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Assessing Processing Speed among Individuals with Intellectual and Developmental Disabilities: A match-to-sample paradigm

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Abstract

Speeded Matching (SpM) is a new processing speed match-to-sample test within the NIH Toolbox Cognitive Battery. It was designed to developmentally extend feasibility to younger children or individuals with intellectual or developmental disabilities (IDD). SpM reduces cognitive demands to tapping an identical match as opposed to judging and indicating whether two stimuli are identical. In this study, we piloted SpM among 148 participants with fragile X syndrome, Down syndrome, or other intellectual disabilities (chronological age mean=17.8 years, sd=5.4; nonverbal mental age mean=65 months, sd=19.4). SpM had a high feasibility (96%) and internal consistency $(r_{xx}=0.98)$. It converged well with other measures of processing speed, fluid cognition, and nonverbal mental age and diverged appropriately from crystallized cognitive skills. The correlation between nonverbal mental age and SpM in the IDD sample was not significantly different than the correlation between chronological age and SpM in a separate sample of 118 neurotypical children (age mean=3.9 years sd=0.8). This study provides initial evidence for the reliability and validity of the new SpM task, which may be appropriate as an outcome measure of processing speed for future clinical trials. It is more feasible than tasks designed for adults; it is brief, easy to administer, and engaging for young children and older individuals with lower mental ages associated with IDD.

Keywords

Processing Speed; Fragile X Syndrome; Down Syndrome; NIH Toolbox; Cognition

Introduction

Informational processing speed, often indexed by reaction time, is a core cognitive skill. It is foundational for many cognitive processes, such that improvements in other domains—especially working memory, attention, and other executive functions—require a

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sufficient prerequisite processing speed ability (Bauer et al., 2013; Mayes & Calhoun, 2007; Salthouse, 1996; Zelazo et al., 2013). The developmental trajectory of processing speed has been well-described. It is slow among young children, increases in adolescence and young adulthood, and then slows among older adults (Kail, 1986; Carlozzi et al., 2015). Differences in processing speed are directly related to cognitive decline in older adults (Salthouse, 2000).

There are numerous types of processing speed tasks. In infants, looking time and novelty preference have been used to index it, where slower formation of novelty preference has been correlated with poorer health outcomes (e.g. Rose, Feldman, & Jankowski, 2002). Among older individuals, tasks require some type of response, with reaction time indexing information processing speed. In a simple reaction time task, a participant would respond whenever a stimulus appears. Choice reaction time tasks require a participant to respond to one of several stimuli. Choice-based tasks also vary in complexity, from tasks where a stimulus appears in one of several locations, corresponding to a choice button (e.g. Deary, Liewald, & Nissan, 2011); tasks that require a judgement as to whether two images are the same or different (e.g. Salthouse, Babcock, & Shaw, 1991); or tasks requiring the participant to identify a direct match and mark it in random or structured arrays (e.g. Della Sala et al., 1992). In all cases, there is an expectation that, had time been unlimited, a respondent would not make any errors (i.e., the tests are designed to be easy). Thus if errors are made, they are likely due to the timed nature of the task rather than task difficulty.

The National Institutes of Health Toolbox for the Assessment of Neurological and Behavioral Function (NIHTB) is a battery of cognitive, sensory, emotional, and motor functioning measures (Gershon et al., 2013). Within the cognitive battery, there is a choice reaction time test modeled after Salthouse's Pattern Comparison Task (Salthouse et al., 1991), which requires the participant to judge whether two images are the same, and respond via tapping "yes" or "no" buttons on a tablet screen (Carlozzi et al., 2013, 2015). Pattern Comparison Processing Speed (PCPS) is included in the NIHTB Cognition Battery for ages 7+ and is available for ages 3–6 as a supplementary measure. This supplementary version requires children to make a judgement as to whether two stimuli are the same or different, and then transform that judgment onto tapping a smiling emoji ("same") or a frowning emoji ("different") for their response (Carlozzi et al., 2013).

