ORIGINAL ARTICLE

Bali Medical Journal (*Bali Med J)* 2019, Volume 8, Number 2: 526-531
P-ISSN.2089-1180, E-ISSN: 2302-2914

Published by DiscoverSys

# Measuring motor evoked-potentials in children with autism spectrum disorders accompanied with cerebral vein thrombosis following intraarterial heparin flushing

Erwin Setiawan[1*], Ristaniah Soetikno[1], Nelly Amalia Risan[1], Shelly[1], Tugas Ratmono[2], Terawan Agus Putranto[2], Ardianto Pramono[2]

## ABSTRACT

**Background:** The use of the term "Autism Spectrum Disorder" has led to confusion over this substance. Prior to DSM-V criteria, symptoms of Autism Spectrum Disorder (ASD) refers to the problems in brain vasculature and brain chemistry most likely affect the children behavior, whereas the authors' findings suggest such problems depicting a similar anomaly in cerebral vein thrombosis case (CVT). Recently, the evoked potentials, that demonstrated in CVT, have a possible prognostic value on patients suffering from ASD. This study purposes to measure the motor evoked potentials (MEPs) on patients following the intervention of intraarterial heparin flushing (IAHF).

**Methods:** A descriptive study was conducted on 17 patients admitted in Cerebrovascular Center of RSPAD Gatot Soebroto, Jakarta, diagnosed with ASD presenting CVT. The MEPs value was measured by conforming the IAHF procedure.

**Results:** The MEPs value (amplitude, latency, CMCT) pre and post-IAHF showed an increasing value. Meanwhile, there was a lowering value of latency and CMCT in left cortical participants after IAHF.

**Conclusion:** The group tends to perform more expected positive MEPs changes after IAHF.

**Keywords:** MEPs, ASD, CVT, IAHF, amplitude, latency, CMCT

**Cite this Article:** Setiawan, E., Soetikno, R., Risan, N.A., Shelly., Ratmono, T., Putranto, T.A., Pramono, A. 2019. Measuring motor evoked-potentials in children with autism spectrum disorders accompanied with cerebral vein thrombosis following intraarterial heparin flushing. *Bali Medical Journal* 8(2): 526-531. DOI: 10.15562/bmj.v8i2.1531

[1]Padjajaran University. Jl. Raya Bandung-Sumedang Km. 21. Jatinangor. Sumedang, Indonesia
[2]RSPAD Gatot Soebroto. Jl. Abdul Rahman Saleh, No.24, Central Jakarta 10410, Indonesia

*Corresponding Author :
Erwin Setiawan;
Padjajaran University. Jl. Raya Bandung-Sumedang Km. 21. Jatinangor. Sumedang, Indonesia.
erwinsps2003@gmail.com

Received: 2019-02-21
Accepted: 2019-03-22
Published: 2019-04-01

## INTRODUCTION

Autism Spectrum Disorders (ASD) is long well known and defined as a neurodevelopmental disorder, which the disease is characterized by a widespread of abnormalities in social interactions, communication, and limited interests with highly repetitive behaviour.[1] Considering its wide array of symptoms manifesting as neuronal disruption, several authors thought autism as a disorder of neural connectivity.[2] autism was termed as a pervasive developmental disorder, where the presentation was necessary prior to 30-month-old, with the presenting symptoms and signs consists of lack of interest in people, gross impairment in communication, and uncommon responses to environmental stimulation and interactions.[5] These conditions are suggested to be present at birth and are diagnosable by 18 months of age. Nowadays, the known ASD case recorded by The Centres for Disease Control and Prevention currently estimates the prevalence rate of Autism Spectrum Disorder (ASD) in the United States alone is approximately 1 of 88 children (1 of 54 boys and 1 of 252 girls)[7] while the male to female sex ratio is 4:1.[8] Most of the children diagnosed with autism how sensory and perceptual abnormalities. They have both hyposensitivity and hypersensitivity to sensory, auditory, and visual stimuli.[9] Besides the known disturbance in sensory and perceptual aspect, there is also gait problems that commonly found in children with ASD which confirmed by the qualitative rating of "body use" on the Childhood Autism Rating Scale (CARS), related to the motor dysfunction. However, when Magnetic Resonance Imaging (MRI) examination was performed on children who suffer from ASD such as poor concentration, repetitive movement and lack of communication, the results showed that there were signs of CVT. Study of de Veber et al. showed that the signs and symptoms of CVT in pediatric patients may differ, but the typical clinical features are seizures, headache, respiratory distress, and focal neurological deficits.[7] Patients whose diagnosed with CVT may also present with deficits related to venous infarction which ranging from developmental delays, learning disabilities, hemiparesis, and hemisensory loss.[7,90]

