RESEARCH ARTICLE

Assessment of the Cambridge Neuropsychological Test Automated Battery test in Saudi children with learning disabilities: A case-control study [version 1; peer review: 1 approved with reservations]

Nouf Al Backer^{1,2}, Koloud Ateeq Alharbi³, Abdulrahman Alfahadi², Syed Shahid Habib⁴, Shahid Bashir^{id}⁵

¹Department of Pediatric Medicine, King Khalid University Hospital, Riyadh, 11461, Saudi Arabia

²College of Medicine, King Saud University, Riyadh, 11461, Saudi Arabia

³College of Medicine, Ibn Sina National College, Jeddah, 22421, Saudi Arabia

⁴Department of Physiology, College of Medicine, King Saud University, Riyadh, 11461, Saudi Arabia

⁵Department of Neurophysiology, Neuroscience Center, King Fahad Specialist Hospital, Dammam, Saudi Arabia

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Abstract

Background: The neuropsychological tests and its subtests are composed of the motor planning task; simple reaction time task and the intradimensional/extradimensional shift (IED) task from the Cambridge Neuropsychological Test Automated Battery (CANTAB) were developed to examine specific components of cognition. The main objective of this study was to examine the reliability of these CANTAB subtests in pediatric patients with learning disabilities (LD) in Saudi Arabia.

Methods: We administered the CANTAB subset test to 92 participants with LD and 68 controls with no LD. The tests performed were motor planning task (MOT), simple reaction time task (SRT) and the intradimensional/extradimensional shift (IED).

Results: There was no significant age difference between the case and the control group (case: 9.2 ± 2.4 years versus controls: 9.0 ± 1.6 years, $p=0.544$). The IED and MOT were significantly longer among patients with LD versus control ($p < 0.001$). LD cases had a longer SRT time than controls (cases: 1050.4 ± 626.5 versus controls: 815.5 ± 133.9 , $p=0.003$). LD patients completed an average of 3.0 stages, than the controls, who were able to complete a mean of 8.4 IED stages ($p < 0.001$). SRT was significantly longer in the case group (965.9 ± 716.4) compared to the controls (747.7 ± 120.7 , $p=0.014$). LD cases made more errors in the motor screening tasks (MOT-Error) compared to the control group (case: 14.6 ± 4.5 versus controls: 12.4 ± 2.7 , $p < 0.001$).

Open Peer Review

Approval Status ?

	1
version 2 (revision) 25 Jun 2019	? view
version 1 15 Mar 2018	? view

1. Maksym V. Kopanitsa^{id}, Imperial College, London, UK

Any reports and responses or comments on the article can be found at the end of the article.

Conclusion: Patients with LD have poor CANTAB subtest results. If these CANTAB subtests do measure cognitive function, this adds to the accumulating evidence of cognitive impairment association in LD, and such studies should remain an active area of research.

Keywords

CANTAB, learning disabilities, cognition, Saudi Arabia

Corresponding author: Shahid Bashir (shahid.bashir@kfs.h.med.sa)

Author roles: **Al Backer N:** Data Curation, Investigation, Methodology, Supervision, Validation, Visualization, Writing – Original Draft Preparation; **Ateeq Alharbi K:** Conceptualization, Data Curation, Methodology, Validation, Writing – Original Draft Preparation, Writing – Review & Editing; **Alfahadi A:** Data Curation, Methodology, Supervision, Validation, Writing – Original Draft Preparation, Writing – Review & Editing; **Shahid Habib S:** Conceptualization, Formal Analysis, Investigation, Methodology, Software, Supervision, Validation, Visualization, Writing – Original Draft Preparation; **Bashir S:** Conceptualization, Data Curation, Formal Analysis, Investigation, Methodology, Software, Supervision, Validation, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing

Competing interests: No competing interests were disclosed.

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Expression of Concern:

18th October 2019: Since publication of this article, the F1000Research editorial team were made aware of potential issues with the manuscript and the accompanying data that could affect interpretation of the results. We are investigating these issues with corresponding author Shahid Bashir, in line with guidance from the Committee of Publication Ethics. Further action will be dependent on the outcome of these discussions and peer review activity has been suspended in the meantime. We request that no one copies or redistributes the material in any medium or format until this issue is resolved.

