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# Validity of the T-ACE in Pregnancy in Predicting Child Outcome and Risk Drinking

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# Abstract

Preventing Fetal Alcohol Spectrum Disorders (FASDs) requires detection of in-pregnancy maternal risk drinking. The widely used T-ACE screen has been applied in various ways although the impact of those different uses on effectiveness is uncertain. We examined relations among different T-ACE scoring criteria, maternal drinking and child outcome. Self-reported acrosspregnancy maternal drinking was assessed in 75 African-American women. The different T-ACE criteria used varied the level of drinking that defined tolerance (2 or 3 drinks) and the total T-ACE score cut-points (2 or 3). Receiver-operator curves (ROCs) and regression analysis assessed the significance of relations. Increasing the total T-ACE score cut-point to 3 almost doubled specificity in detecting risk drinking while maintaining adequate sensitivity, equivalent to that in the original report, and identified substantially more neurobehavioral deficits in children. Redefining tolerance at 3 drinks did not improve T-ACE effectiveness in predicting outcomes. This study is among the first to show the ability of an in-pregnancy T-ACE assessment to predict child neurodevelopmental outcome. In addition, increasing the total T-ACE score criterion (from 2 to 3) improved identification of non-drinking mothers and unaffected children with little loss in detection of drinkers and affected children. Efficient in-pregnancy screens for risk-drinking afford greater opportunities for intervention which could prevent/limit FASDs.

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# Keywords

Alcohol use screens; Fetal Alcohol Spectrum Disorders (FASD); Fetal Alcohol Syndrome (FAS); Pregnancy; T-ACE

Fetal Alcohol Spectrum Disorders (FASDs) are characterized by wide-ranging deficits in growth, behavior, cognition, and central nervous system (CNS) dysfunction (Sokol, et al., 2003; Kodituwakku, 2007; Spadoni, et al., 2007). Fetal Alcohol Syndrome (FAS), the most severe expression of the FASDs, includes characteristic craniofacial malformations as well as growth restriction and neurobehavioral deficits (Bertrand, et al., 2005). The incidence of all FASDs is influenced by many cultural, demographic and medical factors (Abel and Hannigan, 1995; May, et al., 2007) and is estimated to occur in ~10 per 1000 live births in the general population (Manning and Hoyme, 2007; O'Leary, 2004), with 0.3 to 2.0 per 1000 live births for FAS (May and Gossage, 2001; CDC, 2002).

Several relatively simple, quick and economical screens for detecting problem drinking in pregnancy have become important clinical tools and are a first step in targeted prevention of the FASDs (ACOG, 2006). There is as yet no clearly defined minimum amount of alcohol known to be harmful to fetuses, nor any defined "safe" level of drinking during pregnancy (ACOG, 2006; Henderson, et al., 2007; Jacobson and Jacobson, 1994; Sokol, et al., 2003), so screens with high sensitivity to risk alcohol consumption are recommended as part of primary obstetrical care. Fetal risk drinking across pregnancy is defined as an average intake of  $\geq 0.5$  ounces of absolute alcohol per day across pregnancy (AADXP), or about 1 standard drink per day on average (Jacobson and Jacobson, 1994). Risk drinking during pregnancy can also be inferred from self-reported consumption about the time of conception, but before the woman knew she was pregnant, or average peri-conceptional intake of  $\geq 1.0$  ounces of absolute alcohol per day (AAD0), or about 2 standard drinks per day on average. Alcohol screening tools employed to detect drinking during pregnancy have included the Michigan Alcoholism Screening Test (MAST; Selzer, 1971), CAGE (Ewing, 1984), T-ACE (Sokol, et al., 1989), and TWEAK (Chan, et al., 1993). Each of these screens focus on assessing problems associated with drinking and/or tolerance (i.e., the "T" in "T-ACE" and "TWEAK"), and seek to overcome the intrinsic limitation of under-estimated maternal selfreport of alcohol consumption in pregnancy (Ernhart, et al., 1988; Morrow-Tlucak, et al., 1989). The briefer screens maintain ease of use by health care professionals, a critical feature determining a screen's practical value (cf., ACOG, 2004; 2006). Russell, et al. (1994; 1996) compared the CAGE, T-ACE and TWEAK to each other and to the MAST and concluded that the TWEAK and the T-ACE were more sensitive and more specific screens for risk drinking in pregnancy than the CAGE or the MAST.

NIAAA (2005) and the American College of Obstetrics and Gynecology (ACOG, 2004; 2006) recommend the T-ACE as a standard screen for detecting fetal risk drinking in pregnant women. The T-ACE had been devised to optimize sensitivity in detecting risk drinking in pregnant women (Sokol, et al., 1989). However, the utility of the T-ACE in predicting outcomes in the offspring has, to our knowledge, not been tested. The initial aim of the current study was to examine the ability of the T-ACE administered in pregnancy to predict selected child neurobehavioral outcomes known to be affected by prenatal alcohol exposure. Neurobehavioral dysfunctions were chosen because they arguably have the greatest life-long negative impact among the fetal alcohol effects on children and their families (cf, Merrick, et al., 2006; Streissguth, et al., 2004; Streissguth and O'Malley, 2000). Some of these specific neurobehavioral deficits, for example in arithmetic ability and short-term memory, were assessed also because they are particularly consistent deficits in FASD (Chiodo, et al, 2009; Kodituwakku, et al., 2007; Lee et al., 2004; Roebuck, et al., 1999).

The original T-ACE (Sokol et al., 1989), and as now recommended by NIAAA (2005) and ACOG (2004; 2006), maximized sensitivity at the expense of specificity. The original T-ACE defined tolerance as "more than" two (>2) drinks to "feel high" (Sokol et al., 1989) – or more than 3 drinks in another assessment (Russell et al., 1994) – and scores two points for a positive answer on the tolerance question and one point for each of the other 3 questions which ask about problems due to drinking. A total T-ACE score of 2 or more was considered positive for risk drinking (Sokol et al., 1989). Some applications of the T-ACE queried tolerance by asking how many drinks the woman can "hold" before falling asleep or passing out (e.g., Russell, et al., 1996; Chambers, et al., 2006) and defined tolerance as 6 or more drinks by that criterion. Other versions of the T-ACE vary the amount of drinking that defines tolerance, how tolerance is scored, and the "cut-point" used for the total T-ACE score to indicate risk drinking (e.g., Bradley et al., 1998; Chiodo, et al., 2009; Fabbri, et al., 2007; McQuade, et al., 2000; Russell et al., 1994; 1996; Varescon, et al., 2007; Wattendorf and Muenke, 2005). Others applied the T-ACE as an assessment of maternal alcohol "dependence" (e.g., Savage, et al., 2003), an objective for which it was not intended or tested. Nor was the T-ACE designed to assess binge drinking, which is also an important risk factor for FASDs (Abel and Hannigan, 1995; ACOG, 2006). Yet there are different purposes to which the T-ACE can be properly applied, such as identifying pregnant women drinking at any level that may potentially put fetuses at risk – which would provoke one clinical response; versus detecting in-pregnancy problem drinking which is likely to cause fetal harm – which ought to provoke a different and more intense clinical intervention, one that places more demands on limited time and resources. The purpose of the current study was to evaluate the effectiveness of the T-ACE in predicting neurobehavioral outcomes in children and assess how different scorings of the T-ACE would affect sensitivity for identifying maternal risk drinking without significantly increasing the false-positive rate.