As the theory of Excitatory-Inhibitory (E-I) imbalance is one of the possible etiology of ASD, one of the known likely causative is

increased glutamatergic or decreased signaling in GABAergic. Couples of examination tools such as electroencephalogram (EEG) and magnetoencephalography (MEG) possibly can be used to determine the E-I imbalance in ASD alone, or together with Trans Magnetic Stimulation (TMS) which can provide useful biomarkers and outcome measures.[53] Since E-I imbalance is under the scope of neurophysiology, measured by a particular tool is needed. Thus, it used motor evoked potentials (MEPs) which measured by TMS method. According to American Clinical Neurophysiology Society, MEPs are a collection of electrical signals recorded from neural tissue or muscle using a particular tools and techniques following the activation of central motor pathways which also act as a complement to another clinical neurophysiology techniques, for example is somatosensory evoked potentials (SEPs), considering the assessment of the human nervous system. TMS can also be used to investigate cortical and cortico-spinal plasticity mechanisms in a non-invasive way. These mechanisms have also been implicated in the ASD pathophysiology.[27,28]

There are few treatment strategies for ASD presenting with CVT cases in children, but most children receive anticoagulation regimens. The delivery method of anticoagulants therapy may vary between centers. In RSPAD Gatot Soebroto Jakarta, Digital Subtraction Angiography (DSA) method was used both as a diagnostic tool and a therapeutic method after modified by Terawan et al.[93] A modified DSA procedure was a method of delivering anticoagulation therapy directly to the occluded vessels guided by imaging technique in further called IAHF (IntraArterial Heparin Flushing), where the only difference between IAHF and the original DSA was the continuous directed local flushing of heparin into the occluded vessels.[90] There is still limited literature discussing ASD presenting with CVT and IAHF. Thus, this study suggests the motor evoked potentials (MEPs) as the investigation tools because it is well understood that MEPs were directly correlated with the motor performance itself, or accuracy of movement.[18-20]

## METHOD

The participants of this study were obtained from Cerebrovascular Center of RSPAD Gatot Soebroto, Jakarta, who registered as patients that admitted by the pediatricians, then consulted to a group of medical specialties consist of Psychiatrist, Neurologist, Physiatrist, and Interventional Radiologist. All participants, which obtained from their parents, gave their informed written consent before being tested. The procedure was approved by the Cerebrovascular Center of RSPAD Gatot Soebroto, Jakarta and University of Padjajaran Bioethics committee. The methods carried out in this study are in accordance with approved guidelines.

Participants were tested in a sitting position with forearm supported in a pronated position. A standard skin preparation[92] procedure was performed for each electrode placement site. EMG electrodes were placed on the first dorsal interosseous (FDI) muscle of the dominant hand. MEPs size measurement was performed by using TMS Neurosoft Variant 4 (Neurosoft, Ivanovo, Russia). Big ring coil was placed on the vertex, and a single pulse stimulation was given. Side B of the coil (anticlockwise) was used to stimulate left hemisphere, while side A (clockwise) to stimulate right hemisphere. To measure latency (millisecond/ms), amplitude (millivolt/mV), and CMCT (ms), the MEPs value was recorded with stimulation of submaximal threshold 80% MEP at each side. The MEPs value was measured both pre-IAHF and 4 hours post-IAHF procedure.

