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ORIGINAL RESEARCH

New marker using bioimpedance technology in screening for attention deficit/hyperactivity disorder (ADHD) in children as an adjunct to conventional diagnostic methods

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Background: Diagnosis of attention deficit/hyperactivity disorder (ADHD) in children is not straightforward and misdiagnosis may occur, which leads to the possibility of errors in treatment, with numerous possible side effects that could be especially damaging in view of the age of the population. For this reason, a tool that is easy to use, fast, and cost-effective, which provides an addition to conventional diagnosis and treatment monitoring of ADHD children, is needed. In this study, electro interstitial scans (EIS) were used to perform bioimpedance measurements. The results of conductivity measurements taken using forehead electrodes in a group of children conventionally diagnosed with ADHD and in a control group not showing any symptoms of ADHD were compared.

Method: Sixty children without any ADHD symptoms (group 1) and 52 children diagnosed with ADHD following psychiatric examination (group 2) underwent an examination with the EIS system. Statistical analysis was performed to compare the conductivity measurements at the level of the forehead electrodes, using independent *t*-tests and a receiver-operating characteristic curve (ROC) to determine the specificity and sensitivity of the test.

Results: The mean of the conductivity measurements of two pathways between the forehead electrodes (from left forehead to right forehead and from right forehead to left forehead) in the ADHD group was 33.11 micro Siemens (mS) (range 2–113 mS). This was significantly higher ($P < 0.001$) than mean of the conductivity measurements of two pathways between the forehead electrodes of the control group (2.75 mS, range 1.75–27.4 mS). In terms of the ROC results, comparing the two groups using the reference of the mean of conductivity measurements of the two pathways between the forehead electrodes, the test showed a specificity of 98% and sensitivity of 80% and $P = 0.0001$ (95% confidence interval) with a cutoff value at 7.4 mS.

Conclusion: The EIS marker related to the conductivity measurements of the forehead pathway has a high specificity and high sensitivity and use of this could provide practitioners with a noninvasive, low-cost system that is easy to use in the office and could offer an adjunct to the conventional diagnosis of ADHD children. It could also assist in treatment monitoring, and allow for earlier intervention.

Keywords: ADHD, children, electro interstitial scan (EIS), bioimpedance, conductivity measurements

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Introduction

Attention deficit/hyperactivity disorder (ADHD) is a heterogeneous disorder manifesting itself in various behavioral dimensions including inattention, hyperactivity, and impulsivity, often co-occurring with other child behavioral disorders including

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comorbid oppositional defiant disorder and conduct disorder.[1] It is likely that different neurotransmitter systems and the relative balance between them have varying degrees of influence over these behavioral dimensions.[2] Variations in genes involved in these neurotransmitter systems are likely to mediate this delicate balance and have an effect on the function of these chemicals in the brain.[2]

A central premise in the catecholamine hypothesis[3] of ADHD is that dopamine dysfunction leads to clinical symptoms. The theory, however, overlooks the phenotypic complexity of the disorder and the possible interactions between the dopamine and serotonin (5-HT) neurotransmitter systems.[4–7]

Diagnostic criteria for ADHD children are defined by the American Association of Psychiatry in the *Diagnostic and Statistical Manual of Mental Disorders: Text Revision; DSM-IV-TR*® (DSM-IV).[8]

Questionnaires are also used for parents and children to learn as much as possible about the situation.[8]

Additional procedures are also now used, including:

- electroencephalography
- axial tomography (cerebral scan)
- T2 relaxometry.

Diagnosis of ADHD children is not straightforward and misdiagnosis may occur, which leads to the possibility of error in treatment, with numerous possible side effects that could be especially damaging in view of the age of the population.

The last consideration arises, in part, from the clinical efficacy of methylphenidate medication (Ritalin®; Novartis International AG, Basel, Switzerland), as well as evidence from brain imaging studies that suggest reduced activity in frontal-striatal regions.[9]

Bioimpedance is the response of living tissue to externally applied electric current, and it has been shown that applying electric current is a safe technique when used in a number of biomedical applications.

One explanation as to why conductivity increases in the forehead pathway of ADHD children could be related to reduced activity in the frontal-striatal regions and altered cerebral blood flow as shown from brain imaging studies.[9]

A second explanation as to why conductivity increases could be related to the detection of hypoxia/ischemia, as suggested by Seoane et al, who used bioimpedance to detect hypoxia in the perinatal brain.[10]

The objective of this study was to compare conductivity measurements in the pathways between forehead electrodes using electro interstitial scans (EIS) in a group conventionally diagnosed with ADHD and a control group. The comparison was clinical and did not take into account comorbidity.