11th November 2019: Since being made aware of the potential problems with the data in this article, the F1000Research editorial team have continued to communicate with corresponding author, Shahid Bashir, in attempt to identify and promptly resolve the issues identified. After further investigation and discussion with co-authors, Dr Bashir has provided evidence to show that the current findings are inaccurate as a result of honest error in the handling and transfer of data files. Dr Bashir is working closely with the editorial team to correct and reanalyse the data from the raw files. In line with [F1000Research policies for permanency of content](#), we will soon be publishing a revised 'corrected' version of this article to ensure the data are corrected and fully reliable. This policy takes into account current [best practice](#) in the scholarly publishing and library communities, and ensures the integrity and completeness of the scholarly record. Corrections and changes relative to the previous version will be clearly summarised in the 'Amendments' section at the start of the new version.

Introduction

Cognitive impairment of executive dysfunctions (EFs) is very common in individuals diagnosed with learning disabilities (LD)¹⁻³. The EFs profile contains several brain functions including planning, organization, self-monitoring, mental representation of tasks essential driven to prefrontal cortex to perform complex behavior task throughout life^{2,4-6}. There are a number of experimental studies showing EFs in individuals with LD disorders, across a wide range of functional levels and ages. These studies have reported that response inhibition, working memory, cognitive flexibility, planning, fluency and vigilance problems in these children⁷⁻¹⁰. EFs, including response inhibition, set-shifting, working memory, and planning, have been found to be impaired in children with attention deficit hyperactivity disorder (ADHD) and with LD¹⁰⁻¹³.

The computer-controlled system known as the Cambridge Neuropsychological Test Automated Battery (CANTAB) is a nonverbal (visually presented) set of tasks developed to recognize areas of the brain for cognition¹⁴⁻²¹.

Three CANTAB subtests, the Motor task, simple reaction time, and the Intradimensional/Extradimensional (IED) tasks, test the functions of prefrontal cortex region of the brain, which contains the planning and programming areas of the human brain. Neuroimaging data has provided support in exploring their roles. Thus, cognitive impairments associated with LD, and their neural underpinnings can be studied by CANTAB.

EFs refers to neuropsychological processes that enable physical, cognitive, and emotional self-control in LD children.

EFs are often present in neurodevelopmental disorders, but examinations of the specificity of these deficits and direct comparisons with age matched controls are few. Therefore, we conducted the current study investigated EFs in children with LD in comparison to age matched healthy controls. We hypothesized that the LD group would have more severe cognitive dysfunctions than healthy controls.

Method

Participants

Recruitment and testing of participants with learning disorders took place at the King Saud University Medical City (KSU-MC), Riyadh, Saudi Arabia. Participants were recruited for both case and controls, were aged between 6 and 15 years old from the neurology consultation clinics of KSU-MC coming for their follow up visits. The study was conducted from June 2016 to December 2017. A case (test) group was recruited together with a control group. The case group was formed of diagnosed patients with neurodevelopmental disorders, particularly those with learning disabilities and ADHD. Neurology consultants performed extensive interviewing for the control group, which was formed of individuals without neurodevelopmental conditions, psychopathology, or learning disabilities. Control group consisted of healthy children with age matching with LD group. These subjects did not have any family history of LD. They were recruited from pediatric clinics when visiting for follow up appointments.

Written consent was obtained from the parents of the patients upon joining the study. Ethical consent was obtained from the Institutional Review Board of the College of Medicine, King Saud University, Riyadh, Saudi Arabia [Project No: E-13-983].

CANTAB testing

The three subtests from the [CANTAB](#) computerized battery were administered and responses were recorded directly with a touch-sensitive screen. Multiple training trials to learn the requirements of each task were given to each participant.

Before the actual test is started orientation trials were given to familiarize the subjects with the tests. The coinvestigators were trained for CANTAB testing and they administered the tests to the participants under the supervision of their consultant.

Motor Screening Task (MOT)

[MOT task](#) provides an assessment (speed, accuracy and number of errors) involving the selection of colored crosses in different locations on the screen as quickly and accurately as possible by the participant.