Unfortunately, there was poorer performance (i.e., lower than anticipated number of children able to follow instructions and respond at greater than chance levels) on the NIHTB PCPS test among 3- and 4-year-olds in the normative sample on this test (Carlozzi et al., 2015). In previous research, PCPS has also shown lower feasibility among older individuals of similar mental age with an intellectual or developmental disability (IDD; Hessl et al., 2016; Shields et al., 2020). While the NIHTB PCPS may be supplementary for young children, the lack of feasibility among older individuals with an IDD is potentially more concerning given its potential use as a treatment trial outcome. Processing speed is impaired relative to the neurotypical population in many individuals with IDDs (Mayes & Calhoun, 2007), and cognitive limitations such as slowed mental processing are key diagnostic features. On PCPS, we have found a left-right response pattern—originally primed on practice items (Shields et al., 2020). There are multiple possible reasons for patterned responding,

ome less focused or engaged over

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including that they may forget the test instructions, become less focused or engaged over time, or may have difficulty with the same/different judgment required to complete the task. These may be developmentally appropriate behaviors for individuals with a 3- or 4-year mental age, and thus may also partially explain the lower feasibility of the PCPS among young children. Alternating response patterns have also been noted in a previous study in which neurotypical 4-year-olds had to choose between two puppets after being asked questions regarding characteristics about them (Brosseau-Liard & Birch, 2010).

The goal for the current study was to develop and pilot a new choice reaction time processing speed test. We sought for it to have a higher feasibility among participants with IDD, given the lower mental age associated with these conditions. Additionally, the task should be designed such that it would not require making a judgement as to whether two stimuli were the same or different, but rather use a match-to-sample response. This reduces the cognitive demands from judgement as to whether stimuli are the same or different to the simpler task of identifying similarities. In this way, the novel Speeded Matching (SpM) is more like a cancellation paradigm with a structured array, where a direct match is marked. We hypothesized that SpM would have improved feasibility among an IDD sample, and that it would show a high split-half reliability. Further, we hypothesized that it would show good convergent validity correlations with other fluid cognition and processing speed measures, and that these would be stronger than putative divergent measures, such as crystallized verbal measures. As exploratory analysis, performance on SpM was compared across the IDD diagnostic groups. Lastly, the relationship between SpM and nonverbal mental age among the IDD sample was contrasted with the relationship between SpM and chronological age from a separate study of neurotypical young children.

Materials and Methods

Participants

IDD Sample—This study was ancillary to a larger longitudinal study evaluating the performance of the NIHTB Cognitive Battery in IDD. There were three subsamples, two of which were composed of syndromic forms of IDD (fragile X syndrome [FXS] and Down syndrome [DS]) and a third group which was composed of other individuals meeting diagnostic criteria for an intellectual disability (i.e. deficits in intellectual functioning and adaptive behavior) who did not have FXS or DS. This third group was composed of individuals primarily with idiopathic IDD, though a limited number had other types of syndromic IDD. There were three clinical sites recruiting for the samples. The local IRB for each site reviewed and approved all human subjects research. Eligibility for the parent study was chronological age between 6 and 25 years at the first visit, mental age above 3 years, IQ below 80, and documented adaptive behavior deficits. Exclusion criteria were uncorrected vision impairment, uncontrolled seizures, motor impairment affecting touchscreen use, and a history of head trauma, brain infection, or stroke.

Neurotypical Comparison Sample—Given that the limitations of the NIHTB PCPS were first noted with the IDD sample, these primary analyses utilized the IDD sample described above. However, PCPS is considered a supplementary test in the NIHTB for

ages 3–6, likely due to limited feasibility in younger typically-developing children (Carlozzi et al., 2015). We were interested in whether the SpM would have better performance in younger neurotypical children as well. In a separate study, the feasibility and performance of SpM was assessed among 118 neurotypical children between 30 to 71 months old collected via a market research firm. This chronological age overlaps the targeted mental age for a large portion of this study sample. We calculated the split-half reliability and the relationship with chronological age in this sample as well. As the focus of that study was on measure development and test characteristics, IRB review determined that it did not involve human subjects research. Parental permission was, nonetheless, provided prior to administration of SpM.

