Chapter 7

Executive Function in Children with Attention Deficit/ Hyperactivity Disorder

Akira Yasumura and Masumi Inagaki

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/60669

Abstract

In recent years, deficit in executive function has been noted as a core symptom of attention deficit hyperactivity disorder (ADHD). Previously, with the aim of quantitatively assessing the characteristics of children with ADHD from the viewpoint of inhibition among executive functions, we have considered behavioral and frontal brain functions with regard to inhibition vis a vis color word interference. In this study we also undertook additional collections of data at a number of facilities and investigated usefulness as a differential diagnosis aid. A total of 38 ADHD children and 46 typical developing children, matched in terms of age, gender, dominant arm and non-verbal intelligence, were the subject of analysis in this study. Utilising a Reverse Stroop Task (RST), we measured prefrontal area activity during task performance with near-infrared spectroscopy (OEG-16). Results were: 1) Behavioral results: in the RST, the ADHD children recorded a higher rate of interference than the TD children. 2) Brain activity: as regards brain activity during the RST, right lateral prefrontal activity was significantly lower in the ADHD children than in the TD children. These results suggest that RST results and changes in brain activity during task performance allow quantitative assessment of the clinical symptom of ADHD.

Keywords: attention-deficit hyperactivity disorder, executive function, frontal lobe function, near-infrared spectroscopy (NIRS), children

1. Introduction

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder, which specifically affects behaviour. Until the publication of the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* (*DSM-IV-TR*), ADHD was classified as a disruptive behaviour disorder, alongside oppositional defiant disorder and conduct disorder. In the most recent version, the fifth edition of the *DSM* (*DSM-5*), ADHD has been re-classified as a neurodevelopmental disorder, alongside autism spectrum disorders (ASD) [1]. As this change shows, in the past, the focus of ADHD was on antisocial and non-adaptive problem behaviours. Currently, however, ADHD is classified as one distinct type of developmental disorder, based on the assumption of a dysfunction in the brain. Thus, the focus is now on a more central cause. In addition, while the *DSM-5* does not present any major changes, compared to the *DSM-IV-TR*, in terms of diagnostic criteria for ADHD, the age of manifestation was revised from 7 years old to 12 years old. Thus, the *DSM-5* emphasizes ADHD as a developmental disease, which can afflict both adolescents and adults.

2. Deficits in executive functions as the core symptom of ADHD

Attention deficit and hyperactivity/impulsivity are cited as the primary clinical symptoms of ADHD [1]. Several studies have suggested that the core symptom is a deficit in executive functions [2]. Executive functions, which are related to high-level cognitive and behavioural control, are cognitive functions that are necessary in order to effectively accomplish human goal-oriented activities. The neural basis of these functions is generally considered to be located in the prefrontal cortex [3, 4]. For example, achieving the goal of "get to school by 9:00 AM" entails going directly to school, while suppressing the impulses to look in a display window of a toy store along the route to school and play with friends.

Based on recent developments in cognitive psychology, various theoretical models of executive functions have been proposed. There are two main models: a simple model, which asserts that executive functions are simple functions, and a complex model, in which executive functions are divided into multiple elements [5, 6]. With regard to the latter model, based on the results of a series of cognitive tasks, Miyake et al. reported that the three crucial components of executive functions are "inhibition", "attention shifting", and "updating (working memory)" [6]. Of these three, it is suggested that the clinical symptoms of ADHD strongly relate to "inhibition" in particular [4, 7, 8]. This function is necessary for intentionally inhibiting inappropriate and predominant behaviours in a given situation. Typical tasks for assessing this function include the Stroop test and the reverse Stroop test [8, 9]. The former test assesses the inhibition of Stroop interference. Stroop interference refers to the interference that occurs when receiving incongruent information regarding a colour and its name. In a Stroop test, when the word "yellow" is written in red, the correct answer is the colour in which the word is written (in this case, red). Providing this answer results in interference from the meaning of the word, known as semantic interference. In the latter reverse Stroop test, the correct answer