We hypothesized that while the current recommendations to clinicians on the use of the T-ACE (e.g., ACOG, 2006) maximize sensitivity for detecting *any* risk drinking, more stringent criteria would improve specificity for child outcomes. We further hypothesized that certain applications of the T-ACE would optimize prediction of specific neurobehavioral deficits in a sample of prospectively identified 4- to 5-year-old inner-city African-American children. A more stringent criterion for the T-ACE capable of predicting neurobehavioral outcomes in offspring may serve as a better indicator of problem drinking in pregnancy and to whom intensive follow-up intervention ought to be directed.

# MATERIALS AND METHODS

This study was reviewed and approved by the WSU Institutional Review Board. All adult participants provided informed consent for themselves and their children prior to participation.

#### Participants

The sample consisted of 75 African-American, inner-city mothers and their children who were participants in a larger (N=332) ongoing study of the long-term effects of prenatal alcohol exposure and nutrition on pregnancy outcome and development (e.g., Beblo, et al., 2005; Chiodo, et al., 2009; Stark, et al., 2005b, a; 2005b). The mothers were recruited initially at their first antenatal clinic visit to a large, inner-city maternity hospital serving primarily African-American women (92%). Women were included if they reported periconceptional alcohol consumption averaging at least 1.0 ounce of absolute alcohol per day (AAD) – the equivalent of about two standard drinks per day. A random sample representing ~8% of the abstainers and lower level drinking women who received antenatal care at the clinic were invited to participate as a comparison group. Maternal exclusion criteria were a first antenatal visit later than 28 weeks gestation, metabolic disorders, or a known positive

HIV status. From the 332 mother-infant dyads completing the original study, 75 children were selected, as previously detailed in Chiodo, et al. (2009), for neurobehavioral assessment at 4 to 5 years of age. Approximately half of the sample (50.6%) drank above 1.0 AAD around the time of conception; 49.4% drank below this level and were used as the comparison group.

#### Assessment of Maternal Alcohol Use

Antenatal interviews at each prenatal clinic visit solicited the mother's self-reported alcohol consumption during the previous two weeks. Each gravida was questioned about her drinking on a day-by-day basis over 1) the preceding two weeks, just prior to the initial antenatal clinic visit, which on average occurred at the 16<sup>th</sup> week of gestation (range: 5 to 28 weeks), 2) retrospectively for the two weeks around the peri-conceptional period, and 3) for the two weeks preceding each subsequent antenatal visit, using a semi-structured interview validated in pregnant women (Sokol et al., 1989). Drinking volume was noted for each day, converted to average ounces of absolute alcohol per day (AAD) for each period based on beverage type, and then data from all visits were used to generate a measure of average consumption across pregnancy (AADXP) which has demonstrated predictive validity for various prenatal alcohol-related outcomes (e.g., Beblo, et al., 2005; Jacobson, et al., 1994; 1998; 2002; Nordstrom-Bailey, et al., 2004). An AADXP ≥ 0.5 defined in-pregnancy risk drinking and was used originally to validate the quick T-ACE screen (Sokol, et al., 1989; Russell, et al., 1996). As effective as quantity and frequency measures of alcohol consumption (like AADXP) can be in defining "at-risk" drinking and/or predicting neurobehavioral outcomes in research studies (cf., Chiodo, et al., 2009; Jacobson and Jacobson, 1994; Russell, et al., 1994), they are more difficult to collect on clinic patients than screens like the T-ACE (ACOG, 2006). Another goal of the current study was to evaluate relations between the various forms of the T-ACE screen and AADXP, a key quantity/frequency measure of maternal at-risk alcohol consumption.

The relatively simple T-ACE screen consists of four items assessing tolerance and signs of problem drinking (Table 1). A positive response on the tolerance question (the "T" in T-ACE) yields a score of two points. One point is scored for each positive answer to the other three ('ACE') questions. The typical, recommended form of the tolerance question asks about the minimum number of drinks needed to feel the effects of alcohol, "feeling high" (e.g., Sokol et al., 1989;Russell, et al., 1996). Two or more drinks ( $\geq 2$ ) is the current standard for a positive response. For the current analyses, we also defined tolerance using an additional cut-point considering tolerance to be  $\geq 3$  drinks needed to feel high. A total T-ACE score of 2 or more is the usual criterion indicating clinically significant risk or problem drinking (ACOG, 2006;Sokol et al., 1989). For the current analyses, we also analyzed the predictive ability of the T-ACE using other total scores with "cut-points" of 2 or 3 consistent with Russell, et al. (1994;1996) and Bradley, et al. (1998). (See also Sokol, et al. (1989), Table V, p. 866.)

#### **Neurobehavioral Assessments**

At 4 to 5 years of age, children were tested in the laboratory with a selected battery of tests assessing intelligence, attention, memory, visual-motor integration, fine motor skills, and behavior, all outcomes associated previously and consistently with FASDs. Briefly, for the present analyses we focused on measures that assess deficits that are among the most reliably recognized as components of a putative neurobehavioral "profile" of prenatal alcohol effects on cognition and behavior (see Kodituwakku, 2007; Lee et al, 2004; Mattson and Riley, 1998; O'Callaghan, et al., 2007; Rasmussen, 2005). The Wechsler Preschool and Primary Scale of Intelligence (WPPSI; Wechsler-R, 1989), a widely used measure of

general cognitive function in preschool children was used to yield scores for total IQ, verbal and performance IQ scales, and 12 individual subtests, including arithmetic.

