reduced executive function, decreased visuospatial function and perception, and possible language deficits, other studies do not support this conclusion. In fact, most studies have shown mixed results on cognitive outcomes. With regard to neuropsychological outcomes and ECT in adolescents, several studies were conducted during the 40's and 50's and focused on general intellect (Rey & Walter, 1997). In one of the earliest studies examining cognition in

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ECT in children, Bender reported that ECT treatment was unrelated to intellectual functioning (1947). In another study conducted by Bender and Keeler (1952), "children were asked to draw human figures and perform the visual motor gestalt test" before undergoing ECT treatment (p. 336). The findings established that irregularities with cognitive functioning "lasted up to 6 hours after each daily ECT and increased throughout the course, but they cleared up approximately 36 hours after the last treatment" (Bender & Keeler, 1952, p. 353). More recently, a study conducted by Cohen et al. (2000) examined possible cognitive side effects in ECT treatment in an adolescent population. They compared cognitive profiles of 10 adolescents with severe mood disorders who had undergone ECT treatment on average 3 years earlier to a group of 10 adolescents on an inpatient unit with other psychiatric illnesses. The authors concluded that all but one of the depressed patients had a profile similar to the non-treated group including short-term memory, attention, new learning, and objective memory measures.

Studies focusing on specific neuropsychological domains in adolescents reported mixed results. For example, Kyte et al. (2005) reported no executive function impairments or verbal memory deficits in ECT. In contrast, other studies have reported declines in performance in these two domains (Matthews et al., 2008). However, it is also important to note that depression alone may also confer cognitive consequences. As Baune et al. notes "neurobiological disruptions in depressed individuals are particularly concerning for young people who are undergoing neurobiological and neuropsychological development" (Baune, Czira, Smith, Mitchell & Sinnamon, 2005; p. 442). Since adolescence is a time when the brain is still developing, it is also a time where a mood disorder, such as depression, could negatively impact that adolescents' neuropsychological development. Baune et al. (2012) found that depressed patients between the ages of 13-25, who suffer from depression showed "impairments on several neuropsychological domains of executive functioning" such as that of attention and working memory (p.445).

Previous studies on neuropsychological functioning have shown an association between how long a patient has suffered from depression, how severe it is, as well as the chronic stress associated with experiencing a depressive episode (MacQueen et al., 2003). A study by Fossati et al. (2004) found that adults who had suffered only one depressive episode did not display memory impairments, but those who had recurring depressive episodes did, which supports the notion that the duration as well as the severity of depression may immediately influence neuropsychological functioning.

Although ECT treatment is associated with positive response in adults and adolescents, it is also apparent that there are few studies examining the impact of ECT as well as depression on an adolescents' neuropsychological functioning. Because there are relatively few studies conducted on this to date, we examined whether ECT or depression affects neuropsychological functioning in adolescents. We hypothesized that at baseline, adolescents referred for ECT treatment due to severe depression would demonstrate neuropsychological deficits in processing speed, memory, intellectual, and executive functioning (Hypothesis 1; H1). In addition, at follow-up, we hypothesized that patients who have undergone ECT would demonstrate no changes in comparison to baseline neuropsychological functioning, or possibly improvements (Hypothesis 2; H2).

Method

Participants

Participants included in these analyses were patients who were referred for pre- or post-treatment evaluation for the years spanning 1995 to 2014 who had both pre- and post-ECT cognitive testing. Data comes from a retrospective chart review, approved by the IRB. A total sample of 73 patients were seen for routine clinical evaluations for their pre-ECT care, however, only a subgroup of these patients was seen at a follow up evaluation post-ECT (n=15; 53%

Female; Mage = 15.9 years, SD = 2.69; Mgrade = 9.7). Of those seen for post-treatment evaluation, both baseline inpatient testing and outpatient follow-up testing ranged between 1 and 36 months, with a mean follow up of 9.67 months (SD = 8.75). For baseline evaluations, patients were examined in their rooms in the inpatient unit. Follow-up evaluations were conducted on an outpatient basis in a clinic.