http://dx.doi.org/10.5772/60669

is the word itself (yellow). Providing this answer results in interference from the colour (colour word interference). Both tests use oral responses and matching responses. Oral responses indicate the fluency and accuracy of reading aloud, while matching responses assess the accuracy and speed of selection by means such as pointing. With oral responses, the reverse Stroop effect (colour word interference) seldom occurs, compared to the Stroop effect (semantic interference). Therefore, reports of the reverse Stroop effect are extremely rare and the development process of its neural basis has yet to be reported. However, in contrast to oral responses, matching responses, in which the subject must select the colour of the word written from among a patch of multiple colours (for example, if the word "red" is written in green, the correct answer would be to point to red), are known to produce reverse Stroop interference [10-12]. Some researchers have indicated that, when a reverse Stroop test is performed on children with ADHD or ADHD tendencies, an ADHD-associated specificity, which is not seen in a Stroop test, is observed [13, 14].

Another typical assessment of inhibition is the Go/No-go task. This cognitive task assesses inhibition by asking subjects to either perform an appropriate action (Go response) or to appropriately withhold a response (No-go response), in accordance with a situation. One previous study compared children with ADHD to typical developing (TD) children, while another compared children with ADHD before and after medication [15, 16]. In the former test, the children with ADHD demonstrated poorer outcomes in No-go responses than the TD children. In the latter test, increased activity was observed in the right prefrontal cortex, following medication.

Another study has reported on the link between symptoms of ADHD and deficit in working memory, which is an element in executive function. Westerberg et al. have stated that the difference in outcomes of non-verbal working memory tasks between TD children and children with ADHD tend to increase with age [17].

These studies suggest that clinical symptoms of ADHD are strongly associated with the executive functions of inhibition and working memory.

3. Brain function measurements for children with ADHD

As can be seen from the English listing of "neurodevelopmental disorder" in the *DSM-5*, the main cause of developmental disorders, including ADHD, is generally considered to be brain function specificity [1]. Thus, in order to aid differential diagnosis of ADHD and assess ADHD before and after intervention, methods for quantitatively measuring brain function are called for. However, many children with ADHD present with hyperactivity and other behavioural problems, which easily result in artefacts that are caused by the child's movement during measurement. Therefore, as it is usually difficult to measure while the child is awake, assessment tools, such as functional magnetic resonance imaging, can only be used when the child is asleep. Of the currently existing testing modalities, near infrared spectroscopy (NIRS) can measure cerebral blood flow even when the head is moving. It is, therefore, capable of reflecting

the function of the prefrontal cortex, which is the seat of executive function. Thus, NIRS is well suited for measuring the brain function in children with ADHD.

As previously stated, a number of previous studies have examined inhibition in ADHD. However, there is a dearth of studies on brain function, particularly involving children, which address the differences in results between tasks or support disorders. Therefore, we used the Stroop test (ST) and the reverse Stroop test (RST) in order to assess executive functions, particularly functions that are related to the inhibition of interference (Figure 1).