Multiple age-appropriate aspects of executive function, fine motor skills and other neurobehavioral domains were assessed using the *Neurobehavioral Test Battery* (NTB). The NTB (Rohlman et al., 2003) is a composite test including items from the wide-ranging Behavioral Assessment and Research System (BARS; Anger et al., 1996) and the Pediatric Environmental Neurobehavioral Test Battery (PENTB; Amler and Gilbertini, 1996): the Purdue Pegboard Test (Gardner and Broman, 1979; Tiffin and Asher, 1948), Object Memory Test (Mahurin et al., 1992), Digit Span, Symbol Digit, and Finger Tapping, plus Match to Sample, the Continuous Performance Test (CPT), Divided Attention and Visual Motor Integration. See Chiodo et al., 2009 for more details on the neurobehavioral assessment.

#### **Data Analyses**

Prior to analyses, checks were performed for missing and out-of-range data, and normality. Receiver-Operator Curves ("ROC curves") examined the sensitivity and specificity of various cut-points for tolerance level within the T-ACE (i.e.,  $\geq 2$  or  $\geq 3$  drinks) and for total T-ACE scores (2 or 3) in predicting across-pregnancy maternal risk drinking (ounces of Absolute Alcohol Per Day Across Pregnancy [AADXP]). The impact of altering the total T-ACE score criterion from 2 to 3 was also assessed using logistic regression. The T-ACE with the cut-point set at 2 was entered in the first step and at 3 in the second step. The logistic analysis presented is for the total T-ACE score cut-point as the sensitivities were very similar for tolerance regardless of cut-point (see below). To examine the ability of the T-ACE to predict neurobehavioral outcomes in the offspring, the four different T-ACE criteria (i.e., 2 total cut-points  $\times$  2 drink tolerance values: T-ACE\_2-2; T-ACE\_2-3; T-ACE\_3-2; and T-ACE\_3-3) were correlated with 31 different outcome variables. Differences among the four T-ACE criteria in predicting neurobehavioral outcomes were tested using the Wilcoxon sign rank test.

# RESULTS

# **Sample Characteristics**

Maternal and child characteristics in Table 2 are detailed in Chiodo, et al. (2009). Briefly, on average the mothers were 25.7 years old and at 16 weeks gestation at their first antenatal visit. Only 35% obtained prenatal care during their first trimester. The mothers were predominantly lower SES, only 7% were married, and they were poorly educated: >35% had not graduated from high school and <1% had a college degree. The children were 4.4 years old (SD=0.4) at testing, 53.2% were male, and only 3 children were not in the custody of their biological mother; one mother was deceased. Although the children in this study performed ~1 standard deviation lower than national norms on the WPPSI assessment of intelligence (Chiodo, et al., 2009), this is consistent with results from other research groups evaluating urban African American children in this mid-western site (Jacobson, et al., 2004;Nordstrom-Bailey, et al., 2004).

#### Relations between the T-ACE and Across-Pregnancy Drinking

The relations between total T-ACE score and other across pregnancy drinking measures are provided in Table 3. As is evident, the T-ACE total score is highly related to other measures of across-pregnancy drinking as well as to other screens assessing problems due to drinking. Note that both the TWEAK and the CAGE have items that overlap with the T-ACE.

To examine the particular T-ACE criteria that yield the highest levels of predictive validity, ROC curve sensitivity and specificity analyses using each tolerance and total T-ACE score cut-point in relation to across-pregnancy drinking (AADXP) are presented in Table 4. A change in the total T-ACE score cut-point from 2 to 3 increased the specificity almost two-fold (from 0.40–0.65 to 0.80–0.83), while reducing the sensitivity by <17% (~0.16). In addition, the positive predictive value in this sample increased 24% to 63%, from 0.36–0.50 to 0.60–0.62 (depending on the tolerance cut-point), while the negative predictive value decreased only about 5% from 0.94–0.97 to ~0.91. This represents a significantly increased ability of the T-ACE to correctly identify those mothers who were not drinking at risk levels in pregnancy (i.e., AADXP  $\ge$  0.5) with very little change in the ability to predict those who were. In contrast, sensitivities were identical within each total T-ACE score cut-point whether the tolerance cut-point was 2 or 3 drinks (see Tables 4 and 5). Finally, positive and negative likelihood ratios were more predictive of risk drinking using a total T-ACE score of 3 than they were using a total score of 2.

Logistic regression was used to assess the magnitude of the impact of shifting the T-ACE total score criterion from 2 to 3, using the two-drink definition of tolerance. The 2-point T-ACE score was entered in the first step, followed by the 3-point T-ACE in the second step. The results of the regression analyses revealed that the total T-ACE score set at 2 significantly predicted risk drinking across pregnancy ( $\beta$ =2.50, p<0.02, R<sup>2</sup>=0.11 [proportion of variance in risk drinking explained by predicted scores in logistic regression]). Explained variance increased significantly ( $\chi^2$ =12.70, df= 1, p<0.001,  $\Delta R^2$  =0.20) with the addition of T-ACE\_3-2 (total score of 3 and tolerance at 2 drinks). In the final model when both T-ACE\_2-2 and T-ACE\_3-2 were included, using the currently recommended tolerance cutpoint of 2 of more drinks, a total T-ACE score cut-point of 2 did not significantly predict across-pregnancy drinking (p=0.36) whereas the total T-ACE score to 3 did= ( $\beta$ =2.35, p<0.001), demonstrating that increasing the total T-ACE score cut-point from 2 to 3 improved predicting maternal at-risk drinking in pregnancy whereas increasing the tolerance cut-point from 2 to 3 did not.

