*Acta Psychiatr Scand 2007: 116: 129–136*
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DOI: 10.1111/j.1600-0447.2007.01008.x



*ACTA PSYCHIATRICA SCANDINAVICA*

# Stability of executive function deficits into young adult years: a prospective longitudinal follow-up study of grown up males with ADHD

Biederman J, Petty CR, Fried R, Doyle AE, Spencer T, Seidman LJ, Gross L, Poetzl K, Faraone SV. Stability of executive function deficits into young adult years: a prospective longitudinal follow-up study of grown up males with ADHD.

**Objective:** Although individuals with attention deficit-hyperactivity disorder (ADHD) commonly exhibit deficits in executive functions that greatly increase the morbidity of the disorder, all available information on the subject is cross sectional.
**Method:** Males ($n = 85$) 9–22 years with ADHD followed over 7 years into young adulthood were assessed on measures of sustained attention/vigilance, planning and organization, response inhibition, set shifting and categorization, selective attention and visual scanning, verbal and visual learning, and memory. A binary definition of executive function deficits (EFDs) was defined based on a subject manifesting at least two abnormal tests 1.5 standard deviations from controls.
**Results:** The majority of subjects maintained EFDs over time (kappa: 0.41, $P < 0.001$; sensitivity: 55%, specificity: 85%, positive predictive value: 69%, and negative predictive value: 75%).
**Conclusion:** Considering the morbidity of EFDs, these findings stress the importance of their early recognition for prevention and early intervention strategies. EFDs are stable over time.

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Key words: executive functions; attention deficit-hyperactivity disorder; neuropsychology; stability

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Accepted for publication January 2 2007

**Significant outcomes**

- Eighteen out of the 26 subjects with executive function deficits (EFDs) at their first assessment met our definition of EFDs at follow-up, giving a positive predictive value of 69%.
- Forty-four out of the 59 subjects without EFDs at the first assessment in adolescence did not have EFDs at follow-up, giving a negative predictive value of 75%.
- Stability was low (intraclass correlations $< 0.30$) for Rey copy and delay organization and WCST failure to maintain set, moderate (intraclass correlations $> 0.30$ and $< 0.70$) for WCST perseverative errors, CVLT/WRAML, Stroop color-word, and high (intraclass correlations $\geq 0.70$) for freedom from distractibility.

**Limitations**

- Although our cut-off for EFDs, defined as two or more tests 1.5 standard deviations from the mean of the controls has face validity as a clinically relevant standard of EFDs which has been validated in prior work with children and adults, we recognize that dichotomizing a continuous variable may result in the loss of some information.
- As the majority of our subjects were Caucasians, our results may not generalize to other ethnic groups.
- Because the sample was referred, we do not know if our results will generalize to children with ADHD in the general population.

## Introduction

One source of the disability associated with attention deficit-hyperactivity disorder (ADHD) has been deficits in a group of neuropsychological functions known as executive functions (EFs). These are higher cortical mental processes that direct thought, action, and emotion, particularly during active problem solving. A consistent literature of published studies addressing neuropsychological performance in individuals with ADHD has found a pattern of neuropsychological deficits across the lifecycle in the executive system, similar to the literature documenting psychopathology (1–5). This literature, which has been recently summarized by several meta analyses (6–9), showed that individuals with ADHD commonly exhibit deficits in a wide range of executive functions including sustained attention, working memory, verbal fluency, as well as executive processing speed (6, 10, 11).

Although neuropsychological testing provides many useful dimensional measures of functioning of value, clinicians also need a means of sorting patients into groups for planning treatments. To facilitate that process, we created and validated a definition of executive function deficits (EFDs) that required an individual to have at least two impaired EF measures on a battery of eight neuropsychological tests of EFs (12). We showed that the presence of EFDs in youth with ADHD was associated selectively with an increased risk for school deficits, including grade retention, need for tutoring and placement in special classes, as well as a decrease in academic achievement relative to other youth with ADHD without EFDs. These results confirmed prior work by finding partial independence between neuropsychological and psychopathological outcomes in ADHD youth (13, 14).