Materials and methods

This study was approved by the regional ethics committee, and adhered to the ethical principles of the Declaration of Helsinki. Each patient's parent (in view of the age of the subjects) signed an informed consent form, and confidentiality was maintained for all participants.

Subjects

The study included 112 children aged 3–18 years. Children were excluded: if their parent had a neurological disorder precluding the ability to sign a consent form; if, in the opinion of the investigator, a child was clinically unsuitable as a candidate for the trial; and/or if there were any contraindications to use of the EIS system. Use of the EIS system is contraindicated in the presence of an external defibrillator; skin lesions likely to come into contact with the electrodes; excessive perspiration; any implanted electronic device; inability to remain still for three minutes; metallic pins or prostheses in digits or joints; or absence of a limb.

Fifty-two children diagnosed with ADHD following psychiatric examination and 60 children without any symptoms of ADHD, underwent an examination with the EIS system.

The composition of the two groups was:

- Group 1: 60 children assumed to be non-ADHD, showing no symptoms of the condition and not undergoing any treatment (mean age: 8.7 years; 27 females).
- Group 2: 52 children diagnosed with ADHD according to the DSM-IV and further examinations, and not undergoing any treatment (mean age: 8 years; 14 females).

Materials

The Electro Interstitial Scan system (LD Technology, Miami, FL) is a programmable electromedical system comprising a universal serial bus (USB) plug and hardware including an interface box, disposable electrodes, reusable plates, and reusable cables, with software installed on a computer. The system uses bioimpedance in bipolar mode with direct current, and measures the electrical conductivity of eleven pathways of the body through six tactile electrodes placed symmetrically on the palms of the hands, soles of the feet, and on the forehead. Each pathway is recorded twice from anode to cathode and then from cathode to anode. Electrode polarization does not affect the bioimpedance measurement,[11] and transmission of the current from the electrode to the hardware is performed by chronoamperometry.[12]

With direct current, the plasma membrane acts as an insulator and the current is not able to penetrate the cell, so most of the current flows around the cell and, therefore, in the interstitial fluid.[10] Analysis of the direct current at the cathode and anode in electrolytic solution is performed at both the anode and the cathode.[11]

The electrochemical reaction at the cathode is:

$$2H_2O + 2e \rightarrow H_2(\text{gas}) + 2\ OH^- \ (\text{base})$$

The electrochemical reaction for water at the anode is:

$$2H_2O \rightarrow O_2\ (\text{gas}) + 4H^+ + 4e^- \ (\text{acid})$$

Statistical analysis

Statistical analysis was performed using MedCalc® statistical software (MedCalc Software bvba, Mariakerke, Belgium).[13]

Statistical analysis was conducted between the two groups using independent sample *t*-tests and receiver-operating characteristic curves (ROCs) to determine the specificity and sensitivity of detection of ADHD children with the EIS data. Independent sample *t*-tests and ROCs were constructed for the conductivity measurements of the pathway of the forehead electrodes for Groups 1 and 2.

Determination of the sample size

According to the previous studies related to the EIS system[14,15] the number of patients needed for the study was calculated to be 100 on the basis of $\alpha = 5\%$, at 80% power, taking into account the judgment criteria Δ at approximately 100 (5% error). A *P* value of <0.05 was accepted as being statistically significant.

Results

To determine the differences between ADHD and the control group in the conductivity values of the pathway of the forehead electrodes, comparison of the means via independent sample *t*-test was conducted. Table 1 presents the *t*-test results for conductivity scores in the ADHD group and the control group. It shows the number of measurements per group used in the analysis, the means, the standard deviation, degrees of freedom, *t* value and the significance of the test (*P* value). The findings in Table 1 indicate that the mean of the conductivity measurements of two pathways between the forehead electrodes (from left forehead to right forehead and from right forehead to left forehead) in the ADHD group was 33.11 micro Siemens (mS) (range 2–113 mS). This was significantly higher ($P < 0.001$) than mean of the conductivity measurements of two pathways between the forehead electrodes of the control group (2.75 mS, range 1.75–27.4 mS).

Table 1 Independent sample T-test for forehead pathways between ADHD and control groups

	N	Mean	SD	DF	T	*P*-value
ADHD	104	33.11	3.8	224	2.48	0.000
Control	120	2.75	2			

Abbreviations: ADHD, attention deficit/hyperactivity disorder; SD, standard deviation; DF, degrees of freedom.

In terms of the ROC results, comparing the two groups using the reference of the mean of conductivity measurements of two pathways between the forehead electrodes, the test showed a specificity of 98% and sensitivity of 80% and $P = 0.0001$ (95% confidence interval) with a cutoff value at 7.4 mS (Figure 1).