#### **Relations between the T-ACE and Neurobehavioral Endpoints**

To examine the relative ability of the various T-ACE criteria to predict neurobehavioral outcomes in the children, the four different T-ACE scores were correlated with the 31 neurobehavioral outcome variables (Table 5). First, with the tolerance definition set at a cutpoint of 2, significant relations were seen between the T-ACE with the total score cut-point set at 2 (i.e., T-ACE\_2-2) and 7 outcomes, including effects in IQ, memory, far-sightedness, and Digit Span Forward - a measure of short term memory and attention. In contrast, with the total T-ACE score cut-point set at 3 (i.e., T-ACE\_3-2), significant relations were seen with 17 outcomes. The total T-ACE score with a cut-point of 3 was related significantly to 2.4 times more neurobehavioral outcomes than with a cut-point of 2, (T-ACE 2-2 vs. T-ACE\_3-2; z-score= -2.67, p=0.008). There was a similar significant effect of increasing the total T-ACE score cut-point to 3 when the tolerance cut-point was set at 3 (T-ACE\_2-3 vs. T-ACE\_3-3; z-score= -3.05, p=0.002), such that the T-ACE with the higher total score cutpoint was related to 2.3 times more outcomes (6 vs. 14; see Table 5, last row). Similar to predicting AADXP (above), increasing the tolerance cut-point from 2 to 3 did not significantly alter the number of neurobehavioral outcomes predicted with the total T-ACE cut-point set either at 2 (7 vs 6 outcomes; z=-.33, p>0.05) or at 3 (17 vs 14 outcomes; z=-.33, p>0.05) or at 3 (17 vs 14 outcomes; z=-.33, p>0.05) or at 3 (17 vs 14 outcomes; z=-.33, p>0.05) or at 3 (17 vs 14 outcomes; z=-.33, p>0.05) or at 3 (17 vs 14 outcomes; z=-.33, p>0.05) or at 3 (17 vs 14 outcomes; z=-.33, p>0.05) or at 3 (17 vs 14 outcomes; z=-.33, p>0.05) or at 3 (17 vs 14 outcomes; z=-.33, p>0.05) or at 3 (17 vs 14 outcomes; z=-.33, p>0.05) or at 3 (17 vs 14 outcomes; z=-.33, p>0.05) or at 3 (17 vs 14 outcomes; z=-.33, p>0.05) or at 3 (17 vs 14 outcomes; z=-.33, p>0.05) or at 3 (17 vs 14 outcomes; z=-.33, p>0.05) or at 3 (17 vs 14 outcomes; z=-.33, p>0.05) or at 3 (17 vs 14 outcomes; z=-.33, p>0.05) or at 3 (17 vs 14 outcomes; z=-.33, p>0.05) or at 3 (17 vs 14 outcomes; z=-.33, p>0.05) or at 3 (17 vs 14 outcomes; z=-.33, p>0.05) or at 3 (17 vs 14 outcomes; z=-.33, p>0.05) or p>0.05) or p>0.05) or p>0.05) or p>0.05-1.73, *p*>0.05).

#### DISCUSSION

The T-ACE, a simple clinical screen for problem drinking validated in pregnant women (Sokol et al., 1989; Russell et al., 1994; 1996), is recommended by the CDC (2002) and

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ACOG (2004; 2006; Floyd, et al., 2006) and NIAAA (2004). The current study assessed the utility of different applications of the T-ACE and the results confirmed our *a priori* hypothesis that increasing the total T-ACE score cut-point from 2 to 3 improved specificity while maintaining high sensitivity in detecting maternal risk alcohol consumption during pregnancy. These results also demonstrate that detection of children with neurobehavioral effects related to prenatal alcohol exposure is possible with the T-ACE, and that the T-ACE is better at this with the higher than with the lower total T-ACE score cut-point. On the other hand, increasing the tolerance cut-point from 2 to 3 drinks did not significantly improve the ability of the T-ACE to either predict maternal risk drinking or detect neurobehavioral effects in the children.

This is the first study to test the ability of the highly recommended T-ACE screen to predict neurobehavioral outcomes due to prenatal alcohol exposure such as decreased cognitive ability or attention problems (Coles et al., 2002; Kable and Coles, 2004; Kodituwakku, 2007; Mattson and Riley, 1999). Even prenatal alcohol exposures of one or two drinks per day on average have been associated with significant group decrements in cognition and problems in behavior (e.g., Striessguth, et al., 1990; Jacobson, et al., 1993, 1994; Jacobson and Jacobson, 1999; Kodituwakku, 2007). The fact that children with apparently similar levels of prenatal alcohol exposure assessed by levels of maternal consumption show variable neurobehavioral effects - whether diagnosed with FASDs or not - suggests that current measures of maternal intake alone may not be adequately discriminating the fetal risk drinking that produces fetal alcohol effects (Aros, et al., 2006; Chiodo, et al., 2009; Vaurio, et al., 2008), perhaps because of variable under-reporting of quantity and frequency. Setting a higher cut-point to define tolerance in the current study did not improve prediction of outcomes, whereas increasing the total T-ACE score criterion to 3 did. This meant that women could not be classified as risk drinkers solely on the basis of tolerance, consistent with the objective of others who varied the scoring of the T-ACE to limit the relative value of the tolerance question. For example, McQuade et al. (2000) increased specificity by scoring only one point for the tolerance question, but at the expense of sensitivity. The present results also suggest that tolerance alone - which itself may not mean "problem drinking" - is not as sensitive or specific an indicator of fetal risk as multiple measures of problem drinking (the 3 "ACE" questions), or tolerance plus at least one more of the other T-ACE questions.

One possible limitation to these findings is that the current sample, though intensively studied, was relatively small and was restricted to low-SES, urban African-American women and their children, and the reliability of maternal alcohol use/abuse screens may differ across populations (Nardini et al., 2006; Bradley et al., 1998; Ewing, 1984; Sokol et al., 1989; Chan, et al., 1993). These analyses will need to be replicated in a larger cohort, which we plan to do in the future. Also, in addition to unreliable reporting in maternal alcohol use, variable fetal susceptibility to alcohol due to differences in genetics, metabolism, nutrition, or patterns of exposure can also account for variable outcomes children (cf., Abel and Hannigan, 1995; Sokol et al., 1986). Among the patterns of exposure, binge drinking is an important risk factor for FASDs (cf, Abel and Hannigan, 1995; ACOG, 2006), and the T-ACE may be limited because it does not directly assess binge drinking.

Assessing fetal risk levels of prenatal alcohol exposure in the clinical setting can be time consuming, difficult, and/or uncertain using quantity/frequency patterns of maternal self-reported consumption. Improving the utility of a simple clinical screen in predicting maternal problem drinking – especially a screen that also predicts child outcomes – is important for prevention and treatment of FASDs. Increasing the total T-ACE score criterion from 2 to 3 should allow for intervention with fewer "false positives," reducing physician time with these patients and allowing a more intensive targeted clinical response for

pregnant women correctly identified as drinking at fetal risk levels. The current application of the T-ACE, with a total score cut-point set at 3, addresses screening needs identified by Savage et al. (2003, p. 444) for detecting fetuses exposed to risk levels of alcohol but whose mother's are not "alcohol dependent," for planning "appropriate levels of intervention with the mother," and aiding early identification and treatment for the child.