Intradimensional/Extradimensional (IED) Shift

IED is a test that assesses the shifting and flexibility of attention in the fronto-striatal areas of the brain and takes about 7 minutes. There are two dimensions that are used in this test: color-filled shapes and white lines. The simple stimuli are the color-filled shapes and the compound stimuli are both the color-filled shapes and the white lines. This test started with two simple stimuli appearing in the screen and the subject has to learn the correct stimuli and respond by touching it. Feedbacks teach the subject the correct stimuli. After 6 correct responses, the

stimuli and/or the rule changes. IED test assesses the errors, and the number of trial and stages completed. The detail description of the task described above is available from the [CANTAB website](#).

Statistical analysis

Analysis of the data were performed by [Statistical Package for Social Sciences](#) (SPSS) version 23 (SPSS Inc., IBM, Chicago, Illinois, USA). The CANTAB sets and subsets between cases and controls were compared using an independent t-test. A p value of <0.05 was considered statistically significant.

Results

A total of 160 participants participated in the study, 92 (57.5%) for the case group and 68 (42.5%) in the control group. The participants in control group were less because age matched selection was difficult. The mean age for all participants was 9.1 ± 2.1 years, ranging from 6 to 15 years old. [Table 1](#) shows the demographic characteristics and the results of the CANTAB test and subsets of all participants. There were no significant

differences between the case and the control group (case: 9.2 ± 2.4 years versus controls: 9.0 ± 1.6 years, $p=0.544$)

[Table 2](#) shows the comparison of the three CANTAB subsets between cases and controls. The IED and MOT were significantly greater/longer among patients with learning disabilities (cases) compared to those without a disability (control). P values were <0.001 and <0.001, respectively. Patients with learning disabilities (cases) had a longer SRT time than controls (cases: 1050.4 ± 626.5 versus controls: 815.5 ± 133.9 , $p=0.003$).

[Table 3](#) shows the results of further analysis of each of the CANTAB subsets between cases and controls. Those with learning disabilities (cases) were able to complete an average (mean) of 3.0 stages, which was significantly lower than the controls, who were able to complete a mean of 8.4 IED stages ($p<0.001$, [Figure 1](#)). The maximum time to react (SRT-Maximum) was significantly longer in the case group (965.9 ± 716.4) compared to the controls (747.7 ± 120.7), $p=0.014$, [Figure 1](#). Patients with

Table 1. Demographic profile and CANTAB set and subset test results for all participants. Cambridge Neuropsychological Test Automated Battery (CANTAB), motor planning task (MOT), simple reaction time task (SRT), intradimensional/extradimensional shift (IED), Standard deviation (SD), Percent (Per) and Median (MED).

Variables	Mean	SD
Age in years	9.1	2.1
IED	82.6	80.1
IED completed stages	5.3	3.9
MOT	1532.5	1087.2
MOT_MED	1419.3	1143.9
MOT_Error	13.7	3.9
SRT	950.6	495.7
SRT Maximum	873.1	558.2
SRT_Per	73.7	33.9
BMI	25.0	4.6

Table 2. Results in the three main CANTAB subsets [mean (SD)] between cases and controls. Cambridge Neuropsychological Test Automated Battery (CANTAB), motor planning task (MOT), simple reaction time task (SRT), intradimensional/extradimensional shift (IED), Standard deviation (SD), Percent (Per) and Median (MED).

CANTAB subsets	Cases n=92	Controls n=68	p value
IED	118.4 (88.5)	34.2 (21.8)	<0.001
MOT	2014.4 (1210.8)	880.5 (251.8)	<0.001
SRT	1050.4 (626.5)	815.5 (133.9)	0.003

Table 3. Results of further analysis of each of the CANTAB subsets (mean and SD) between cases and controls. Cambridge Neuropsychological Test Automated Battery (CANTAB), motor planning task (MOT), simple reaction time task (SRT), intradimensional/extradimensional shift (IED), Standard deviation (SD), Percent (Per) and Median (MED).