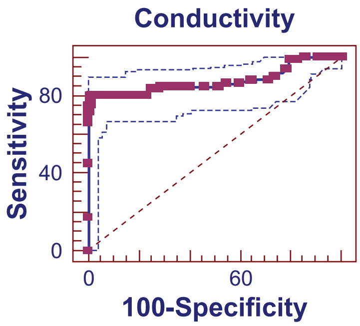
Discussion

ADHD is a complex and heterogeneous disorder that is characterized not only by cognitive deficits but also by affective dysfunctions, both motivational and emotional.[16,17] Nevertheless, the neural bases of affective dysfunctions have barely been explored in relation to this disorder, in contrast to extensive research that has examined the neural correlates of its main cognitive deficits (attention, response inhibition, and working memory). The diagnostic criteria to classify children and adolescents as having ADHD are the classic symptoms listed in the DSM-IV.[8] However, today these criteria are challenged due to the many errors of diagnosis and new forms of diagnosis are being considered.[18] For this reason, a tool that is easy to use, fast, and cost-effective and that could provide a new marker is warranted as an adjunct to the conventional diagnosis and treatment monitoring of ADHD children. It is well-known that a child with ADHD who benefits from treatment and adequate supervision can blossom and follow a normal path in school.

US researchers have published a study[9] on children suffering from ADHD, using functional magnetic resonance. T2 relaxometry shows anomalies at the level of the putamen, the cerebral structure implicated in the regulation of motor behavior.[18,19]

Currently, studies are looking at the role of genes in the hyperkinetic syndrome. Researchers are primarily studying the relation that may exist between genetic deficits, attention problems, and hyperactivity. There may be a genetic predisposition to this hyperactive syndrome.[20–23]

However, these techniques using magnetic resonance and genetic tests are expensive, require qualified personnel to



Variable	Conductivity
Classification variable	Diagnosis
Sample size	202
Positive group: Diagnosis = 1	80
Negative group: Diagnosis = 0	122
Disease prevalence (%)	39.6
Area under the ROC curve (AUC)	0.876
Standard error[a]	0.0305
95% confidence interval[b]	0.823 to 0.918
z statistic	12.349
Significance level *P* (Area = 0.5)	<0.001

[a]DeLong et al 1988[24]
[b]Binomial exact

Figure 1 Receiver-operating characteristic curve comparing the conductivity value measurements of the forehead pathway for the ADHD group and non-ADHD group.
Abbreviations: ADHD, attention deficit/hyperactivity disorder; AUC, area under the curve; ROC, receiver-operating characteristic curve.

perform, and cannot be used on a large scale or in treatment follow-ups.

Heart-rate variability and galvanic skin response devices have also been tested as methods of detecting ADHD in children,[25–28] but they do not provide adequate specificity, sensitivity, or cutoff.

Conclusion

The EIS marker related to the conductivity measurement of the forehead pathway has a high specificity and high sensitivity and use of this could provide practitioners with a noninvasive, low-cost, and easy-to-use system, which could offer an adjunct to the conventional diagnosis of ADHD in children, be used in treatment monitoring, and could allow for earlier intervention. Longitudinal studies are under way to confirm these findings.

The object of this study was to identify a measurable marker to assist in the conventional diagnosis of ADHD in children. Diagnosis of ADHD in children cannot be made solely with this marker. The marker may be useful for the diagnosis of ADHD, but additional validation using greater numbers of affected and control subjects is needed to confirm its usefulness.

Disclosure

This study was not sponsored and the author reports no conflicts of interest in this work.