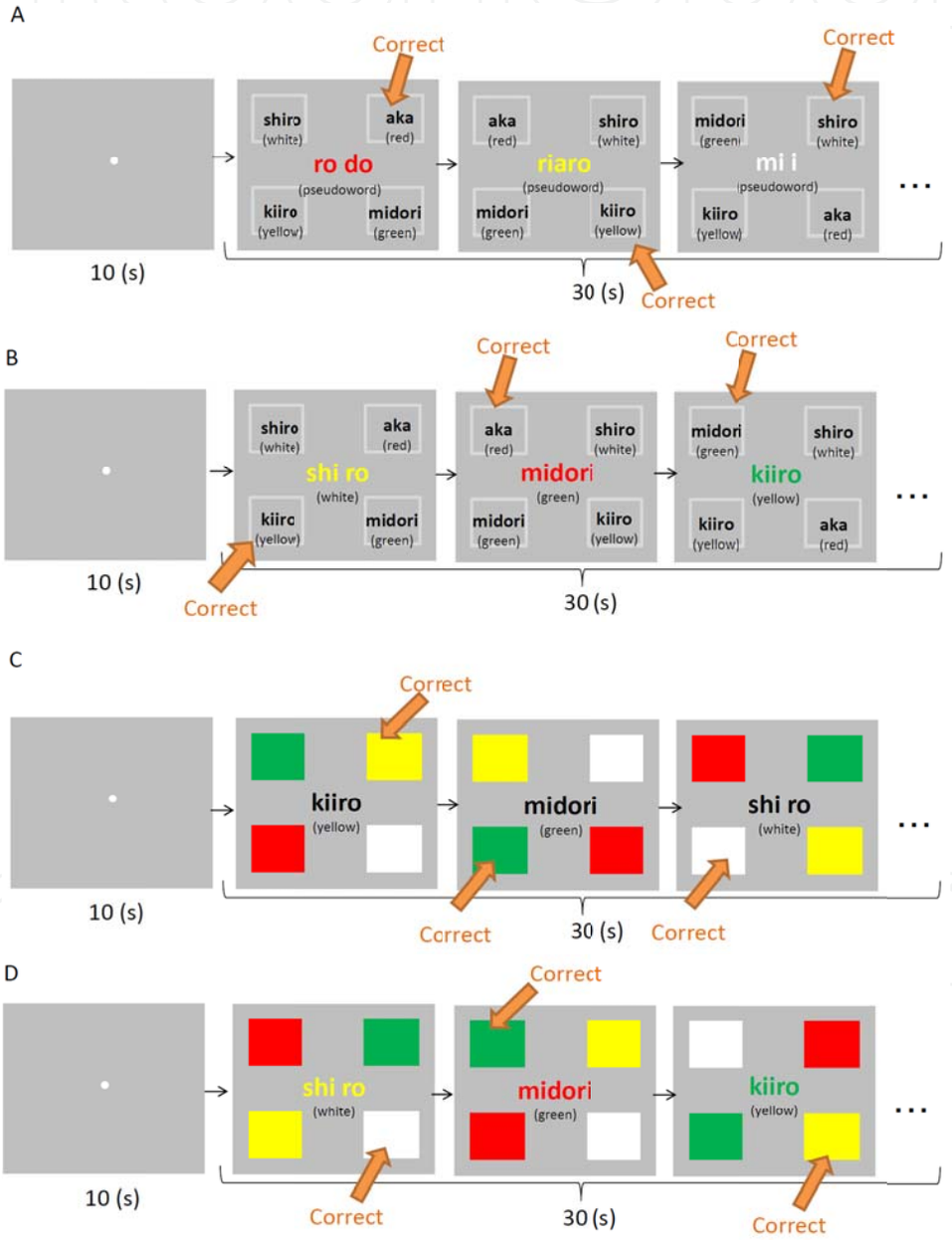

Figure 1. Schematic illustration of the protocol for the neutral condition of the Stroop task (A), incongruent condition of the Stroop task (B), neutral condition of the reverse Stroop task (C) and incongruent condition of the reverse Stroop task (D).

http://dx.doi.org/10.5772/60669

We began our research with the objective of determining the specificity of brain function in children with ADHD [7]. In particular, we also examined children with autism spectrum disorders (ASD), which are considered difficult to differentially diagnose from ADHD, and attempted to abstract differences in the developmental disorders. The subjects were 10 children with ADHD (age: 11.2±2.2), along with 15 TD children (age: 9.6±1.5) and 11 children with ASD (age: 10.5±2.3), who were matched with the children with ADHD in terms of age, sex, intelligence, and verbal capacity ($p>0.1$). The ST and RST were conducted with touch panels and matching responses. During both tasks, an NIRS device (OEG-16; Spectratech, inc. Japan) was mounted over the prefrontal cortex in order to measure the changes in cerebral blood flow (Figure 2).