Using the same approach, we found that EFDs significantly increased the risk for both educational and occupational under-attainment in adults with ADHD relative to other adults with ADHD without these deficits indicating that all the areas required for functional executive functions are taxed, including planning, organizing, and inhibition (15). Although these cross-sectional findings in pediatric and adult samples support the clinical importance of identifying EFDs in individuals with ADHD and suggest that EFDs would be stable through the lifecycle, the cross-sectional nature of these studies preclude inferences about the temporal stability of EFDs.

Whether EFDs are stable over time has important implications. If EFDs reflect a fluctuating state that varies with motivation, treatment or environmental circumstances, then we would expect low levels of stability. In contrast, if EFDs express an underlying trait reflecting cognitive dysfunction, we would expect relatively high levels of stability. Clinically, a stable working definition of EFDs in individuals with ADHD would be beneficial to clinicians dealing with individuals with ADHD for treatment planning. For example, different interventions may be needed in remediation of specific academic areas as well as interventions preceding particular occupational pursuits in individuals with ADHD and associated EFDs. Finally, having a valid definition of EFDs with known stability would assist the development of treatment approaches for EFDs.

### Aims of the study

To address these issues, we evaluated the stability of EFDs in a large sample of boys with ADHD grown up at the 7-year follow-up into young adult years. We hypothesized that psychometrically defined EFDs would be stable over time. To the best of our knowledge, this is the first systematic evaluation of the stability of EFDs in a prospective longitudinal sample of males with ADHD.

## Material and methods

### Subjects

Detailed study methodology has been previously reported (16, 17). Briefly, subjects were derived from a longitudinal case–control family study of boys with and without ADHD (16, 17). This study originally ascertained families on the basis of male (16) subjects aged 6–18 years with ($n = 140$) and without ($n = 120$) DSM-III-R ADHD from pediatric and psychiatric referral sources. Potential subjects were excluded if they had been adopted, or if their nuclear family was not available for study. We also excluded potential subjects if they had major sensorimotor handicaps (paralysis, deafness, blindness), psychosis, autism, inadequate command of the English language, or a Full Scale IQ less than 80. All of the ADHD subjects met full DSM-III-R diagnostic criteria for ADHD at the time of the clinical referral; at the time of recruitment they all had active symptoms of the disorder.

The psychiatrically referred group was ascertained from consecutive referrals to a pediatric psychopharmacology program at a major academic medical center. The pediatrically referred group was ascertained from the computerized records of a major Health Maintenance Organiza-

tion (HMO). At each ascertainment source we selected comparison subjects without ADHD. We have previously demonstrated no clinically or statistically significant differences between ADHD subjects ascertained from these two referral sources on measures of psychopathology, cognitive performance or psychosocial functioning (18).

We used a three-stage ascertainment procedure to select subjects. We used this approach because screening is known to decrease false-positive diagnoses and improve the accuracy of psychiatric diagnoses (19, 20). For ADHD subjects, the first stage was their referral, resulting in a clinical diagnosis of ADHD by a child psychiatrist or pediatrician. As many different clinicians using different clinical standards had made these diagnoses, we included a second, systematic screening using DSM-III-R criteria. This second stage confirmed the diagnosis of ADHD by screening all children positive at the first stage using a telephone questionnaire with their mother. Eligible case children meeting study entry criteria were recruited for the study and received the third stage, a diagnostic assessment with a structured interview. Only patients who received a positive diagnosis at all three stages were included in the final analysis.

We also screened potential non-ADHD controls in three stages. First, as stated above, we ascertained them from referrals to medical clinics for routine physical examinations at both the psychiatric and pediatric ascertainment sources. In stage 2, the control mothers responded to the DSM-III-R ADHD telephone questionnaire. Eligible controls meeting study entry criteria were recruited for the study and received the third stage, a diagnostic assessment with a structured interview. Only subjects classified as not having ADHD at all three stages were included in the control group. Using repeated measurements to determine case and control status, and only accepting subjects with consistent results, provides additional assurance that we have not incorrectly specified the diagnosis of our subjects. Parents and adult offspring provided written informed consent to participate, and parents also provided consent for offspring under the age of 18. Children and adolescents provided written assent to participate. The human research committee at Massachusetts General Hospital approved this study.