References

1. National Institute of Mental Health. *Attention Deficit Hyperactivity Disorder (ADHD)*. Bethesda, MD: National Institutes of Health; 2008. Available from: http://www.nimh.nih.gov/publicat/adhd.cfm. Accessed July 26, 2011.
2. Kelland MD, Chiodo LA. Serotonergic modulation of midbrain dopamine systems. In: Ashby CR Jr, editors. *The Modulation of Dopaminergic Neurotransmission by Other Neurotransmitters*. Boca Raton, FL: CRC Press; 1996:87–122.
3. Spivak B, Vered Y, Yoran-Hegesh R, et al. Circulatory levels of catecholamines, serotonin and lipids in attention deficit hyperactivity disorder. *Acta Psychiatr Scand*. 1999;99(4):300–304.
4. Gainetdinov RR, Wetsel WC, Jones SR, Levin ED, Jaber M, Caron MG. Role of serotonin in the paradoxical calming effect of psychostimulants on hyperactivity. *Science*. 1999;283(5400):397–401.
5. Waldman ID, Rowe DC, Abramowitz A, et al. Association and linkage of the dopamine transporter gene and attention-deficit hyperactivity disorder in children: heterogeneity owing to diagnostic subtype and severity. *Am J Hum Genet*. 1998;63(6):1767–1776.
6. Jucaite A, Fernell E, Halldin C, Forssberg H, Farde L. Reduced midbrain dopamine transporter binding in male adolescents with attention-deficit/hyperactivity disorder: association between striatal dopamine markers and motor hyperactivity. *Biol Psychiatry*. 2005;57(3):229–238.
7. Kapur S, Remington G. Serotonin-dopamine interaction and its relevance to schizophrenia. *Am J Psychiatry*. 1996;153(4):466–476.
8. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*: *Text Revision*; *DSM-IV-TR*®. 4th ed. Arlington, VA: American Psychiatric Association; 2000.
9. Teicher MH, Anderson CM, Polcari A, Glod CA, Maas LC, Renshaw PF. Functional deficits in basal ganglia of children with attention-deficit/hyperactivity disorder shown with functional magnetic resonance imagery relaxometry. *Nat Med*. 2000;6(4):470–473.
10. Seoane F, Lindecrantz K, Olsson T, Kjellmer I, Flisberg A, Bågenholm R. Spectroscopy study of the dynamics of the transencephalic electrical impedance in the perinatal brain during hypoxia. *Physiol Meas*. 2005;26(5):849–863.
11. Grimmes S, Martinsen ØG. *Electrolytics in Bioimpedance and Bioelectricity Basics*. San Diego, CA: Academic Press; 2000.
12. Cottrell FG. Application of the Cottrell equation to chronoamperometry. *Z Physik Chem*. 1902;42:385.
13. MedCalc. Statisical literature [web page on the Internet]. Mariakerke: MedCalc Software; 2011 [updated 2011 Jun]. Available from: http://www.medcalc.org/literature.php. Accessed July 26, 2011.
14. De Abreu DS. Bioimpedance and chronoamperometry as an adjunct to prostate-specific antigen screening for prostate cancer. *Cancer Manag Res*. 2011;3:109–116.
15. Alexeev VG, Kuznecova LV. Bioimpedance in monitoring of effects of selective serotonin reuptake inhibitor treatment. *Psychol Res Behav Manag*. 2011;4:81–86.
16. Martel MM. Research review: a new perspective on attention-deficit/hyperactivity disorder: emotion dysregulation and trait models. *J Child Psychol Psychiatry*. 2009;50(9):1042–1051.
17. Nigg JT, Casey BJ. An integrative theory of attention deficit/hyperactivity disorder based on the cognitive and affective neurosciences. *Dev Psychopathol*. 2005;17(3):785–806.
18. The MTA Cooperative Group. A 14-month randomized clinical trial of treatment strategies for attention-deficit hyperactivity disorder. *Archives of General Psychiatry*. 1999;56(12):1073–1086.
19. Brunner D, Buhot MC, Hen R, Hofer M. Anxiety, motor activation, and maternal-infant interactions in 5HT1B knockout mice. *Behav Neurosci*. 1999;113(3):587–601.

20. Khan SA, Faraone SV. The genetics of ADHD: a literature review of 2005. *Curr Psychiatry Rep*. 2006;8(5):393–397.
21. Pine DS, Coplan JD, Wasserman GA, et al. Neuroendocrine response to fenfluramine challenge in boys. Associations with aggressive behavior and adverse rearing. *Arch Gen Psychiatry*. 1997;54(9):839–846.
22. Reuter M, Kirsch P, Hennig J. Inferring candidate genes for attention deficit hyperactivity disorder (ADHD) assessed by the World Health Organization adult ADHD self-report scale (ASRS). *J Neural Transm*. 2006;113(7):929–938.
23. Sonuga-Barke EJ. Causal models of attention-deficit/hyperactivity disorder: from common simple deficits to multiple developmental pathways. *Biol Psychiatry*. 2005;57(11):1231–1238.
24. Desman C, Petermann F, Hampel P. Deficit in response inhibition in children with attention deficit/hyperactivity disorder (ADHD): impact of motivation? *Child Neuropsychol*. 2008;14(6):483–503.
25. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. *Biometrics*. 1988;44:837–845.
26. Tonhajzerova I, Ondrejka I, Adamik P, et al. Changes in the cardiac autonomic regulation in children with attention deficit hyperactivity disorder. *Indian J Med Res*. 2009;130(1):44–50.
27. Luman M, Oosterlaan J, Hyde C, van Meel CS, Sergeant JA. Heart rate and reinforcement sensitivity in ADHD. *J Child Psychol Psychiatry*. 2007;48(9):890–898.
28. Börger N, van Der Meere J, Ronner A, Alberts E, Geuze R, Bogte H. Heart rate variability and sustained attention in ADHD children. *J Abnorm Child Psychol*. 1999;27(1):25–33.