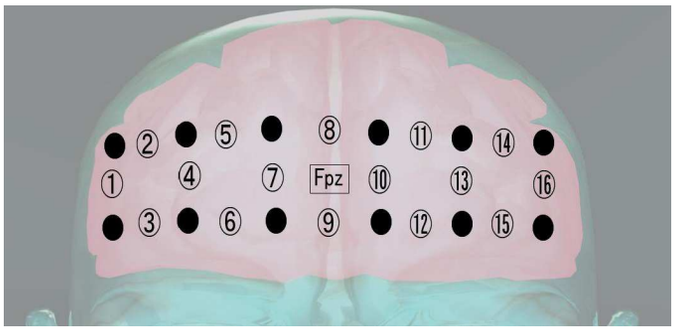

Figure 2. Experimental settings. The NIRS probe was attached to the prefrontal area. The centre of the probe matrix was place on Fpz (International 10-10 system).

We found no differences among the three groups in the ST ($p>0.1$). However, in the RST, in comparison with the TD children, the children with ADHD demonstrated behavioural abnormalities, i.e., a higher rate of interference ($p<0.01$) and a greater number of incorrect responses ($p<0.05$). Furthermore, with regard to changes in brain activity during the RST, the children with ADHD demonstrated lower activation of the prefrontal cortex than the TD children ($p<0.05$). In addition, the ADHD group demonstrated a tendency towards a negative correlation between brain activity and severity of attention deficit, which were evaluated by the Japanese versions of the Swanson, Nolan and Pelham, version-IV Scale (SNAP- IV) [18] ($r=-0.60$, $p=0.07$). These results demonstrated that inhibition of colour word interference is diminished in ADHD children. In addition, the weakness of interference inhibition was suggested to be associated with the severity of attention deficit and affected by the low activity level of the prefrontal cortex.

We also accumulated additional data from multiple institutions in order to investigate the usefulness of NIRS as a differential diagnosis aid. The subjects of this examination were 38 children with ADHD (age: 10.4±2.3, 12 children taking medication) and 46 TD children (age: 10.2±1.7), matched in terms of age, sex, dominant arm and non-verbal intelligence ($p>0.1$). In order to assess Stroop inhibition, frontal lobe activity was measured with an NIRS device (OEG-16) during the performance of RST. Among behaviour outcomes, we re-confirmed that children with ADHD demonstrated a higher rate of interference on the RST than the TD children ($p<0.01$). Within the ADHD group, the rate of interference demonstrated positive

correlations with the severity of attention deficit ($r=0.48$, $p<0.01$) and severity of hyperactivity/ impulsivity ($r=0.40$, $p<0.05$) (Figure 3).