Analysis of stability was limited to the ADHD subjects assessed at first assessment ($n = 85$) because only 12% of controls were previously reported to have EFDs (12). We thought it sensible to focus on the ADHD sample, as this is the group of most interest to clinicians. ADHD subjects ranged from 9 to 22 years of age at first neuropsychological assessment, with a mean of 14.2 years (standard deviation = 2.9 years). ADHD subjects ranged from 16 to 30 years of age at follow-up, with a mean of 21.2 years (standard deviation = 3.2 years). The mean time between first assessment and follow-up assessment was 7.0 years (standard deviation = 1.1 years).

### Neuropsychological assessments

We assessed domains of neuropsychological functioning thought to be important in ADHD and to be indirect indices of frontosubcortical brain systems. These include measures of sustained attention/vigilance, planning and organization, interference control, set shifting and categorization, selective attention and visual scanning, verbal and visual learning, and memory.

First, we examined measures that were included in the dichotomous definition of EFD from our previous analyses. These included: i) the copy and delay organization scores of the Rey-Osterrieth Complex Figure (21, 22); (scored by the Waber–Holmes method (23)); ii) total errors score of an auditory continuous performance test (CPT) (24); iii) the perseverative errors and loss of set scores of the computerized version of the Wisconsin Card Sorting Test (WCST) (25); iv) the per cent of total words learned on the California Verbal Learning Test (CVLT) (26) for individuals 17 and older or on the Wide Range Assessment of Memory and Learning (WRAML) (27) for youth 16 years and under; v) The color-word score of the Stroop Color Word Interference Test (28); and vi) an additive combination of the WISC-R Digit Span and Oral Arithmetic subtests (29, 30) to approximate the Freedom From Distractibility Index of the Wechsler Intelligence Scale for Children-Third Edition (WISC-III) (31). In addition to the measures used in the original EFD definition, we examined the WISC-R digit symbol subtest, the separate oral arithmetic and digit span subtests (29). WISC–R Vocabulary and Block Design subtests, and the WRAT-R Reading and Arithmetic Scores (29, 32). Follow-up assessments paralleled the baseline battery, with some measures utilizing updated versions of tests. These included the WISC-III, the WRAT-III, the CVLT-C to replace the WRAML, and a different auditory CPT (33). Raters who applied the neuropsychological battery at follow-up were blind to the results from the first assessment. Testing conditions at first assessment paralleled the follow-up assessment including order of tests, training of psychometricians, and supervision. Subjects with neuropsychological data at first assessment who were lost to follow-up ($n = 36$)

did not significantly differ on any of the eight neuropsychological measures used to define EFDs compared with subjects who returned at follow-up (all $P > 0.20$).

### Statistical analysis

As previously described (12), a subject was considered to have EFDs if two or more of the eight neuropsychological measures above were considered impaired as defined by 1.5 standard deviations (93rd percentile for non-normal distributions) from the mean of the controls' scores. Cut-off points at first assessment were calculated for developmentally distinct age groups, 9 years old or less, 10–13 years old, 14–17 years old, and 18 years old or above. For follow-up assessments, age groups were used in accordance with those used by Kaplan (34): 16–19 years old and 20 years old or above. The analysis was done within age groups that were based on the normative data validated in the Delis–Kaplan Executive Function System. Thus the males with and without ADHD were stratified within those age ranges and compared with each other. These specific ranges were chosen due to the large national standardization study that the D-KEFS underwent. Stability over time of individual neuropsychological measures was assessed with the kappa statistic for EFDs and intraclass correlations for individual test measures. Effects of time were calculated using McNemar's test for binary data and paired *t*-test for continuous data. Stability and change over time were not assessed for the CPT due to the use of a different version of the CPT at follow-up. However, this new version of the CPT was used to define binary EFDs at follow-up since it was the best approximation of the test used at first assessment. All tests were two-tailed with alpha set at 0.05.