## RESULTS

Seventeen participants with ASD (11 males; aged 6-16 years old) took part in this study. The participants were measured for the MEP results before and 4 hours after the IAHF procedure (as seen in Table 1).

Table 1 shows the difference between MEPs value pre and post-IAHF procedure. All the MEPs value seems to be increased both in left and right cortical. In the right cortical, the average MEP amplitude value has increased 0.3 point while the latency value has increased as much as 2.344 point. It's also shown at CMCT value, which has increased 0.72 point. Meanwhile, in the left cortical, the average amplitude value has increased as much as 0.757 point while the latency value and CMCT values also increased as much as 0.78 and 0.27 point, respectively.

As shown in Table 2, there was a significant difference to be noticed in its value on participants' MEP in both hands post-IAHF. Amplitude and CMCT value of MEPs in the right cortical were increased, while the latency value was decreased. On the other hand, the amplitude of MEPs in the left cortical was significantly decreased, while the latency and CMCT value of MEPs was slightly increased.

## DISCUSSION

Children age group which ranges from 6 to 16 years was suffered from Autism Spectrum Disorder (ASD). The patients passed some essential

**Table 1. General MEPs Value pre and post-IAHF procedure**

| Variables (n=17) | Pre-IAHF | Post-IAHF | Δ |
|---|---|---|---|
| **Left hand** (μ) | | | |
| Amplitude | 0.60 | 0.9 | 0.3 |
| Latency | 17.8 | 20.133 | 2.344 |
| CMCT | 8.203 | 8.92 | 0.72 |
| **Right hand** (μ) | | | |
| Amplitude | 0.7 | 1.474 | 0.757 |
| Latency | 17.089 | 17.87 | 0.78 |
| CMCT | 7.56 | 7.82 | 0.27 |

**Table 2. MEP Results in Right and Left-cortical post-IAHF**

| Variables (n=17) | Right Cortical | | | Left Cortical | | |
|---|---|---|---|---|---|---|
| | Amplitude | Latency | CMCT | Amplitude | Latency | CMCT |
| **Increased** | 8 (47%) | 10 (58%) | 7 (41%) | 12 (70%) | 7 (41%) | 8 (47%) |
| **Decreased** | 9 (52%) | 7 (41%) | 10 (58%) | 5 (29%) | 10 (58%) | 9 (52%) |

examination from several specialties such as Pediatrician, Psychiatrist, Neurologist, and also Intervention Radiologist to make sure the patient condition is suitable for this procedure and make sure the safety of the patient. Numerous studies already reported that there was a possibility of motor deficits that might coexist in individuals with ASD, including alterations in motor milestone development[46], clumsiness, motor incoordination, disturbances in reach-to-grasp movement[64-86], deficits in gross and fine motor movement[87], and also impaired postural control.[16-88] Once after MEPs value was obtained, further examination such as Magnetic Resonance Imaging (MRI) was needed. Problems in brain anatomy development as a causative factor in ASD is also possible, and based on the experience in RSPAD, most of children suffered from ASD will most likely have abnormality in their brain vasculature, therefore the MRI which include Magnetic Resonance Venography (MRV) and Magnetic Resonance Perfusion (MRP) is performed. However, the abnormality in brain vasculature also found in Cerebral Vein Thrombosis (CVT) cases in pediatric patients. CVT diagnosis was established by an anticoagulant therapy with catheter guide help using a digital imaging technique called Digital Subtraction Angiography (DSA), which has been developed and modified by Interventional Radiologist team in RSPAD Gatot Soebroto, Terawan, now specifically called Intraarterial Heparin Flushing (IAHF).[90] This supported by the findings in de Veber study. When MRI examination was performed on children who suffer from symptoms resembled an ASD such as poor concentration, repetitive movement, and lack of communication, the results showed that there were signs of CVT. The sign and symptoms of CVT in pediatric children may vary, but most common clinical features are seizures, headache, respiratory distress, and focal neurological deficits.[91]

In general population of this study, there was no significant difference in MEP values pre and post-IAHF procedure, but there were some significant differences in amplitude, latency, and CMCT when the results were categorized into left and right-cortical post-IAHF, which possibly showed a typical positive outcome in left cortical participants, seemed to depict a motor recovery and improvement in these participants' clinical condition. This improvement was measured by the psychiatrist using Childhood Autism Rating Scale (CARS) and also from the patient parents or legal guardians testimony, which described such more positive changes in patient behavioral status.