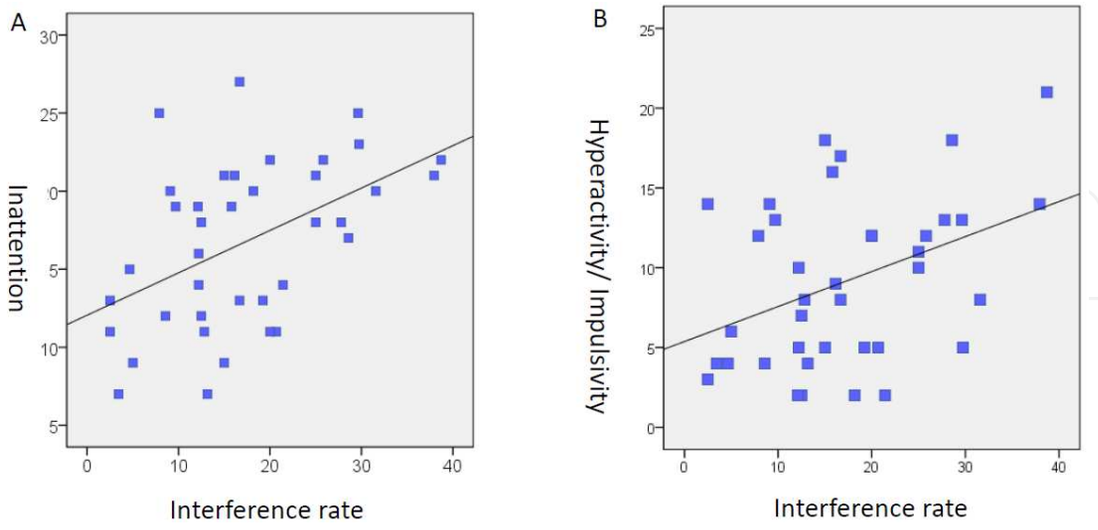

Figure 3. Correlation between the interference rate of the reverse Stroop task and the inattention score from Swanson, Nolan and Pelham scale (SNAP) in children with attention deficit hyperactivity disorder (ADHD) (A). The correlation between the interference rate of the reverse Stroop task and the hyperactivity/ impulsivity score from SNAP in the ADHD group (B).

Among the results related to brain activity, the children with ADHD demonstrated significantly lower activity in the right lateral prefrontal cortex during the RST than the TD children ($p<0.05$) (Figure 4).

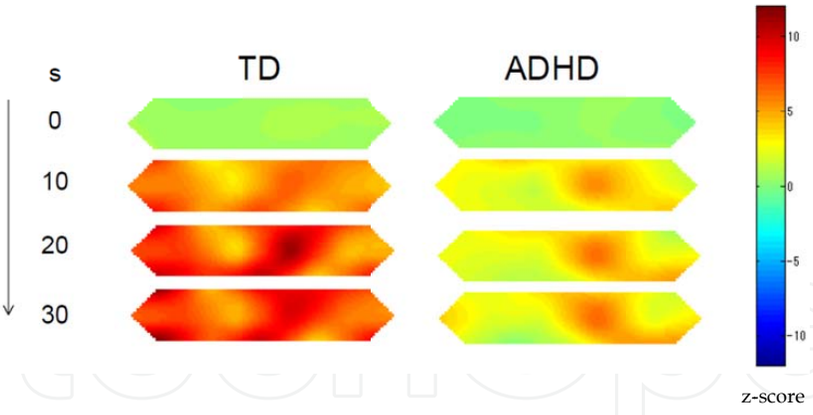

Figure 4. Changes in oxygenated haemoglobin (oxy-Hb) during the reverse Stroop task, using the mean z-scores from all of the subjects, as measured by near-infrared spectroscopy. Pseudocolor images plot regional changes in oxy-Hb across the prefrontal cortex for typically developing children (TD, left) and children with attention deficit hyperactivity disorder (ADHD, right). The bar graphs below each of the pseudocolor image series plot the mean signals over the right and left hemispheres.

Furthermore, when we performed a discriminant analysis, based on the diagnostic results with regard to the rate of interference and prefrontal cortex activity, we obtained an overall discrimination rate of 79.8%. A correlation was observed between the rate of interference and severity of ADHD in the RST. Children with ADHD demonstrated lower right lateral

prefrontal cortex activity during the RST than the TD children. These findings suggested that changes in RST outcomes and changes in brain activity during the RST could be used to linearly assess the clinical symptoms of ADHD. In order to construct a linear model with a higher discrimination rate, future studies may need to include greater numbers of participants and additional selection of indicators, as well as children with developmental disorders other than ADHD.