## Results

### Stability of binary definition of EFDs

Our binary definition of EFDs (at least two abnormal tests, one and a half standard deviations from controls) had a moderate and significant kappa of 0.41 ($P < 0.001$, Fig. 1). Eighteen out of the 26 subjects (69%) with EFDs at their first assessment met our definition of EFDs at follow-up. Thus, the positive predictive value (PPV) of EFD at the first assessment as a predictor of EFD at the 7-year follow-up was 69%. Forty-four out of the 59 subjects without EFDs at the first assessment in adolescence did not have EFDs at follow-up giving a negative predictive value (NPV) of

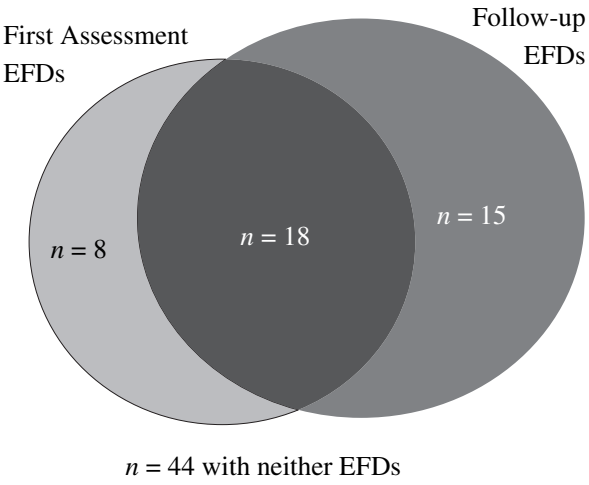


*Fig. 1.* Stability of EFDs at follow-up.

75%, i.e. the probability of not having EFD at follow-up was 75% if the subject did not have EFD at the first assessment. The sensitivity of the first EFD assessment was 55%; the specificity was 85%. Although a higher percentage of ADHD boys had EFDs at follow-up compared with first assessment, there was not a significant effect of time on the rate of EFDs ($\chi^2_{(1)} = 2.1$, $P = 0.14$).

### Stability of individual neuropsychological testing

Intraclass correlations were used to measure stability of individual neuropsychological testing used between Time 1 and Time 2 assessments (Table 1). For measures used to define EFDs, intraclass correlations were low ($<0.30$) for Rey copy and delay organization and WCST failure to maintain set, moderate ($>0.30$ and $<0.70$) for WCST perseverative errors, CVLT/WRAML, and Stroop color-word, and high ($\geq 0.70$) for freedom from distractibility. All intraclass correlations were statistically significant ($P < 0.01$) except for Rey copy organization and WCST failure to maintain set. The effect of time was also tested for each neuropsychological score (Table 1). Significant improvements (on average) from first assessment to follow-up assessment were observed for Rey copy organization, Rey delay organization, Stroop color-word, freedom from distractibility, and WCST perseverative errors.

For secondary measures assessed (i.e. not used to define EFDs), intraclass correlations were moderate ($>0.30$ and $<0.70$) for oral arithmetic, digit span, and digit symbol, and high ($\geq 0.70$) for full scale IQ, WISC block design, WISC vocabulary, WRAT arithmetic, and WRAT reading. All intraclass correlations were statistically significant

Table 1. Intraclass correlations and mean differences for individual tests between first neuropsychological assessment and follow-up neuropsychological assessment in ADHD subjects