CANTAB variables within subsets	Cases n=92	Controls n=68	p values
IED completed stages	3.0 (3.6)	8.4 (0.9)	<0.001
MOT_MED	1924.7 (1288.8)	735.5 (155.1)	<0.001
MOT_Error	14.6 (4.5)	12.4 (2.7)	<0.001
SRM	56.6 (17.6)	70.7 (13.9)	<0.001
SRT Maximum	965.9 (716.4)	747.7 (120.7)	0.014
SRT_SD	617.9 (387.8)	595.2 (123.2)	0.642
SRT-Per	55.5 (34.9)	98.3 (2.7)	<0.001

Figure 1. Motor task response time, intradimensional / extradimensional shift (IED) stages completed and response time for cases and control subjects.

learning difficulties had significantly more errors in the motor screening tasks (MOT-Error) compared to the control group (case: 14.6 ± 4.5 versus controls: 12.4 ± 2.7 , $p < 0.001$, Figure 2). MOT-MED was significantly larger among the case group than the control group ($p < 0.001$). SRT-Per was significantly lower among the cases than the control group ($p < 0.001$, Figure 2).

Dataset 1. Data containing test scores for all participants

<http://dx.doi.org/10.5256/f1000research.13695.d196379>

Discussion

The present study aimed to measure cognitive performance by using CANTAB tests for Saudi volunteers with and without a learning disability (LD). LD subjects had lower performances on tests of visual sustained attention, performance time, and learning abilities function in the present study. The key observations in our study were that children with LD have impairments

in shifting and flexibility of attention (IED), general alertness, correct responses & errors of commission and omission (SRT) and motor performance (MOT).

These findings provide evidence that LD in early life is a risk factor for cognitive decline. Previous studies showed impairment in word fluency, memory and speech in LD populations^{9,10,22}.

To our knowledge, this is the first study to study the cognitive function by CANTAB selected cognitive tests for Saudi LD volunteers. The IED tests, which activates the frontal cortex^{16,17,21} according to what we have mentioned earlier in IED explanation, and assesses working memory and strategy based on an individual's ability to retain, manipulate, and remember spatial information. The MOT test motivates the fronto-striatal circuits for sustained attention, while the SRT test activate the fronto-parietal functions and subcortical areas that regulate the planning, and execution of the motor action and psychomotor speed processing^{23,24}.

Figure 2. Motor task (MOT) error rate, simple reaction time (SRT) percentage, response time in SRT and maximum response time in SRT condition for cases and control subjects.

Education levels is one factor of limitation in this study, which has been mentioned in previous study using of CANTAB system for cognition²⁴ since they were admitted in different educational schools for LD children.

In the literature CANTAB and neuroimaging showed that reduced episodic memory is associated with diminished hippocampal volume, with reciprocal influences among neuroanatomical and cognitive variables²⁵. The second limitation is that we did

not use neuroimaging to correlate neuroanatomical changes with CANTAB results. The present evidence provides support of cognitive impairment association in LD and such studies should remain an active area of research.

Data availability

Dataset 1: Data containing test scores for all participants
10.5256/f1000research.13695.d196379²⁶

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Version 1

Reviewer Report 14 December 2018

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Maksym V. Kopanitsa

UK Dementia Research Institute , Imperial College, London, UK

The reviewed manuscript "Assessment of the Cambridge Neuropsychological Test Automated Battery test in Saudi children with learning disabilities: A case-control study" presents a useful dataset that compares performances of children with learning disabilities and those without them in several CANTAB tasks. These data confirm the notion that CANTAB can sensitively detect differences in executive function parameters in children with different learning ability. To enhance the value of the obtained data, I'd like to suggest that the authors consider the following points (perhaps revising their submission):

1. It is not quite clear what methods were used to diagnose children with LD.
2. The authors correctly cite the lack of neuroimaging data as a limitation of the study, however, perhaps they should mention if any of the subjects with LD had any genetic testing? Ideally, some statement about whether any of the subjects has syndromic or non-syndromic intellectual disability and results of any genetic tests should be included.
3. We believe that more studies where CANTAB was used for assessment of children with LD/ADHD could be discussed in the Discussion section. The Bibliography section on Cambridge Cognition web-site could be helpful in this regard:
<http://www.cambridgecognition.com/login/bibliography>.