4. Autism spectrum disorders and deficit in executive function

A deficit in executive functions has also been indicated in developmental disorders other than ADHD, such as in ASD. For example, because the stereotypical symptoms of ASD can be understood as sustained, inflexible symptoms, they are suspected to be associated with a deficit in executive functions. Among executive function tasks, particularly tasks that assess attention shifting, which require a flexible conversion of attention, children with ASD are known to demonstrate poorer behavioural outcomes. Therefore, we performed behavioural analysis and examined cerebral blood flow, with the objective of determining the pathology regarding the neural basis of attention shifting in children with ASD [19]. The subjects were 14 children with high-functioning ASD (age: 9.6±1.4), diagnosed in accordance with the diagnostic criteria in the *DSM-IV-TR*, and 20 TD children (age: 9.2±1.6), who matched with the ASD children in terms of age, sex and intelligence. The task we used was a modified version of the Dimensional -Change Card Sort (DCCS) task [20], in which the rules are frequently altered (Figure 5).

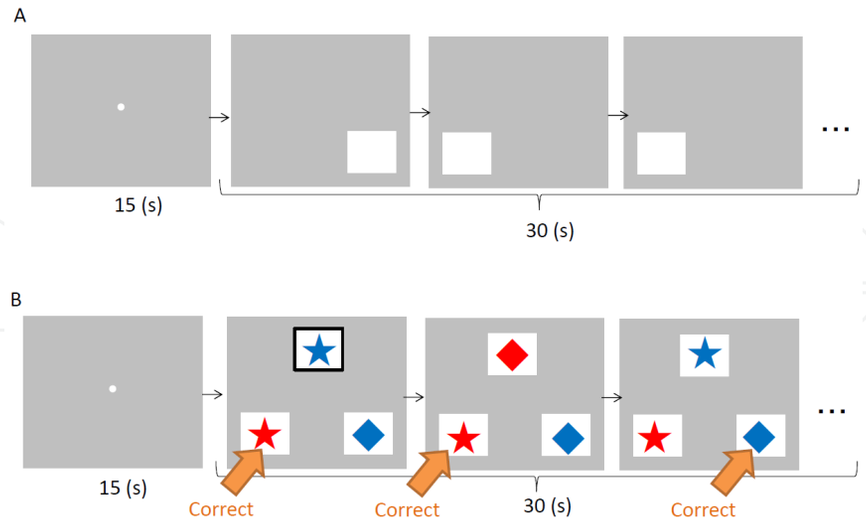

Figure 5. Illustration of the protocol of the baseline (a) and dimensional change card sort (DCCS) (b) tasks. In the baseline task, the participants had to indicate the side of the screen on which the white square appeared. In the DCCS task, if the upper card was hemmed in black, the participants had to select the lower card with the same shape as the one that was printed on the upper card. If the upper card was not hemmed in black, they had to select the lower card of the same colour as that of the upper card.

We also measured the changes in blood flow in the prefrontal cortex during task performance, using NIRS (OEG-16). In addition, in order to assess the guardians' needs in supporting their children with ASD, we asked them to complete a shortened version of the Paediatric Anxiety Rating Scale (PARS) [21]. The results from the PARS showed that children with ASD have greater support needs than TD children. In the DCCS task, the children with ASD had fewer correct responses than the TD children. Furthermore, as for cerebral blood flow, the children with ASD demonstrated less activity than the TD children in the vicinity of the right dorsolateral prefrontal cortex, the frontal pole and the left inferior prefrontal cortex (Figure 6).