Measures

The primary measure utilized herein is the novel SpM test. It was built within the NIHTB iPad application shell as an experimental measure. The test consists of instructions presented as a demonstration, four practice items, and then 130 live items. For each item, there is a line drawing of an animal face at the top of the screen and four line drawings on the bottom half of the screen, one of which is an exact-match to the target. We expect feasibility to improve with SpM, insofar as it increases the number of answer choices (two to four), couples a more intuitive objective (matching), and response modality (tapping the match). We defined *feasibility* as the participant's ability to pass practice and respond meaningfully to the test stimuli to obtain a valid score (i.e., without a discernable pattern). Each item was monochromatic, but color varied across items to improve engagement. An example item is provided in Figure 1. When a participant selected a response option, the background changed shades to signify that it had been selected and the tablet emitted a click sound. A participant had 120 seconds to complete as many of the live items as possible (the full test time, including instructions, practice, live items, and inter-item intervals was less than 5 minutes). In order to accommodate the unlikely event that a participant was able to complete all items in the allotted time, we used a rate-based scoring procedure: the number correct per second of active item administration time.

In order to measure if or how SpM improved feasibility for this population, the NIHTB Cognition Battery was co-administered, including PCPS. The NIHTB Fluid, Crystalized, and Total Cognition Composites were considered for validity evidence, when participants were able to complete all of the tests for these composites. Additionally, the raw score from the Wechsler Preschool and Primary Scales of Intelligence (WPPSI-IV; Wechsler, 2012) Bug Search processing speed measure and the Woodcock-Johnson (WJ-III; Woodcock, McGrew, & Mather, 2001) Letter-Word Identification were collected as evidence for convergent and divergent validity, respectively. The approach of out-of-range testing, or using raw scores from tests for chronologically younger children among individuals with syndromic IDD, is somewhat common, and is often the recommended (or only) option available when examinees cannot achieve a score above the floor of the test within their chronological age (c.f. Soorya et al., 2018). We considered using the processing speed tests from the Wechsler Intelligence Scale for Children, but in previous studies, approximately half of individuals with FXS received a score on the floor of the test (Hessl et al., 2009). The Stanford-Binet 5 (Roid, 2003) also provided evidence for convergent validity, and the Vineland Adaptive

Behavior Scales—3 (Sparrow, Cicchetti, & Saulnier, 2016) was used to describe participant functioning levels.

Data cleaning and scoring

After every participant visit, an administration form was used to record whether the individual tests were considered valid—which was the primary factor to determine test feasibility. Excluding the feasibility results, analyses were restricted to valid scores. Before conducting analyses, raw data and bivariate correlations were visually assessed for normality, the presence of outliers, and floor or ceiling effects.

Statistical Analyses

All analyses were conducted using R version 4.0.2 (R Core Team, 2020). Participant demographics and group differences were compared using linear models, with posthoc pairwise comparisons using the emmeans package (Lenth et al., 2020), or with chi-square tests for nominal data, with post-hoc residual analyses conducted using the chisq.posthoc.test package (Ebbert, 2019). The difference between independent and dependent correlations was calculated using functions from the psych package (Revelle, 2019). All other analyses were conducted using the base functions within R, code written for this project, or the functions included within the extended tidyverse suite (Wickham et al., 2019). An RMarkdown file with code and results is available as supplementary online material.

To calculate the internal consistency, we correlated split-half reliability between rate scores for even- and odd-numbered items. To account for reducing each test by half, we applied the Spearman-Brown formula to the obtained correlation to index the internal consistency of the full-length test. We hypothesized that the reliability of SpM would be high (>0.80).

As evidence for the validity of the SpM test, the overall rate was correlated with other tests from the validity measures. Given that all tests related to cognitive abilities, even the divergent validity measures were anticipated to have a moderate relationship with SpM. As such, we tested whether the convergent and divergent validity coefficients were significantly different from one another using William's tests (Steiger, 1980). We hypothesized that the rate for SpM would be more strongly correlated with measures of processing speed (specifically) or fluid cognition (in general) than crystalized abilities such as reading skills. Likewise, it was hypothesized that SpM would be more strongly correlated with nonverbal mental age than chronological age, given that participants had an IDD herein.

Results

Participants

There were 148 participants across three clinical sites that participated in this ancillary study protocol. There were 54 diagnosed with FXS between the chronological age (CA) of 8 and 27 years, 54 participants with DS between 9 and 27 CA, and 40 participants were in the OID group between 6 and 27 CA. Table 1 presents sample characteristics overall and by clinical group for the IDD sample. (For the neurotypical comparison sample, see Supplementary

Table 1 for demographic information). Few significant differences emerged across groups, except that the participants in the OID group had a higher IQ than the participants in the FXS and DS groups (which did not differ from each other). While the sex assigned at birth distribution was initially significant, after correcting for multiple comparisons, the groups did not differ. For race/ethnicity, other underrepresented groups (including multiracial and unknown) was also more frequently observed among participants in the OID group and less frequently among participants with FXS. The proportion of parent-reported ASD diagnosis also differed significantly among groups.