The research implications of this study include the need to validate the results on a larger and more heterogeneous population, and the possibility of exploring relations of the more specific application of the T-ACE to biomarkers of problem drinking. Of clinical import, while the T-ACE was intended first to be a very sensitive screen for risk or problem drinking in pregnant women, the current application is also a sensitive and specific indicator of negative consequences in the offspring of those women. An improved application of the T-ACE may have implications for diagnoses because knowledge of "significant" or "heavy" or "substantial" maternal alcohol consumption during pregnancy is necessary for a diagnosis of non-FAS FASDs and greatly facilitates a diagnosis of FAS (Astley, 2006; Bertrand, et al., 2004; 2005; Hoyme, et al., 2005; Stratton, et al., 1996). It is premature to argue from the current study that the T-ACE alone may be a sufficient indicator of that "substantial" level of drinking, but a positive T-ACE with a total cut-point of 3 should signal a compelling need for more detailed assessment of maternal alcohol consumption patterns and intervention. In addition, the significant relations between the more specific application of the T-ACE and neurobehavioral outcomes mean that a positive T-ACE ought to be sufficient indication for careful postnatal assessment of exposed infants, and vigilant follow-up into childhood, thereby reducing the possibility of missing affected children and allowing for earlier intervention.

In conclusion, increasing the total T-ACE score cut-point to 3 increased specificity and maintained adequate sensitivity equal to that of the original report (Sokol et al., 1989) for the identification of risk drinking, without identifying an excessive number of false positives, and had greater predictive validity for detecting alcohol-related neurobehavioral effects. There are no clearly defined threshold doses for any of the wide-ranging morphological or neurobehavioral effects of alcohol on embryos and fetuses (Hendersen et al, 2007; Jacobson and Jacobson, 1994; Martínez-Frías, et al., 2004), and of course a more effective T-ACE cut-point is not a threshold. Therefore, current standards of care (ACOG, 2006), and recommendations from the Surgeon General (DHHS, 2005; NIAAA, 2005) and the CDC (Bertrand, et al., 2004; 2005) remain that physicians monitor alcohol consumption carefully in their pregnant patients and counsel that "no amount of alcohol consumption can be considered safe during pregnancy" (Chang, 2005; NIAAA, 2000; 2004; 2005; DHHS, 2005).

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# References

Abel EL, Hannigan JH. Maternal risk factors in fetal alcohol syndrome: Provocative and permissive influences. Neurotoxicol Teratol 1995;17:445–462. [PubMed: 7565491]

- American College of Obstetricians and Gynecologists. At-risk drinking and illicit drug use: Ethical issues in obstetric and gynecologic practice. American College of Obstetrics & Gynecology Committee Opinion No 294. Obstet Gynecol 2004;103:1021–1031. [PubMed: 15121596]
- American College of Obstetricians and Gynecologists. Washington D.C: American College of Obstetrics & Gynecology; 2006. Drinking and reproductive health: A fetal alcohol spectrum disorders prevention tool kit. [cited 2008 Jan 28]. Available from: http://www.acog.org/departments/healthIssues/FASDToolKit.pdf
- Amler, RW.; Gibertini, M., editors. Pediatric environmental neurobehavioral test battery. Atlanta, GA: US Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry; 1996.
- Anger WK, Rohlman DS, Sizemore OJ, Kovera CA, Gibertini M, Ger J. Human behavioral assessment in neurotoxicology: Producing appropriate test performance with written and shaping instructions. Neurotoxicol Teratol 1996;18:371–379. [PubMed: 8866527]
- Aros S, Mills JL, Torres C, Henríquez C, Fuentes A, Capurro T, Mena M, Conley M, Cox C, Signore C, et al. Prospective identification of pregnant women drinking four or more standard drinks (> or = 48 g) of alcohol per day. Subst Use Misuse 2006;41:183–197. [PubMed: 16479683]
- Astley SJ. Comparison of the 4-digit diagnostic code and the Hoyme diagnostic guidelines for fetal alcohol spectrum disorders. Pediatrics 2006;118:1532–1545. [PubMed: 17015544]
- Beblo S, Stark K, Murthy M, Janisse J, Rockett H, Whitty JE, Buda-Abela M, Martier SS, Sokol RJ, Hannigan JH, et al. Effects of alcohol intake during pregnancy on docosahexaenoic acid and arachidonic acid in umbilical cord vessels of Black women. Pediatrics 2005;115:194–203. [PubMed: 15630008]
- Bertrand J, Floyd LL, Weber ML. Guidelines for identifying and referring persons with fetal alcohol syndrome. MMWR Recomm Rep 2005;54:1–14. [PubMed: 16251866]
- Bertrand, J.; Floyd, RL.; Weber, MK.; O'Connor, M.; Riley, EP.; Johnson, KA.; Cohen, DE. National Task Force on FAS/FAE. Fetal Alcohol Syndrome: Guidelines for Referral and Diagnosis. Atlanta, GA: Centers for Disease Control and Prevention; 2004.
- Bradley KA, Boyd-Wickizer J, Powell SH, Burman ML. Alcohol screening questionnaires in women: A critical review. JAMA 1998;280:166–171. [PubMed: 9669791]
- Center for Disease Control. Fetal Alcohol Syndrome Alaska, Arizona, Colorado and New York, 1995–1997. MMWR Morb Mortal Weekly Rep 2002;51:433–435.
- Chambers CD, Kavteladze L, Joutchenko L, Bakhireva LN, Jones KL. Alcohol consumption patterns among pregnant women in the Moscow region of the Russian Federation. Alcohol 2006;38:133– 137. [PubMed: 16905438]
- Chan AW, Pristach EA, Welte JW, Russell M. Use of the TWEAK test in screening for alcoholism/ heavy drinking in three populations. Alcohol Clin Exp Res 1993;17:1188–1192. [PubMed: 8116829]
- Chang G. Screening and brief intervention in prenatal care settings. Alcohol Res Health 2005;28:80– 84. [PubMed: 19006995]
- Chiodo LM, Janisse J, Delaney-Black V, Sokol RJ, Hannigan JH. A metric of maternal prenatal risk drinking predicts neurobehavioral outcomes in preschool children. Alcohol Clin Exp Res 2009;33:634–644. [PubMed: 19183137]
- Coles CD, Platzman KA, Lynch ME, Freides D. Auditory and visual sustained attention in adolescents prenatally exposed to alcohol. Alcohol Clin Exp Res 2002;26:263–271. [PubMed: 11964567]
- Ernhart CB, Morrow-Tlucak M, Sokol RJ, Martier S. Underreporting of alcohol use in pregnancy. Alcohol Clin Exp Res 1988;12:506–511. [PubMed: 3056071]
- Ewing JA. Detecting alcoholism: The CAGE questionnaire. JAMA 1984;252:1905–1907. [PubMed: 6471323]
- Fabbri CE, Furtado EF, Laprega MR. Alcohol consumption in pregnancy: performance of the Brazilian version of the questionnaire T-ACE. Rev Saude Publica 2007;41:979–984. [PubMed: 17923888]
- Floyd RL, O'Connor MJ, Bertrand J, Sokol RJ. Reducing adverse outcomes from prenatal alcohol exposure: a clinical plan of action. Alcohol Clin Exp Res 2006;30:1271–1275. [PubMed: 16899029]