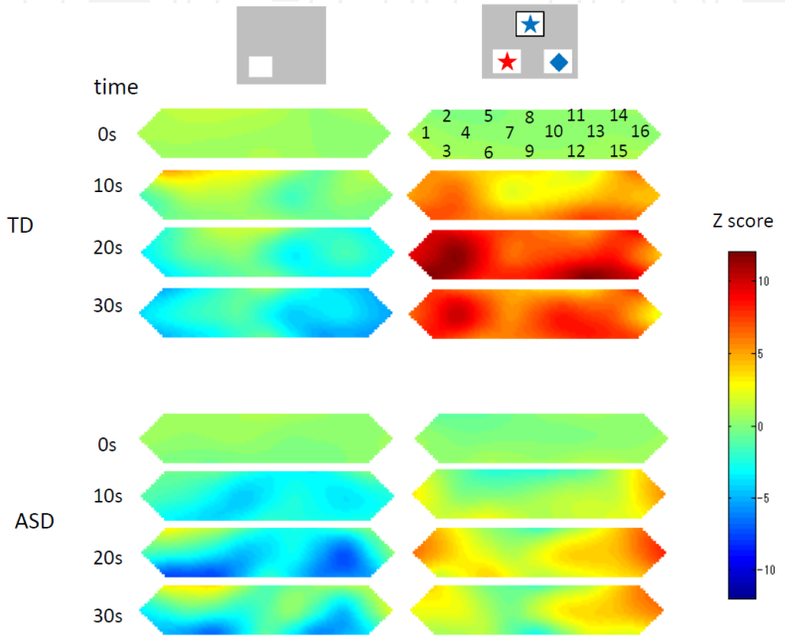

Figure 6. Time course of near-infrared spectroscopy topography using the mean z-scores from all of the subjects. The numbers on the first image on the second row indicate the locations of the channels. The left side of the figure indicates the brain activities during the baseline task - typically developing children (TDC, upper) and autism spectrum disorder (ASD, lower). The right side of the figure indicates the brain activities during the dimensional change card sort task - TDC (upper) and ASD (lower).

The above results suggest that children with ASD have a diminished ability to shift their attention, which is consistent with previous studies [22]. This can be inferred as a reflection of the specific stereotypes in ASD. In addition, the brain function results during the task performance suggested that reduced prefrontal cortex activity is related to the pathology of ASD. This, in turn, suggests that NIRS findings could serve as an objective indicator for clinical diagnoses of ASD in children. Future studies will need to investigate whether the DCCS task can be applied in differential diagnosis of other developmental disorders, as well as whether it can be applied as an indicator for assessing the effects of medication and behavioural therapy.

5. Conclusion

In this report, we discussed the relationships of ADHD and ASD, which are neurodevelopmental disorders, with executive functions. The seat of executive functions is generally

considered to be located in the prefrontal cortex. We discussed NIRS as a useful method for measuring this activity. It is possible that the core symptoms of ADHD may be quantified by NIRS. Progress in functional neuroimaging research on ADHD and ASD is expected to enable highly precise measurements of the severity of developmental disorders. In addition to differentiating severity, future research will need to determine the optimal intervention (drug therapy, behavioural therapy, etc.) on a case-by-case basis when selecting treatment.

Acknowledgements

This work was supported in part by the TMC Young Investigator Fellowship and an Intramural Research Grant (25-6; Clinical Research for Diagnostic and Therapeutic Innovations in Developmental Disorders) for Neurological and Psychiatric Disorders of National Center of Neurology and Psychiatry (NCNP); Grant-in-Aid for Young Scientists (A) from JSPS KAKENHI (15H05405 to Akira Yasumura) and Grant-in-Aid for Challenging Exploratory Research from JSPS KAKENHI (15K13167 to Akira Yasumura). We would like to thank the following people for their cooperation in collecting data: Dr. Tasuku Miyajima, Department of Pediatrics, Tokyo Medical University; Dr. Masao Aihara, Department of Pediatrics, University of Yamanashi; Dr. Yushiro Yamashita, Department of Pediatrics, Kurume University; Dr. Tatsuya Koeda, Graduate School of Regional Sciences, Tottori University; and Dr. Toshihide Koike, Department of Special Needs Education, Tokyo Gakugei University.

The authors have no conflicts of interest to declare.

Author details

Akira Yasumura* and Masumi Inagaki

*Address all correspondence to: yasumura@ncnp.go.jp

Department of Developmental Disorders, National Institute of Mental Health, National Center of Neurology and Psychiatry, Kodaira, Tokyo, Japan

References

[1] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-5). American Psychiatric Publishing; 2013.

[2] Barkley RA, et al. Frontal Lobe Functions in Attention Deficit Disorder with and Without Hyperactivity: A Review and Research Report. J Abnorm Child Psychol. 1992; 20(2) 163-188.