| Neuropsychological measure | Intraclass correlation | *P*-value | Mean difference ± SD (Follow-up − first assessment) | *t*-statistic | *P*-value |
|---|---|---|---|---|---|
| CPT errors | NA | NA | NA | NA | NA |
| Rey copy organization | 0.15 | 0.10 | 1.5 ± 4.6 | 2.99 | 0.004 |
| Rey delay organization | 0.28 | 0.006 | 2.3 ± 4.5 | 4.54 | <0.001 |
| WCST – perseverative errors | 0.50 | <0.001 | −3.9 ± 8.4 | −3.66 | <0.001 |
| WCST – failure to maintain set | 0.01 | 0.48 | −0.2 ± 1.6 | −1.22 | 0.23 |
| CVLT/WRAML | 0.58 | <0.001 | 0.02 ± 0.1 | 1.59 | 0.12 |
| Stroop color-word | 0.43 | <0.001 | 9.1 ± 8.7 | 9.49 | <0.001 |
| Freedom from distractibility | 0.75 | <0.001 | 1.4 ± 3.5 | 3.56 | <0.001 |
| Oral arithmetic | 0.65 | <0.001 | 0.2 ± 2.6 | 0.70 | 0.49 |
| Digit span | 0.68 | <0.001 | 1.2 ± 2.2 | 4.94 | <0.001 |
| Digit symbol | 0.63 | <0.001 | −1.2 ± 2.5 | −4.14 | <0.001 |
| Full scale IQ | 0.84 | <0.001 | 0.6 ± 7.8 | 0.68 | 0.50 |
| Block design | 0.82 | <0.001 | −1.9 ± 9.5 | −1.76 | 0.08 |
| Vocabulary | 0.70 | <0.001 | 1.6 ± 11.9 | 1.18 | 0.24 |
| WRAT arithmetic | 0.79 | <0.001 | −0.4 ± 11.4 | −0.31 | 0.76 |
| WRAT reading | 0.81 | <0.001 | 0.9 ± 9.5 | 0.86 | 0.39 |

CPT, continuous performance test; WCST, Wisconsin Card Sorting Test; CVLT, California Verbal Learning Test; WRAML, Wide Range Assessment of Memory and Learning; NA, not appropriate due to different tests at first assessment and follow-up.

($P < 0.01$). Significant improvement (on average) from first assessment to follow-up assessment was observed for digit span. Digit symbol was significantly poorer on average over time.

Figure 2 shows scatterplots of first assessment versus follow-up scores for each of the eight neuropsychological measures used to define EFDs. The $y = x$ line is provided to reference the differences in first assessment and follow-up scores (except for CPT scores because of different tests at first assessment and follow-up). That is, the closer a data point is to this reference line, the more similar the subject's first assessment and follow-up scores were.

## Discussion

This 7-year followup of boys with ADHD grown up found that the majority of those who had EFDs in adolescence continued to have EFDs in young adult years. These longitudinal results into young adult years confirm and extend our previous findings by mid-adolescence by documenting that a sizeable minority of ADHD children grown up continue to be afflicted with EFDs. Our previous paper on youth included both males and females, however the percentage of the subjects with EFDs (33%) is similar to the percentage found in the present study (39%). Considering the morbidity associated with EFDs in individuals with ADHD, these findings stress the importance of early recognition of EFDs for prevention and early intervention strategies.

The finding of a PPV of 69% should alert clinicians that for the majority of cases EFDs will be stable from mid-adolescence to adulthood. The NPV of 75% indicates that most adolescents who do not have EFDs will not develop EFDs in adulthood. Nonetheless, this should also alert clinicians and patients to the possibility that a large minority (25%) of ADHD adolescents without EFDs will show EFDs in adulthood. In considering these results, clinicians should be aware that the predictive values we cite are influenced by the base rates of EFD in the settings to which they are applied. For clinicians working in settings having a lower rate of EFDs, we would expect the PPV to be lower and the NPV to be higher than what we have reported. For those working in settings having higher rates of EFDs, we would expect the PPV to be higher and the NPV to be lower. In contrast, sensitivity and specificity are not influenced by base rates so these can be applied to any setting with confidence.

Although further work is needed to understand the sources of stability and instability for EFDs, several possibilities are worthy of comment. From our meta-analysis of follow-up studies (35) we know that some cases of ADHD remit over time. Further work should determine if EFD remission is predicted by ADHD remission. The onset of new EFDs might have been due to changes in the environment. The transition from adolescence to adulthood is fraught with many challenges that stress executive functions and might possibly lead to the expression of EFDs. It is also possible that changes in the brain mediate changes in EFD. For example, there is an age dependent decline of dopamine transporter activity in the brain (36) and some brain volumes that are reduced in ADHD