## CONCLUSION

The group tends to perform more expected positive MEPs changes after IAHF.

## ACKNOWLEDGMENTS

The authors want to express a high gratitude to Padjajaran University and RSPAD Gatot Soebroto (Army Central Hospital) for their support in the process of this study.

## ETHICAL CLEARANCE

This study has obtained ethics approval from the Ethics Committee of Padjajaran University prior to the study conducted.

## CONFLICT OF INTERESTS

The authors declare that there were no conflicts of interest in the process of this study.

## FUNDING

The authors are responsible for the study funding without the involvement of grant, scholarship, or any other resources of funding.

## AUTHOR CONTRIBUTION

All of authors are equally contributed to the study from the study framework, data gathering, data analysis, until reporting the result of study.

## REFERENCES


1. Eikeseth S. Outcome of comprehensive psycho-educational interventions for young children with autism. Res Dev Disab. 2009; 30: 158–78.
2. Coben R, Chabot RJ, Hirshberg L. EEG analyses in the assessment of autistic disorders. In M. F. Casanova, A. S. El-Baz, and J. S. Suri (Eds.). Imaging the Brain in Autism. 2013; 349–370.
3. Volkmar FR, State M, Klin A. Autism and autism spectrum disorders: diagnostic issues for the coming decade. J Child Psychol Psychiatry. 2009; 50:108–15.
4. Baker JP. Autism at 70-redrawing the boundaries. N Engl J Med. 2013; 369:1089–91.
5. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 3rd ed. Washington, DC: American Psychiatric Association; 1980.
6. Kuban KC, O'Shea TM, Allred EN, Tager-Flusberg H, Goldstein A, Leviton A. Positive screening on the Modified Checklist for Autism in Toddlers (M-CHAT) in extremely low gestational age newborns. J Pediatr. 2009; 154(122): 535-540.
7. DeVeber G, Andrew M, Adams C, Bjornson B, Booth F, Buckley D.J, et al. Cerebral Sinovenous Thrombosis in Children. N Engl J Med. 2001;345:417–23.
8. Taurines R, Segura M, Schecklmann M, Albantakis L, Grünblatt E, Walitza S,et al. Altered peripheral BDNF mRNA expression and BDNF protein concentrations in blood of children and adolescents with autism spectrum disorder. J Neural Transm. 2014; 121:1117–1128.
9. Watling R, Deitz J, White O. Comparison of Sensory Profile Scores of young children with and without autism spectrum disorders. Am J Occup Ther. 2001;55:416–23.
10. Fogassi L, Ferrari PF, Gesierich B, Rozzi S, Chersi F, Rizzolatti G. Parietal lobe:from action organization to intention understanding. Science 308. 2005; 5722:662-67
11. Damasio AR, Maurer RG. A neurological model for childhood autism. Archives of Neurology. 1978; 35(12):777-78.
12. Vilensky JA, Damasio AR, Maurer RG. Gait disturbances in patients with autistic behavior: A preliminary study. Archives of Neurology. 198; 38(10):646-49.
13. Lai MC, Lombardo MV, Baron-Cohen S. Autism. Lancet. 2014; 383:896–910.
14. Fournier KA, Hass CJ, Naik SK, Lodha N, Cauraugh JH. Motor coordination in autism spectrum disorders: a synthesis and metaanalysis. Journal of Autism and Developmental Disorders. 2010; 40(10):1227–40.
15. Gowen E, Hamilton A. Motor Abilities in Autism: A Review Using a Computational Context. J Autism Dev Disord. 2012.
16. Kohen-Raz R, Volkmar FR, Cohen DJ. Postural control in children with autism. Journal of Autism and Developmental Disorders. 1992; 22(3):419-432.