Materials and Procedure

Because patients were evaluated as a part of their clinical care, specific tests varied by patient; however, certain domains were included for every evaluation and are listed below. Patients' referrals were received by the clinic and patients were evaluated in their hospital rooms at baseline. Follow-up testing occurred on an outpatient basis. Because patients were tested over a span of several years, and because different tests were updated over the course of the years included in this analysis, some scores were computed based on composite computations. For example, estimated Full Scale IQ scores were computed based on three administered measures or estimated using a 2-subtest estimate. Sattler (2001) provides estimated Full Scale IQ scores for those cases and the scores were included for this analysis. Data were analyzed using IBM-SPSS version 19.1 (IBM Corp, 2010).

Intellectual functioning. Patients were assessed using one of four standardized measures of intellectual functioning. Currently the Wechsler Adult Intelligence Scale is in its fourth edition (WAIS-IV; Wechsler, 2008). However, earlier testing sessions used the WAIS-III [or third revision] (Wechsler, 1997). Both the WAIS-III and the WAIS-IV are comprised of 10 core subtests that go into the computation of the Full Scale IQ score. These measures are for patients aged 16 years and older. For patients ranging in age from six to sixteen years at the time of testing, the Wechsler Intelligence Scale for Children – Fourth Edition (WISC-IV; Wechsler, 2003) was administered. This measure also has 10 core subtests that comprise the Full Scale IQ

score. In addition, some patients were administered the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 2007), which includes measures of verbal and nonverbal reasoning skills, which are combined to compute a Full Scale IQ score. These measures were subsequently converted to a "domain" score labeled intellectual functioning. Each score reported has a mean of 100 and a standard deviation of 15. In addition, in some cases, the 2-subtest abbreviated Full Scale IQ was estimated using the formula provided by Sattler (2001).

Academic achievement. Patients were provided a brief screening of their reading abilities using the Wide Range Achievement Test-Fourth Edition (Jastak & Wilkinson, 1993), a 73-item word list. Administration of this test differs depending on the age of the patient. A patient that is between 5 and 7 years of age is administered a 15-25 minute test, while a patient who is 8 years of age or older is administered a 35-45 minute test (Wilkinson & Robertson, 2006). Scores reported are standard scores with a mean of 100 and a standard deviation of 15.

Verbal fluency. Patients were also administered measures of phonemic and semantic fluency, which assesses expressive language and executive skills. During the COWA test, a patient is asked to name words beginning with a specific letter (phonemic condition) or category (semantic condition) as quickly as possible in 1 minute. Obtained raw scores are compared to normative information including age, gender and education for conversion to a standardized score. (Semrud-Clikeman & Ellison, 2007).

Memory. Because memory difficulty is a frequent complaint in patients that undergo ECT, patients were administered story memory tasks from the Wechsler Memory Scale Third or Fourth Edition (WMS-III Wechsler, 1997; WMS-IV; Wechsler, 2009). The WMS-III is a comprehensive measure of both verbal and visual memory including story memory tasks (Wechsler, 1997). The Logical Memory subtest was used from this measure and includes an immediate free recall and a delayed recall trial. Obtained scores are compared to normative data

stratified by age and education, with standard scores reported with a mean of 100 and a standard deviation of 15. Verbal memory was assessed using the California Verbal Learning Test-Second Edition (CVLT-II; Delis, Kramer, Kaplan, & Ober, 2000). The CVLT-II test is a list learning measure comprised of 15 items from a 'shopping list,' and also includes an immediate and delayed recall trial. Like the other measures, obtained scores are transferred to standard scores based on age, and education and reported as standard scores. Visual memory was assessed by administering the Rey-Osterrieth Complex Figure Test, also known as the ROCF (Kimura, 1984). The Rey-Osterrieth Complex Figure Test material consists of Rey's complex figure, which is a complicated line drawing, which the subject is first instructed to copy. During immediate and delayed recall trials, patients are instructed to replicate what they saw during initial learning trials. Obtained scores are also transformed into standard scores with a mean of 100, and a standard deviation of 15.