Minor points:

1. The article should undergo careful language editing from the point of view of grammar and syntax. There are multiple instances of grammatically and contextually incorrect sentences. Below are very few selected examples:
 - a) The title of the study should be revised, because it was not an "Assessment of the ...test in Saudi children", but rather "Assessment of performance of Saudi children with learning disabilities by using the Cambridge Neuropsychological Test Automated Battery".
 - b) The second sentence of the Results section, "The participants in control group were less because age matched selection was difficult", should be written as "There were fewer

participants in control group because age matched selection was difficult”.

c) The fifth sentence of the Results section should read “There were no significant differences in the ages between case and control groups (case: 9.2 ± 2.4 years versus controls: 9.0 ± 1.6 years, $P = 0.544$)” (“in the ages” was not mentioned in the original sentence).

d) In addition, the term “EF” refers to “executive function” (which is correct) in some parts of the text and to “executive **dys**function” in other parts. For example: “EFs refers to neuropsychological processes that enable physical, cognitive, and emotional self-control in LD children” (*function*) but “There are a number of experimental studies showing EFs in individuals with LD Disorders...” (*dysfunction*).

2. There is no description of SRT in the methods.
3. The use of the Student’s *t*-test is contingent on the normal distribution of data in the compared groups, however there was no evidence this was checked prior to the comparison in this study.
4. As the data are clearly presented in the Tables, there is probably no reason to repeat the same numbers in the text. P-values also can be in a separate column in the Table. Likewise, because the data are quite straightforward, the Figures are not necessary as they just illustrate what is presented in the Tables. Ideally, we would recommend presenting the data as box and whisker plots with all individual values being represented by small dots. This would be the most informative format compared to current Tables and slightly less detailed Figures.

Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?

Partly

Are all the source data underlying the results available to ensure full reproducibility?

No

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: cognitive behaviour in preclinical disease models, in vitro electrophysiology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 27 Feb 2019

Shahid Bashir, King Fahad Specialist Hospital, Dammam, Saudi Arabia

The reviewed manuscript "Assessment of the Cambridge Neuropsychological Test Automated Battery test in Saudi children with learning disabilities: A case-control study" presents a useful dataset that compares performances of children with learning disabilities and those without them in several CANTAB tasks. These data confirm the notion that CANTAB can sensitively detect differences in executive function parameters in children with different learning ability. To enhance the value of the obtained data, I'd like to suggest that the authors consider the following points (perhaps revising their submission):

1. It is not quite clear what methods were used to diagnose children with LD.

We have added the statement "The case group was formed of diagnosed patients with neurodevelopmental disorders based on their medical records and following up with their regular child neurology consultant, particularly those with learning disabilities and ADHD"

2. The authors correctly cite the lack of neuroimaging data as a limitation of the study, however, perhaps they should mention if any of the subjects with LD had any genetic testing? Ideally, some statement about whether any of the subjects has syndromic or non-syndromic intellectual disability and results of any genetic tests should be included.

Thanks for this very valid point, but sorry we don't have genetic assessment. We do genetic testing when we find parents or other siblings showing similar patterns. Secondly, as this was not part of the objectives of the study, we need to have ethical approval for getting genetic results.

3. We believe that more studies where CANTAB was used for assessment of children with LD/ADHD could be discussed in the Discussion section. The Bibliography section on Cambridge Cognition web-site could be helpful in this regard:
<http://www.cambridgecognition.com/login/bibliography>.

We have revised the discussion part.

Minor points:

1. The article should undergo careful language editing from the point of view of grammar and syntax. There are multiple instances of grammatically and contextually incorrect sentences. Below are very few selected examples: a) The title of the study should be revised, because it was not an "Assessment of the ...test in Saudi children", but rather "Assessment of performance of Saudi children with learning disabilities by using the Cambridge Neuropsychological Test Automated Battery".

Thanks for the feedback. We have revised the title.

b) The second sentence of the Results section, "The participants in control group were less because age matched selection was difficult", should be written as "There were fewer participants in control group because age matched selection was difficult".

Done.

c) The fifth sentence of the Results section should read "There were no significant differences in the ages between case and control groups (case: 9.2 ± 2.4 years versus controls: 9.0 ± 1.6 years, $P = 0.544$)" ("in the ages" was not mentioned in the original sentence).

Done.

d) In addition, the term "EF" refers to "executive function" (which is correct) in some parts of the text and to "executive **dys**function" in other parts. For example: "EFs refers to neuropsychological processes that enable physical, cognitive, and emotional self-control in LD children" (*function*) but "There are a number of experimental studies showing EFs in individuals with LD Disorders..." (*dysfunction*).