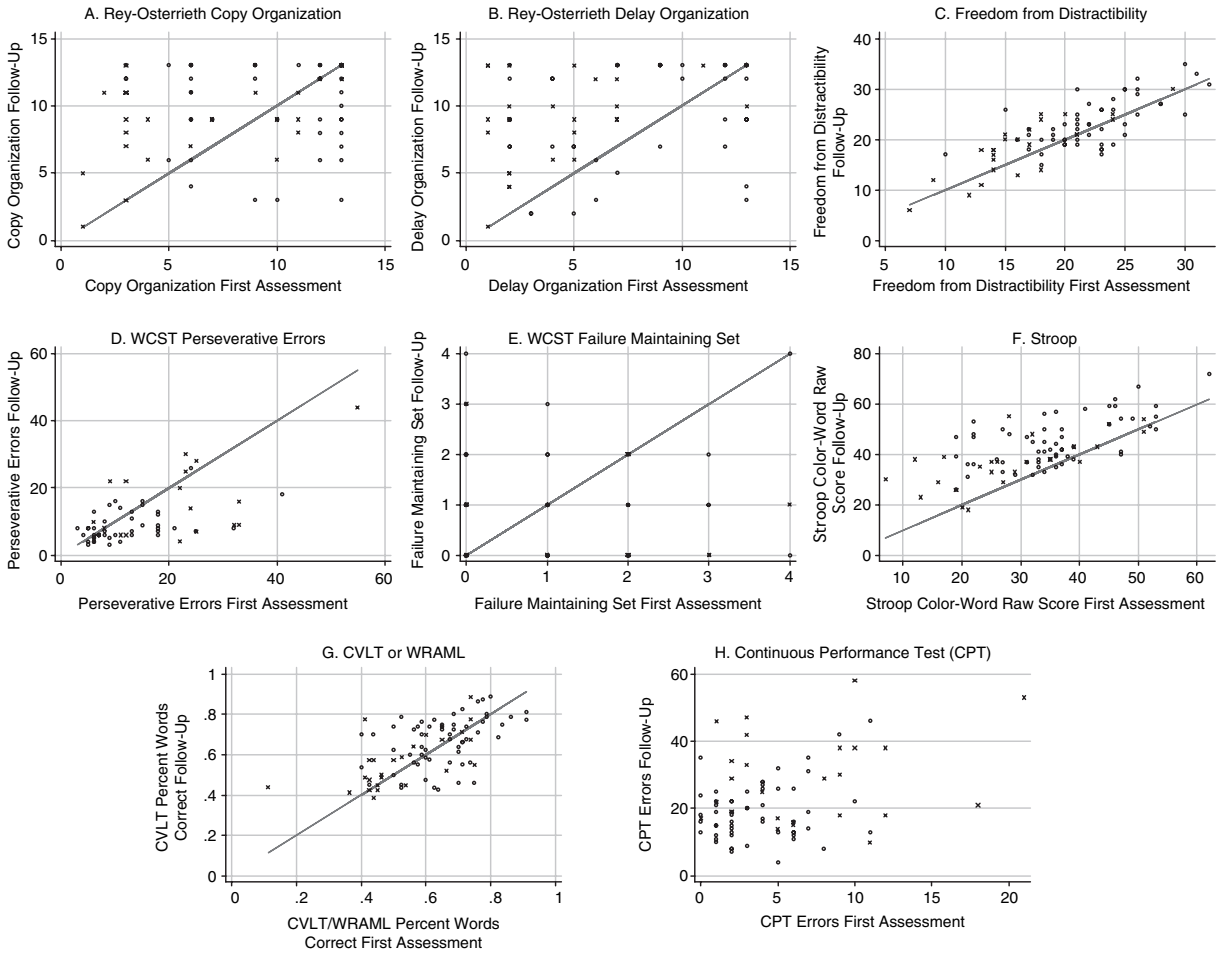


*Fig. 2.* Scatterplots of first assessment and follow-up scores for measures used to determine executive function deficits (EFDs). The y = x line is provided as a reference for how much scores changed from first assessment to follow-up (for measures with comparable tests at both time points). X = EFDs at First Assessment, O = No EFDs at First Assessment

youth show evidence of normalization with aging (37).