Executive functioning. Executive functioning refers to the ability to plan ahead, and flexibly solve problems, and the Wisconsin Card Sorting Test was administered to assess this domain (WCST; Berg, 1948). The Wisconsin Card Sorting Test examines a person's ability to "set-shift" which means "... the ability to display flexibility in the face of changing schedules of reinforcement (Monchi, Petrides, Petre, Worsley, & Dagher, 2001, p. 7733). This task involves having patients sort cards over 64 trials, during which the sorting principle switches without warning. The Trail-making test was also used. *Trail A* requires subjects to trace around a piece of paper with a pencil as quickly as possible connecting digits from 1 to 15. *Trail B* taps more executive skills because it requires alternation between numbers and letters (Arnett & Labovitz, 1995). Both trials involve speed and accuracy. For the purposes of this study, we examined speed. Patient's performance speed was compared to normative age and education data and transformed to standard scores.

Motor functioning. The finger tapping test measures both motor speed and accuracy. In this test, patients place their dominant hand down first, with their fingers extended and their index finger resting on a lever that is attached to a counting device. The patients must tap their index finger as quickly as possible for ten seconds while simultaneously keeping their hand and arm immobile. Patients are required to perform this task over 5 to 10 trials, with a discontinuation criterion involving 5 trials within 5 "taps," or 10 trials total with breaks given. This entire procedure is repeated for the non-dominant hand. Raw scores for the number of taps per hand are computed and compared to age and gender matched normative data, and then transformed into standardized scores with a mean of 100, and a standard deviation of 15.

Mood and emotional functioning. Patients were administered the Beck Depression Inventory-Second Edition (Beck, 1996). This 21- item questionnaire is a brief self-report of depression which assesses symptoms of weight loss, changes in body image, somatic preoccupation, agitation, worthlessness, loss of sleep and energy as well as concentration difficulty.

Results

Baseline Findings

We examined baseline scores for the number of scores that fell 1.5 standard deviations below the normative means for each test. Thus, scores falling below a 78, which corresponds to the borderline range were inspected. As can be seen in Table 1, performance on the Trails B task fell in the borderline range. Notably, intellectual functioning, reading skills, and verbal memory all fell within one standard deviation of the mean or within the expected range.

Post-treatment Outcomes

To examine outcomes after ECT, we computed matched pair *t*- tests comparing subjects' performance prior to ECT treatment to their performance following ECT treatment and these

results are summarized in Table 1. At follow-up, Full Scale IQ scores, COWA, Rey immediate memory scores, and executive functioning scores improved after ECT treatment; however these results did not reach statistical significance. Test scores that slightly improved or remained constant were verbal memory and reading. Patients' scores on visual motor speed worsened or became slower at follow-up when compared to baseline tests. However, finger tapping for both the dominant and non-dominant hand performance showed a significant improvement following ECT treatment.

Discussion

The current study examined baseline neuropsychological performances in adolescent patients referred for ECT. Pre-treatment functioning showed patients performed 1.5 standard deviations below the mean on the Trails B task, a measure of visual motor speed and processing. This suggests that in our sample, depression appeared to effect cognitive efficiency and psychomotor speed.

Importantly, following ECT, patients' performance improved across most domains, particularly memory. Although memory complaints are typical in this group, our findings show that patients' cognitive functioning appears to improve overall, with the exception of processing speed. It is possible that patient complaints related to memory are actually a reflection of slower processing speed. The reasons why we did not find decrements in memory performance is unclear. It is possible that our population is not representative of the population at large as our hospital tends to draw from a relatively affluent and well-educated area. It is also possible that the memory assessments we performed did not directly evaluate the types of memory (i.e., autobiographical memory) usually reported to decline after treatment.