[3] Pennington BF, et al. Executive Functions and Developmental Psychopathology. J Child Psychol Psychiatry. 1996; 37(1) 51-87.

[4] Schroeter ML, et al. Prefrontal Activation Due to Stroop Interference Increases During Development - An Event-related fNIRS Study. Neuroimage. 2004; 23(4) 1317-1325.

[5] Baddeley A. The Episodic Buffer: A New Component of Working Memory? Trends Cogn Sci. 2000; 4(11) 417-423.

[6] Miyake A, et al. The Unity and Diversity of Executive Functions and their Contributions to Complex "Frontal Lobe" Tasks: A Latent Variable Analysis. Cogn Psychol. 2000; 41(1) 49-100.

[7] Yasumura A, et al. Neurobehavioral and Hemodynamic Evaluation of Stroop and Reverse Stroop Interference in Children with Attention-Deficit/Hyperactivity Disorder. Brain Dev. 2014; 36(2) 97-106.

[8] Negoro H, et al. Prefrontal Dysfunction in Attention-Deficit/Hyperactivity Disorder as Measured by Near-infrared Spectroscopy. Child Psychiatry Hum Dev. 2010; 41(2) 193-203.

[9] Stroop JR. Studies of Interference in Serial Verbal Reactions. J Exp Psychol. 1935; 18(6) 643-662.

[10] Jensen AR, et al. The Stroop Color-word Test: A Review. Acta Psychol (Amst). 1966; 25(1) 36-93.

[11] MacLeod CM. Half a Century of Research on the Stroop Effect: An Integrative Review. Psychol Bull. 1991; 109(2) 163-203.

[12] Durgin FH. The Reverse Stroop Effect. Psychon Bull Rev. 2000; 7(1) 121-125.

[13] Song Y, et al. An Asymmetric Stroop/Reverse-Stroop Interference Phenomenon in ADHD. J Atten Disord. 2011; 15(6) 499-505.

[14] Ikeda Y, et al. Stroop/Reverse-Stroop Interference in Typical Development and its Relation to Symptoms of ADHD. Res Dev Disabil. 2013; 34(8) 2391-2398.

[15] Inoue Y, et al. Reduced Prefrontal Hemodynamic Response in Children with ADHD During the Go/Nogo Task: A NIRS Study. Neuroreport. 2012; 23(2) 55-60.

[16] Monden Y, et al. Clinically-oriented Monitoring of Acute Effects of Methylphenidate on Cerebral Hemodynamics in ADHD Children Using fNIRS. Clin Neurophysiol. 2012; 123(6) 1147-1157.

[17] Westerberg H, et al. Visuo-spatial Working Memory Span: A Sensitive Measure of Cognitive Deficits in Children with ADHD. Child Neuropsychol. 2004; 10(3) 155-161.

[18] Inoue Y, et al. Psychometric Properties of Japanese Version of the Swanson, Nolan, And Pelham, Version-IV Scale-Teacher Form: A Study of School Children in Community Samples. Brain Dev. 2014; 36(8):700-706.

[19] Yasumura A, et al. Neurobehavioral and Hemodynamic Evaluation of Cognitive Shifting in Children with Autism Spectrum Disorder. JBBS. 2012; 2(4):463-470.

[20] Moriguchi Y, et al. Neural Origin of Cognitive Shifting in Young Children. Proc Natl Acad Sci U S A. 2009; 106(14) 6017-6021.

[21] Adachi J, et al. Reliability and Validity of Short Version of Pervasive Developmental Disorders (PDD)-Autism Society Japan Rating Scale (PARS): A Behavior Checklist for People with PDD. Seishinigaku 2008; 50(5) 431-438 [in Japanese].

[22] Lopez BR, et al. Examining the Relationship Between Executive Functions and Restricted, Repetitive Symptoms of Autistic Disorder. J Autism Dev Disord. 2005; 35(4) 445-460.

IntechOpen