- Gardner R, Broman M. The Purdue pegboard test: Normative data on 1334 school children. J Clin Psychol 1979;1:156–162.
- Henderson J, Kesmodel U, Gray R. Systematic review of the fetal effects of prenatal binge-drinking. J Epidemiol Community Health 2007;61:1069–1073. [PubMed: 18000129]
- Hoyme HE, May PA, Kalberg WO, Kodituwakku P, Gossage JP, Trujillo PM, Buckley DG, Miller JH, Aragon AS, Khaole N, et al. A practical clinical approach to diagnosis of fetal alcohol spectrum disorders: Clarification of the 1996 Institute of Medicine criteria. Pediatrics 2005;115:39–47.
  [PubMed: 15629980]
- Jacobson SW, Chiodo LM, Sokol RJ, Jacobson JL. Validity of maternal report of prenatal alcohol, cocaine, and smoking in relation to neurobehavioral outcome. Pediatrics 2002;109:815–825. [PubMed: 11986441]
- Jacobson JL, Jacobson SW. Prenatal alcohol exposure and neurodevelopmental development: Where is the threshold? Alcohol Health Res World 1994;18:30–36.
- Jacobson JL, Jacobson SW. Drinking moderately and pregnancy. Effects on child development. Alcohol Res Health 1999;23:25–30. [PubMed: 10890795]
- Jacobson SW, Jacobson JL, Sokol RJ. Effects of fetal alcohol exposure on infant reaction time. Alcohol Clin Exp Res 1994;18:1125–1132. [PubMed: 7847594]
- Jacobson JL, Jacobson SW, Sokol RJ, Ager JW Jr. Relation of maternal age and pattern of pregnancy drinking to functionally significant cognitive deficit in infancy. Alcohol Clin Exp Res 1998;22:345–351. [PubMed: 9581639]
- Jacobson SW, Jacobson JL, Sokol RJ, Chiodo LM, Corobana R. Maternal age, alcohol abuse history, and quality of parenting as moderators of the effects of prenatal alcohol exposure on 7.5-year intellectual function. Alcohol Clin Exp Res 2004;28:1732–1745. [PubMed: 15547461]
- Jacobson JL, Jacobson SW, Sokol RJ, Martier SS, Ager JW, Kaplan-Estrin MG. Teratogenic effects of alcohol on infant development, Alcohol. Clin Exp Res 1993;17:174–183.
- Kable JA, Coles CD. The impact of prenatal alcohol exposure on neurophysiological encoding of environmental events at six months. Alcohol Clin Exp Res 2004;28:489–496. [PubMed: 15084907]
- Kodituwakku PW. Defining the behavioral phenotype in children with fetal alcohol spectrum disorders: A review. Neurosci Biobehav Rev 2007;31:192–201. [PubMed: 16930704]
- Lee KT, Mattson SN, Riley EP. Classifying children with heavy prenatal alcohol exposure using measures of attention. J Int Neuropsychol Soc 2004;10:271–277. [PubMed: 15012847]
- Mahurin RK, Espino DV, Holifield EB. Mental status testing in elderly Hispanic populations: Special concerns. Psychopharmacol Bull 1992;28:391–399. [PubMed: 1296217]
- Manning MA, Hoyme EH. Fetal alcohol spectrum disorders: a practical clinical approach to diagnosis. Neurosci Biobehav Rev 2007;31:230–238. [PubMed: 16962173]
- Martínez-Frías ML, Bermejo E, Rodríguez-Pinilla E, Frías JL. Risk for congenital anomalies associated with different sporadic and daily doses of alcohol consumption during pregnancy: A case–control study. Birth Defects Res A Clin Mol Teratol 2004;70:194–200. [PubMed: 15108246]
- Mattson SN, Riley EP. A review of the neurobehavioral deficits in children with fetal alcohol syndrome or prenatal exposure to alcohol. Alcohol Clin Exp Res 1998;22:279–294. [PubMed: 9581631]
- Mattson SN, Riley EP. Implicit and explicit memory functioning in children with heavy prenatal alcohol exposure. J Int Neuropsychol Soc 1999;5:462–471. [PubMed: 10439591]
- May PA, Gossage JP. Estimating the prevalence of fetal alcohol syndrome: A summary. Alcohol Res Health 2001;25:159–167. [PubMed: 11810953]
- May PA, Gossage JP, Marais AS, Adnams CM, Hoyme HE, Jones KL, Robinson LK, Khaole NC, Snell C, Kalberg WO, et al. The epidemiology of fetal alcohol syndrome and partial FAS in a South African community. Drug Alcohol Depend 2007;88:259–271. [PubMed: 17127017]
- McQuade WH, Levy SM, Yanek LR, Davis SW, Liepman MR. Detecting symptoms of alcohol abuse in primary care settings. Arch Fam Med 2000;9:814–821. [PubMed: 11031387]
- Merrick J, Merrick E, Morad M, Kandel I. Fetal alcohol syndrome and its long-term effects. Minerva Pediatrica 2006;58:211–218. [PubMed: 16832326]