Feasibility

Feasibility of SpM was strong; out of the 148 participants, 146 passed the practice items and moved on to the live test items; 142 had a valid score (96% of the sample). In comparison, among these 148 participants, the convergent validity measures NIHTB PCPS and WPPSI Bug Search were considered valid for 68% and 82%, respectively (n=101 and 122).

Internal Consistency Reliability

Split half reliability was assessed on the rate correct per second, calculated separately for even and odd test items. For those with a valid score, the correlation between the rates was 0.95, p < 0.001; after applying the Spearman Brown formula, the expected internal consistency was 0.98.

Convergent and Divergent Validity

Table 2 shows the correlations between SpM and the validity measures included herein. Consistent with our hypotheses, SpM had moderate-to-strong correlations with all measures, excluding chronological age (n=142, r = 0.14). Of particular relevance, SpM was highly correlated with the two other measures of processing speed (PCPS and Bug Search).

To further examine the hypotheses regarding divergent validity, William's tests were conducted. Table 3 provides the results of these tests, using complete cases for both convergent and divergent measures. Consistent with the study expectations, SpM was more highly correlated with nonverbal mental age than chronological age and with WPPSI Bug Search than the WJ Letter-Word Identification. Evidence from the NIHTB Fluid vs. Crystalized Cognition composites was in the direction of our hypothesis, but due to the small sample size having a valid fluid composite, it failed to reach statistical significance. Contrary to the hypotheses, though, the correlation between SpM and PCPS was not significantly stronger than the relationship between SpM and the WJ Letter-Word Identification.

Group Differences

Exploratory analyses of group differences between participants with FXS, DS, and OID suggested a significant main effect for group (F(2,138)=5.24, p<0.01), but the model did not explain a significant proportion of the score variance (R²=0.07). However, there were significant differences in overall cognitive ability between groups (c.f. Table 1: OID had the highest FSIQ). Adding FSIQ to the linear model significantly improved proportion of explained variance (R²=0.22, F(1,137)=41.337, p<0.01). There remained an overall

statistically-significant effect for study group (F(2,137)=4.89, p<0.01). We used pairwise expected mean difference comparisons, with p-values corrected using the Tukey method. Table 4 shows the unadjusted group means, the expected means after accounting for FSIQ differences, and the standardized mean difference between groups. Adjusting for IQ, there was no significant difference between OID and the other two groups, but DS and FXS were significantly different from each other (p<0.01, SMD=0.61), with DS having poorer performance on SpM.

Comparisons to Neurotypical Children

Data were also available from a separate study of 118 neurotypical children. In that sample, the split-half reliability was 0.90, which was lower than what was obtained in the IDD samples but still within the hypothesized range of an acceptable reliability coefficient. The correlation between chronological age and SpM score was r=0.65. Figure 2 plots the rate score by chronological age in the neurotypical sample, as well as the relationship between mental age and SpM score in the IDD sample. Using the difference test between two independent correlations, these relationships are not significantly different from one another (z=1.27, p=0.20), though the chronologically-older participants with IDD had a higher rate of correct responding.

Discussion

Processing speed is a critical cognitive skill that can be measured early in life and has a clear developmental trajectory. This study provides evidence for the reliability and validity of a novel processing speed task using a matching and cancellation paradigm. It is designed to be used in early childhood and among individuals with neurodevelopmental disabilities. This study provides initial support for its validity among individuals with a mental age between 3 and 10 years old. It has the potential to be used with older children or adults as well, though it has not been tested in those age ranges. The test had a high feasibility among participants with an IDD, a high split-half reliability, and evidence for convergent and divergent validity with other measures of processing speed and cognition. There is a clear age effect in number correct per second across mental age, suggesting that participants with greater cognitive skill answer more items correctly in less time.