The rate of comorbid EFDs in this longitudinal sample of young adults with ADHD is consistent with our recently published study documenting similar percentages of EFDs in adults with ADHD using similar methods (15). That study found that EFDs in adults with ADHD had significant negative effects on school functioning, social class, and educational and occupational attainments. These results indicate that EFDs compound the already compromised workplace functioning of an adult with ADHD. Taken together, these results indicate that EFDs should be seen as a discrete and persistent cognitive comorbidity within ADHD that can have significant effects upon selective aspects of an individual's adaptive behaviour.

These prospective results documenting the stability of EFDs in ADHD children grown up provide further support for our proposed definition of EFDs. Considering that our prior work showed that EFDs selectively predicted educational and occupational attainments (12), the assessment of EFDs clearly provides information that cannot be extracted from assessments of psychopathology. Moreover, in contrast to the stability of the categorical measure of EFDs used, the results observed in the analysis of individual neuropsychological tests were more variable between first assessment and follow-up for individual binary neuropsychological measures. These findings provide further support for the utility of the proposed categorical definition of EFDs based on two abnormal tests to help identify individuals with ADHD suspected of having EFDs.

The strengths of this report include the well-characterized sample, the reliance on well-established neuropsychological testing, and the long-term follow-up period. This is especially important since very few other studies have followed males with ADHD into adulthood, particularly regarding their neuropsychological

profiles. Also, our sample was ascertained from both pediatric and psychiatric sources. As our prior report demonstrated no differences between subjects from these referral sources across a broad range of domains (18), this feature enhances the generalizability of our findings.

On the other hand, our results should be considered in light of several methodological limitations. Although our cut-off for EFDs, defined as two or more tests 1.5 standard deviations from the mean of the controls has face validity as a clinically relevant standard of EFDs which has been validated in prior work with children (12) and adults (15), we recognize that dichotomizing a continuous variable may result in the loss of some information. Yet our prior work suggests that the loss of information is not dramatic because we found high correlations between the factor analyzed test battery and the number of tests impaired (12). Thus, this loss of information seems to be a reasonable trade-off for the applicability and clinical relevance of our method. Although continuous measures provide a more detailed view of a patient's functioning, clinicians need to make binary decisions (e.g. should a child be referred for further testing or for psychoeducational services). Neuropsychologists often struggle with a clear diagnosis of EFDs based on numerous tests that each assesses a different domain of executive functioning. Although knowing these detailed scores is useful for describing a patient's full profile of neuropsychological strengths and weaknesses, having a method for clearly defining a diagnosis of EFDs in a manner similar to DSM diagnoses would be helpful when a binary clinical or research decision is called for. In clinical practice, neuropsychologists vary in terms of what cutoffs are used to reflect clinical impairments, with impairment cutoffs ranging from 1.0 to 2.0 standard deviations. In our prior work, we chose 1.5 as a balance between these extremes in our initial paper on youth and kept it consistent for this paper. One and a half standard deviations corresponds to the 7th percentile so is consistent with the notion of impairment while not being so extreme as to isolate a small subsample and preclude reliable analyses.

Also, as the majority of our subjects were Caucasians, our results may not generalize to other ethnic groups. Because the sample was referred, we do not know if our results will generalize to children with ADHD in the general population. However, because we sampled from both psychiatric and pediatric referrals, our results should generalize to a wide range of referred cases, which are of most interest to clinicians. In addition, because we did not manipulate treatment as an independent variable, we cannot use our study to determine treatment effectiveness (38) nor to describe the untreated course of ADHD. Future work will need to determine what factors, if any, can predict the stability or instability of EFDs. While our aim was to assess the young adult outcome of children with ADHD, a small portion of our sample had not yet reached adulthood.

Despite these considerations, our 7-year follow-up study has confirmed and extended the results from the mid-adolescent assessment showing that psychometrically defined EFDs are relatively stable over time into young adult years. Our proposed categorical definition of psychometrically defined EFDs can help identify a sizeable minority of individuals with ADHD at high risk for deficits in educational and occupational functioning.

## Acknowledgement

This work was supported, in part, by a grant from USPHS (NICHD), grant 5RO1 HD-36317–07 (J.B.).

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