Done.

2. There is no description of SRT in the methods.

Thanks for your feedback and we really apologise for this mistake. We have added this in methods.

3. The use of the Student's *t*-test is contingent on the normal distribution of data in the compared groups, however there was no evidence this was checked prior to the comparison in this study.

4. As the data are clearly presented in the Tables, there is probably no reason to repeat the same numbers in the text. P-values also can be in a separate column in the Table. Likewise,

because the data are quite straightforward, the Figures are not necessary as they just illustrate what is presented in the Tables. Ideally, we would recommend presenting the data as box and whisker plots with all individual values being represented by small dots. This would be the most informative format compared to current Tables and slightly less detailed Figures.

We have removed the table and figures too.

Competing Interests: No competing interests were disclosed.

Author Response 29 May 2019

Shahid Bashir, King Fahad Specialist Hospital, Dammam, Saudi Arabia, Dammam, Saudi Arabia

TITLE: Assessment of performance of Saudi children with learning disabilities by using the Cambridge Neuropsychological Test Automated Battery.

Introduction: The recent meta-analysis have shown that the CANTAB tasks have a well-established sensitivity to a wide range of cognitive effects including ADHD ²².

Method

The case group was formed of diagnosed patients with neurodevelopmental disorders based on their medical records and following up with their regular child neurology consultant, particularly those with learning disabilities and ADHD.

SRT

The Simple Reaction Time task measures simple reaction time, general alertness and motor speed through delivery of a known stimulus to a known location to elicit a known response. The only uncertainty is regarding when the stimulus will occur, by having a variable interval between the trial response and the onset of the stimulus for the next trial. Outcome measures cover latency (response speed), correct responses and errors of commission and omission.

Results:

There were fewer participants in control group because age matched selection was difficult. The IED and MOT were significantly greater/longer among patients with learning disabilities (cases) compared to those without a disability (control) (Table 1). Patients with learning disabilities (cases) had a longer SRT time than controls ($p=0.003$).

Table 2 shows the results of further analysis of each of the CANTAB subsets between cases and controls. Those with learning disabilities (cases) were able to complete an average (mean) of 3.0 stages, which was significantly lower than the controls, who were able to complete a mean of 8.4 IED stages ($p<0.001$, **Table 2**). The maximum time to react (SRT-Maximum) was significantly longer in the case group (965.9 ± 716.4) compared to the controls (747.7 ± 120.7), $p=0.014$, **Table 2**. Patients with learning difficulties had significantly more errors in the motor screening tasks (MOT-Error) compared to the control group (case: 14.6 ± 4.5 versus controls: 12.4 ± 2.7 , $p<0.001$, **Table 2**). MOT-MED was significantly larger

among the case group than the control group ($p < 0.001$). SRT-Per was significantly lower among the cases than the control group ($p < 0.001$, Table 2).

Discussion:

A number of key limitations should be considered when interpreting the findings presented here. First, although the three CANTAB tasks used in this study were selected to evaluate potential cognitive effects in children with LD, complex and diversity of LD may have affected cognitive function in domains that were not tested. Second, because data were analysed at the group level only, potentially clinically significant effect of cognitive function were not examined at individual level. Third, in the literature CANTAB and neuroimaging showed that reduced episodic memory is associated with diminished hippocampal volume, with reciprocal influences among neuroanatomical and cognitive variables²⁶. Fourth limitation is that we did not use neuroimaging to correlate neuroanatomical changes with CANTAB results. The present evidence provides support of cognitive impairment association in LD and such studies should remain an active area of research.

As compared to traditional neuropsychological tasks, the computerized based CANTAB tasks have proven congruence with an accepted and validated measure of cognitive function in subject with EF impairment²⁷. The CANTAB includes several different tasks with sensitivity to particular types of neurocognitive dysfunction. Furthermore, because the tasks are computerized, the CANTAB benefits from reliability of administration and practice effects are minimized by the use of parallel versions across all testing sessions.

Conclusion: This pilot study provides platform for further investigation of cognitive impairment in children and adolescents with LD, and suggests that potential long-term cognitive function assessment may be worthy of further investigation in well-controlled studies.

Competing Interests: No competing interests were disclosed.

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