- Morrow-Tlucak, M.; Ernhart, CB.; Sokol, RJ.; Martier, S.; Ager, J. Underreporting of alcohol use in pregnancy: relationship to alcohol problem history; Alcohol Clin Exp Res. 1989. p. 399-401.http://firstsearchoclc.org/WebZ/FSQUERY? searchtype=hotauthors:format=BI:numrecs=10:dbname=MEDLINE::termh1=Sokol
  - +RJ:indexh1=au%3D:sessionid=fsapp5-38227-fci9c0bz-sy0v8w:entitypagenum=42:0:next=html/ records.html:bad=error/badsearch.html
- Nardini, K.; Anderson, R. Systems State Issue Brief No. 2. Washington, DC: National Association of State Alcohol and Drug Abuse Directors (NARSADAD); 2006. Alcohol research on prenatal alcohol exposure, prevention, and implications for state AOD. [cited 2007 Feb 14]. Available from: http://pubs.niaaa.nih.gov/publications/NASADAD/PrenatalBrief2.htm
- National Institute on Alcohol Abuse and Alcoholism. Fetal alcohol exposure and the brain. Alcohol Alerts 2000;50:1–3.
- National Institute on Alcohol Abuse and Alcoholism. Alcohol An important women's health issue. Alcohol Alerts 2004;62:1–6.
- National Institute on Alcohol Abuse and Alcoholism. Surgeon general updates warning about alcohol use during pregnancy. NIAAA Newsletter 2005;6:2.
- Nordstrom Bailey B, Delaney-Black V, Covington CY, Ager J, Janisse J, Hannigan JH, Sokol RJ. Prenatal exposure to binge drinking and cognitive and behavioral outcomes at age 7 years. Am J Obstet Gynecol 2004;191:1037–1043. [PubMed: 15467586]
- O'Callaghan FV, O'Callaghan M, Najman JM, Williams GM, Bor W. Prenatal alcohol exposure and attention, learning and intellectual ability at 14 years: a prospective longitudinal study. Early Hum Dev 2007;83:115–123. [PubMed: 16842939]
- O'Leary CM. Foetal alcohol syndrome: diagnosis, epidemiology and developmental outcomes. J Paediatr Child Health 2004;40:2–7. [PubMed: 14717994]
- Rasmussen C. Executive functioning and working memory in fetal alcohol spectrum disorder. Alcohol Clin Exp Res 2005;29:1359–1367. [PubMed: 16131842]
- Roebuck TM, Mattson SN, Riley EP. Behavioral and psychosocial profiles of alcohol-exposed children. Alcohol Clin Exp Res 1999;23:1070–1076. [PubMed: 10397293]
- Rohlman DS, Gimenes LS, Eckerman DA, Kang SK, Farahat FM, Anger WK. Development of the Behavioral Assessment and Research System (BARS) to detect and characterize neurotoxicity in humans. Neurotoxicology 2003;24:523–531. [PubMed: 12900065]
- Russell M, Martier SS, Sokol RJ, Mudar P, Bottoms S, Jacobson S, Jacobson J. Screening for pregnancy risk-drinking. Alcohol Clin Exp Res 1994;18:1156–1161. [PubMed: 7847599]
- Russell M, Martier SS, Sokol RJ, Mudar P, Jacobson S, Jacobson J. Detecting risk drinking during pregnancy: a comparison of four screening questionnaires. Am J Public Health 1996;86:1435– 1439. [PubMed: 8876514]
- Savage C, Wray J, Ritchey PN, Sommers M, Dyehouse J, Fulmer M. Current screening instruments related to alcohol consumption in pregnancy and a proposed alternative method. J Ob Gyn Neonatal Nurs 2003;32:437–446.
- Selzer ML. The Michigan alcoholism screening test: The quest for a new diagnostic instrument. Am J Psychiatry 1971;127:1653–1658. [PubMed: 5565851]
- Sokol RJ, Ager J, Martier S, Debanne S, Ernhart C, Kuzma J, Miller SI. Significant determinants of susceptibility to alcohol teratogenicity. Ann N Y Acad Sci 1986;477:87–102. [PubMed: 3468841]
- Sokol RJ, Delaney-Black V, Nordstrom B. Fetal alcohol spectrum disorders. JAMA 2003;290:2996–2999. [PubMed: 14665662]
- Sokol RJ, Martier S, Ager JW. The T-ACE questions: Practical prenatal detection of risk-drinking. Am J Obstet Gynecol 1989;160:863–870. [PubMed: 2712118]
- Spadoni AD, McGee CL, Fryer SL, Riley EP. Neuroimaging and fetal alcohol spectrum disorders. Neurosci Biobehav Rev 2007;31:239–245. [PubMed: 17097730]
- Stark KD, Beblo S, Murthy M, Buda-Abela M, Janisse J, Rockett H, Whitty JE, Martier SS, Sokol RJ, Hannigan JH, et al. Comparison of plasma and erythrocyte total fatty acid composition from African-American women at 24 weeks gestation, infant delivery and 3 months postpartum. J Lipid Res 2005a;46:516–525. [PubMed: 15604519]

- Stark KD, Beblo S, Murthy M, Whitty JE, Buda-Abela M, Janisse J, Rockett H, Martier SS, Sokol RJ, Hannigan JH, et al. Alcohol consumption in pregnant, Black women is associated with decreased plasma and erythrocyte docosahexaenoic acid. Alcohol Clin Exp Res 2005b;29:130–140. [PubMed: 15654301]
- Stratton, K.; Howe, C.; Battaglia, F. Fetal alcohol syndrome: Diagnosis, epidemiology, prevention, and treatment. Washington: National Academy Press; 1996.
- Streissguth AP, Barr HM, Sampson PD. Moderate prenatal alcohol exposure: Effects on child IQ and learning problems at age 7 1/2 years Alcohol. Clin Exp Res 1990;14:662–669.
- Streissguth AP, Bookstein FL, Barr HM, Sampson PD, O'Malley K, Young JK. Risk factors for adverse life outcomes in fetal alcohol syndrome and fetal alcohol effects. J Dev Behav Pediatr 2004;25:228–238. [PubMed: 15308923]
- Streissguth AP, O'Malley K. Neuropsychiatric implications and long-term consequences of fetal alcohol spectrum disorders. Sem Clin Neuropsychiatry 2000;5:177–190.
- U.S. Department of Health and Human Services. U.S. Surgeon General releases advisory on alcohol use in pregnancy. 2005. [cited 2008 Jan 12]. Available from: http://www.surgeongeneral.gov/pressreleases/sg02222005.html
- Tiffin J, Asher J. The Purdue Pegboard: Norms and studies of reliability and validity. J Appl Psychol 1948;32:234–247. [PubMed: 18867059]
- Varescon I, Gaugue J, Wendland J. Alcool et grossesse: Premiére utilisation du questionnaire de dépistage T-ACE dans une population française. [Alcohol and pregnancy: First use of the T-ACE screening test in a French population.]. Alcoologie et Addictologie 2007;29:221–225.
- Vaurio L, Riley EP, Mattson SN. Differences in executive functioning in children with heavy prenatal alcohol exposure or attention-deficit/hyperactivity disorder. J Int Neuropsychol Soc 2008;14:119– 129. [PubMed: 18078538]
- Wattendorf DJ, Muenke M. Fetal alcohol spectrum disorders. Am Fam Physician 2005;72:279–282. 285. [PubMed: 16050451]
- Wechsler, D. Wechsler Preschool and Primary Scale of Intelligence-Revised. San Antonio: The Psychological Corporation; 1989.