Although this is one of the few studies examining neuropsychological outcomes in adolescents who have undergone ECT, and further work needs to be done, an important

consideration is how those treated with ECT report feeling afterward. Although one of our study limitations is that we do not have this kind of information, a study conducted by Tajeb et al., (2001) does report perceptions of ECT treatment. Specifically, these authors sought out "10 patients' and 18 parents' attitudes and experiences towards the use of electroconvulsive therapy in adolescence" (p. 183). Many parents were concerned with possible brain damage, personality changes, and of seizures following ECT treatment. Most parents had difficulty accepting the fact that their children would be given electric shocks to induce seizures; however, it was easier for parents to give approval for ECT out of frustration from the ineffectiveness of other treatments and ultimately, their child's suffering overrode their apprehension with ECT. Another important point that Taieb et al. (2001) acknowledged was that "the efficacy of ECT had reassured them [the parents]" in going through with ECT treatment (p. 186). Although patients complained of memory loss immediately after ECT treatment, both the patients and parents agreed that overall they had positive experiences with ECT. In addition "all patients and parents disagreed with the statement: 'ECT is dangerous and should not be used' and all emphasized the effectiveness of treatment" (Taieb et al., 2001, p. 186). These results paralleled those of a previous study conducted by Walter et al. (1999a), which also showed that both adolescents treated with ECT, and their families viewed the treatment as a positive experience.

The limitations of our study include our sample size thus limiting generalizability. However, getting patients to come for return visits 1 year after treatment is a challenge. It is possible that because they are feeling better, they do not see a need for further evaluation. It is also possible that insurance changes contribute as they may no longer have coverage for neuropsychological services. In addition, as these studies were conducted on an inpatient unit, the distractions associated with this rather artificial setting are unknown. Further, we did not examine the influence of medications at either time point, an important possible contributor to

cognition. In addition, we were not able to more precisely measure depression and its potential influence on mood at baseline.

Future directions include working with insurance companies in understanding the importance of follow up care for this patient population and to build in repeat assessment availability at the start. Secondly, working with primary care physicians in keeping contact and communicating the importance of follow up evaluations to patients would be important.

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Table 1

Baseline & Follow-up means and SD's, t-test and Significance (p) of neuropsychological domain scores

Variable	Baseline Mean (SD)	Follow-up Mean (SD)	Matched Pair t-test	p
Full Scale IQ (standard score)	98.07 (20.52)	102.00 (19.82)	-1.63	.128
Word Reading (standard score)	92.86 (21.20)	92.14 (18.87)	0.25	.810
Verbal Fluency	85.58 (18.88)	87.08 (19.03)	-0.42	.684
Animals	101.92 (17.38)	98.42 (12.19)	0.62	.548
Story Memory (Scaled Score)	100.00 (13.06)	100.29 (12.06)	-0.33	.752
List Learning	99.00 (21.90)	97.00 (11.75)	0.17	.873
Visual Memory (T-score)	36.43 (11.93)	41.00 (11.63)	-0.87	.419
Executive Function- number of concepts	83.90 (18.96)	95.00 (15.62)	-1.76	.112
Finger Tapping: Dominant hand	84.75 (22.95)	101.00 (16.92)	-2.77	.028*
Non-dominant hand	79.50 (23.61)	101.25 (13.29)	-3.31	.013*
Trails A: seconds	86.89 (22.05)	101.44 (12.22)	-1.44	.189
Trails B: seconds	76.88 (19.95)	124.75 (24.16)	-3.83	.006**

Note. Scores reported are standard unless noted otherwise. * p < 0.05; **p < 0.01. Full Scale IQ score generated composite. Word Reading = WRAT-Reading; Story Memory=Logical memory; List learning = CVLT-II; Executive Function=WCST.