We also evaluated whether different diagnostic groups had differential performance on the test. This was an exploratory analysis without any hypothesized group differences, especially as previous research with the NIHTB PCPS test did not find differences among these participant groups (Shields et al., 2020). However, there were significant group differences in performance on SpM. After adjusting for group differences in IQ, the participants with DS had significantly poorer performance than the group of participants with FXS. Participants with OID did not differ from either. The presence of a group difference is unexpected, and should be evaluated further in future studies.

With regard to evidence for the test's validity, we found a strong correlation with nonverbal mental age among participants with IDD. This finding was replicated with a general population sample whose chronological age was similar to the mental age of the IDD participants. The increase in performance is consistent with anticipated developmental trends

From a more structural perspective, SpM also has benefits. Because the objective of the test is clear, fewer instructions are needed to be read by the examiner. This reduces the amount of time between instructions and data collection. Specifically, when administering cognitive tests to young children and participants with IDD, the examiner needs to be mindful of reduced attention spans. Maintaining engagement is vital in collecting valid data and fluidly administering an entire cognitive battery. Additionally, the "clicking" sound of making a selection, regardless of whether their answer was correct or incorrect, provides immediate auditory feedback, which is important in maintaining attention. And finally, SpM varies colors across items, which helps maintain interest and focus. Together, this significantly improves feasibility of processing speed measures at this developmental stage.

Limitations and Next Steps

One limitation of these analyses is that the neurotypical sample did not include measures of convergent or divergent validity. While there is good evidence for the validity of SpM in IDD samples, additional evidence would be beneficial for younger children. Additionally, neither sample examined practice effects or test-retest reliability. Though the split-half reliability was excellent, if the performance was occasion-specific, this approach would not have identified it. Future research should examine the test-retest reliability in both neurotypical and IDD samples. This is especially important, given that practice effects have been reported on other processing speed tests, including PCPS (Carlozzi et al., 2015).

The next step for SpM should be a larger study examining additional psychometric properties. Building on this initial evidence, there is potential for SpM to be included in future versions of the NIHTB as a measure of processing speed in younger children. The current PCPS is supplemental for ages 3–6 and has been suggested as inappropriate altogether for ages 3 or 4 (Carlozzi et al., 2015). However, insofar as processing speed is strongly related to other cognitive skills, having a reliable index of it at the earliest possible age is desirable. Developing age-based norms, then, would support the use of this test.

Conclusions

The novel SpM test holds promise as a measure of processing speed. It may be especially beneficial for individuals with younger chronological and/or mental ages, insofar as it does not require a judgment as to whether something is "the same" or "different." Additionally, it does not require individuals to map that judgement onto a symbol for responding. Instead the examinee searches for an exact match-to-sample, selects it (as in a cancellation paradigm), and moves to the next item as fast as possible. To accommodate individuals who may finish all available items before the time limit, a rate-based score (number correct per second) is recommended for use. This shows a clear developmental trend in both the general population and in an IDD sample. SpM should be considered whenever processing speed is to be assessed among young children and those with IDD and lower mental age.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1: Practice item from Speeded Matching



Figure 2: Relationship between Age in Months and Number Correct per Second GP-CA=General Population—Chronological Age; IDD-MA=Intellectual or Developmental Disability—Nonverbal Mental Age

Table 1:

Participant Demographics

	Overall	FXS	DS	OID	Differences	
Chronological Age (in years)	17.8 (5.4) 148	18.5 (5.0) 54	17.4 (4.9) 54	17.5 (6.4) 40	F(2, 145)=0.63, <i>p</i> >0.10.	
Nonverbal Mental Age (in months)	65.0 (19.4) 142	58.4 (18.7) 53	65.9 (16.9) 52	73.3 (20.5) 37	F(2,139)=7.13, <i>p</i> =0.001 OID > FXS	
SB-5 FSIQz	52.5 (15.3) 146	48.4 (15.6) 53	50.7 (13.4) 53	60.3 (14.6) 40	F(2,143)=8.16, <i>p</i> <0.001 OID > FXS, DS	
NIHTB Total Cognition	59.4 (14.5) 33	59.9 (18.3) 8	55.8 (13.5) 14	63.7 (12.6) 11	F(2,30)=0.93, <i>p</i> >0.10	
Vineland-3 Adaptive Behavior Composite	46.1 (18.5) 139	41.8 (20.0) 49	48.0 (17.1) 53	48.9 (17.5) 37	F(2,136)=2.06, <i>p</i> >0.10	
	Overall	FXS	DS	OID	Differences	
Sex - Male	91 (61%)	39 (72%)	26 (48%)	26 (65%)	$\chi^2(2)=6.9, p=0.03$	
Sex - Female	57 (39%)	15 (28%)	28 (51%)	14 (35%)		
Race – Hispanic or Latinx	25 (17%)	7 (13%)	10 (19%)	8 (20%)	$\chi^{2}(6)=15.9, p=0.01$ OID: Other+ FXS: Other-	
Race – Non-Hispanic White	92 (63%)	39 (72%)	33 (62%)	20 (72%)		
Race – Non-Hispanic Black	11 (7%)	7 (13%)	2 (4%)	2 (5%)		
Race - Other, Multiracial, or Unknown	19 (13%)	1 (2%)	8 (15%)	10 (25%)		
Parent-Reported ASD	62 (42%)	31 (57%)	5 (9%)	26 (65%)	$\chi^2(2)=39.6, p<0.01$	
Parent-Reported non-ASD	83 (56%)	20 (37%)	49 (91%)	14 (35%)	FXS: ASD+, nonASD– DS: ASD–, nonASD+ OID: ASD+, nonASD–	
Any medication use	103 (70%)	45 (83%)	31 (57%)	27 (68%)	$\chi^{2}(2)=8.7, p=0.01$ FXS: noRx-, anyRx+ DS: noRx+, anyRx-	
Any psychotropic medication	67 (45%)	25 (46%)	21 (39%)	21 (53%)	$\chi^2(2)=1.8, p>0.10$	
Seizure medications	6 (4%)	1 (2%)	0 (0%)	5 (13%)	$\chi^{2}(2)=10.3, p<0.01$ OID: noRx-, seizRx+	
Stimulant medications	31 (21%)	15 (28%)	4 (7%)	12 (30%)	$\chi^{2}(2)=9.5, p<0.01$ DS: noRx+, stimRx-	
Mood Stabilizer medications	25 (17%)	13 (24%)	3 (6%)	9 (23%)	$\chi^{2}(2)=7.8, p=0.02$ DS: noRx+, moodRx-	
Thyroid medications	21 (14%)	1 (2%)	18 (39%)	2 (5%)	χ ² (2)=25.8, <i>p</i> <0.001 FXS: noRx+, thyrRx– DS: noRx–, thyrRx+	

NOTE: Three participants from the FXS group were missing parent-reported ASD diagnoses. For continuous data, if two groups are listed in the group differences, the third group was not significantly different than either. In cases where groups are separated by a comma, they are not significantly different from each other, but are different from the third group. For nominal data, a (+) group has more cases than expected while a (-) group has fewer cases in post-hoc comparisons. If no groups are listed, there were no significant pairwise differences after correcting for multiple comparisons

Table 2:

Correlations between Speeded Matching and Validity Measures

Measure	Ν	r
NIHTB Total Composite	32	0.63
NIHTB Fluid Composite	35	0.65
NIHTB Crystallized Composite	127	0.42
NIHTB PCPS	100	0.67
SB5 FSIQ	141	0.49
WPPSI Bug Search	128	0.72
WJ Letter-Word	141	0.55
Chronological Age	142	0.14
Nonverbal Mental Age	136	0.54

Table 3:

Divergent Validity Difference Test Between Dependent Correlations

Convergent	Divergent	N	Convergent Correlation	Divergent Correlation	Correlation between Validity Measures	t-value	р
Nonverbal Mental Age	Chronological Age	136	0.54	0.09	0.11	4.49	< 0.001
NIHTB Fluid	NIHTB Crystallized	35	0.65	0.44	0.57	1.68	0.05
NIHTB PCPS	WJ Letter-Word	100	0.67	0.57	0.51	1.34	0.09
WPPSI Bug Search	WJ Letter-Word	128	0.72	0.54	0.48	2.90	0.00

Table 4:

Groups Differences

Comparison	Expected Rate			SMD			
	FXS	DS	OID	OID vs FXS	OID vs DS	DS vs FXS	
Unadjusted	0.63	0.53	0.67	0.20	0.66*	0.45	
Adjusted for FSIQ	0.66	0.54	0.62	-0.19	0.42	-0.61*	

* Tukey-adjusted p<0.01; SMD=Standardized Mean Difference