# The T-ACE Problem Drinking Screen as Tested in this Study.

Code	Factor	Cut-Points	Score	Question		
"Т"	Tolerance	$\geq 2 \text{ or } \geq 3 \text{ drinks}$	2	"How many drinks does it take to make you feel high?"		
"A"	Annoy	Yes/No	1	Has anybody ever annoyed you by complaining about your drinking?		
"С"	Cut Down	Yes/No	1	Have you ever felt you ought to cut down on your drinking?		
"Е"	"Eye- Opener"	Yes/No	1	Have you ever needed a drink first thing in the morning to get going?		
Total T-ACE Score Cut-Points:		2 or 3				

# Sample Characteristics (N=75)

	Mean (or %)	SD	Min	Max	
Mother					
Age at delivery (years)	25.30	5.6	15.0	38.0	
Average AA <sup>a</sup> per day (AAD)					
At conception	1.21	1.60	0.0	10.0	
At first prenatal visit	0.04	0.12	0.0	0.8	
Across pregnancy	0.32	0.50	0.0	3.3	
Average AA <i>a</i> /drinking day (AAD	Average AA <sup><i>a</i></sup> /drinking day (AADD)				
At conception	2.55	2.56	0.0	10.0	
At first prenatal visit	0.36	0.96	0.0	4.8	
Across pregnancy	2.36	2.43	0.0	10.0	
MAST total score	4.93	8.26	0.0	38.0	
Primary Caregiver					
Biological Mother (%)	96.05				
Education (years)	12.01	1.38	8.0	16.0	
Marital Status (% married)	6.60				
SES: Hollingshead 4-Factor Index	25.74	9.36	11.0	48.0	
Child					
Age at Assessment (years)	4.42	0.38	3.9	5.6	
Sex (% male)	53.20				
WPPSI-R					
Full Scale IQ	82.03	11.77	50.0	107.0	
Verbal IQ	81.63	11.80	55.0	113.0	
Performance IQ	86.72	13.22	51.0	115.0	

 $a_{\text{``AA''}} = \text{``Ounces of Absolute Alcohol''}$ 

Correlation (r) of T-ACE with Other Alcohol Measures

	r
AA/day at conception (AAD0)	.68*
AA/drinking day at conception (AADD0)	.62*
AA/day across pregnancy (AADXP)	.63*
AA/drinking day across pregnancy (AADDXP)	.61*
MAST total	.59*
CAGE total	.79*
TWEAK total	.94*

\*p<0.001

# Specificity and Sensitivity in Detecting Across-Pregnancy Drinking (AADXP)

	Tolera	nce > 2	Tolerance > 3		
	Total T-ACE Cut-point = 2	Total T-ACE Cut-point = 3	Total T-ACE Cut-point = 2	Total T-ACE Cut-point = 3	
Sensitivity	.947 <sup>a</sup>	.789	.947	.789	
Specificity	.404	.808	.654	.827	
Positive Predictive Value	.367	.600	.500	.625	
Negative Predictive Value	.945	.913	.971	.915	
Positive Likelihood Ratio	1.59	4.11	2.74	4.56	
Negative Likelihood Ratio	0.63	0.24	0.37	0.22	

 $^{a}\mathrm{Values}$  in table were obtained from Receiver Operator Curves (ROCs).

# Correlations Between Neurobehavioral Outcomes and the Four T-ACE Criteria

	Tolera	nce ≥2	Tolerance ≥3		
T-ACE Criteria:	Total Score=2	Total Score=3	Total Score=2	Total Score=3	
WPPSI					
Object Assembly Scaled Score	.00 <sup>a</sup>	19	11	18	
Geometric Design Scaled Score	13	07	.02	06	
Block Design Scaled Score	07	16	15	18	
Maze Scaled Score	07	<b>26</b> *	16	<b>25</b> *	
Picture Completion Scaled Score	17	15	−. <b>20</b> <sup>≠</sup>	14	
Animal Pegs Scaled Score	.03	.09	.03	.10	
Information Scaled Score	<b>26</b> *	10	11	08	
Comprehension Scaled Score	01	.05	.11	.03	
Arithmetic Scaled Score	<b>26</b> *	<b>30</b> **	16	<b>32</b> **	
Vocabulary Scaled Score	09	13	13	12	
Similarities Scaled Score	13	14	.01	10	
Sentences Scaled Score	<b>34</b> **	<b>24</b> *	<b>25</b> *	<b>25</b> *	
Verbal Score IQ	16	<b>20</b> <sup>≠</sup>	13	20	
Performance Score IQ	18	27*	<b>20</b> <sup>≁</sup>	<b>26</b> *	
Full Scaled Score IQ	<b>−.21</b> <sup>≠</sup>	<b>24</b> *	16	<b>23</b> *	
Object Memory					
Intrusions Delay Trial	$.22^{\dagger}$	.26*	.26*	.28*	
Total Recognition	.28*	.03	.20	.06	
Vision					
Farsighted	.27*	.31*	.22	.28*	
Nearsighted	.15	.35**	$.25^{\dagger}$	.40**	
CPT # Hits	06	09	10	14	
Digit Span Forward	17	21	<b>24</b> *	23 <sup>≁</sup>	
Divided Attention Word Amount	11	<b>22</b> <sup>≁</sup>	07	<b>24</b> *	
Peg Board Test					
Total	.00	<b>22</b> <sup>†</sup>	15	<b>25</b> *	
Symbol Digit Number Correct	09	<b>27</b> *	09	<b>26</b> *	
VMI Motor T-Score	03	<b>26</b> *	06	<b>22</b> <sup>†</sup>	
Finger tapper					
# Taps Left Hand	.07	12	.03	06	
# Taps Right Hand	08	<b>29</b> *	11	<b>24</b> *	
# Taps Long	02	22 <sup>≁</sup>	04	15	
# Taps Short	.12	14	05	14	

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T ACE Cuitorio	Tolera	nce ≥2	Tolerance ≥3		
I-ACE CITIEITA:	Total Score=2	Total Score=3	Total Score=2	Total Score=3	
# Taps No Sing	01	− <b>.22</b> <sup>†</sup>	04	16	
# Taps Sing	01	<b>25</b> *	07	20	
Number of Outcomes Predicted <sup>b</sup>	7	17***	6	14***	

 $^{\dagger}p<0.10;$ 

\* p<0.05;

\*\* p<0.01;

\*\*\* *p*<0.001;

 $^{a}$ Values in table are correlation coefficients.

 $^{b}$  = Significance relative to respective total T-ACE score of 2 with the same tolerance cut-point.