17. Kanner. Autistic disturbances of affective contact. Nervous child. 1943; 2:217-250.
18. Davare M, Andres M, Cosnard G, Thonnard JL, Olivier E. Dissociating the role of ventral and dorsal premotor cortex in precision grasping. J Neurosci. 2006; 26:2260–68.
19. Pearce AJ, Kidgell DJ. Corticomotor excitability during precision motor tasks. J Sci Med Sport. 2009; 12:280–83.
20. Classen J, Liepert J, Wise SP, Hallett M, Cohen LG. Rapid plasticity of human cortical movement representation induced by practice. J Neurophysiol. 1998; 79:1117–23.
21. Buie T, Campbell DB, Fuchs GJ 3rd, et al. Evaluation, diagnosis, and treatment of gastrointestinal disorders in individuals with ASD: a consensus report. Pediatrics. 2010;125:S1–18.
22. Choudhury PR, Lahiri S, Rajamma U. Glutamate mediated signaling in the pathophysiology of autism spectrum disorders. Pharmacol Biochem Behav. 2012; 100:841–49.
23. Oberman LM, Pascual-Leone A, Rotenberg A. Modulation of corticospinal excitability by transcranial magnetic stimulation in children and adolescents with autism spectrum disorder. Frontiers in Human Neuroscience. 2014; 8:627.
24. Courchesne E, Karns CM, Davis HR, Ziccardi R, Carper RA, Tigue ZD, et al. Unusual brain growth patterns in early life in patients with autistic disorder: an MRI study. Neurology. 2001; 57(2), 245-254.
25. Geschwind DH, Levitt P. Autism spectrum disorders: developmental disconnection syndromes. Curr Opin Neurobiol. 2007; 17(1):103-111.
26. Dolen G, Bear MF. Fragile x syndrome and autism: from disease model to therapeutic targets. J Neurodev Disord. 2009; 1(2):133-140.
27. Markram H, Rinaldi T, Markram K.The intense world syndrome--an alternative hypothesis for autism. Front Neurosci. 2007; 1(1): 77-96.
28. Oberman LM, Pascual-Leone A. Cortical plasticity: A proposed mechanism by which genomic factors lead to the behavioral and neurological phenotype of autism spectrum and psychotic spectrum disorders. Behavioral and Brain Sciences. 2008; 31:241–320.
29. Rubenstein JLR, Merzenich MM. Model of autism:Increased ratio of excitation/inhibition in key neural systems.Genes, Brain and Behavior. 2003; 2(5):255–267.
30. Folsom TD, Fatemi SH. The involvement of reelin in neurodevelopmental disorders. Neuropharmacology. 2013; 68:122–135.
31. Robertson CE, Baron-Cohen S. Sensory perception in autism. Nat. Rev. Neurosci. 2017; 18:671–684.
32. Baker AE, Lane A, Angley MT, Young RL. The relationship between sensory processing patterns and behavioural responsiveness in autistic disorder: a pilot study. J Autism Dev Disord. 2008; 38:867–75.
33. Leekam SR, Libby SJ, Wing L, Gould J. Describing the sensory abnormalities of children and adults with autism. J Autism Dev Disord. 2007;37:894–910.
34. Tomchek SD, Dunn W. Sensory processing in children with and without autism: a comparative study using the short sensory profile. Am J Occup Ther. 2007; 61:190–200.
35. Baranek GT, David FJ, Poe MD, Stone WL, Watson LR. Sensory experiences questionnaire: discriminating sensory features in young children with autism, developmental delays, and typical development. J Child Psychol Psychiatry. 2006;47:591–601.
36. Hussman JP. Suppressed gabaergic inhibition as a common factor in suspected etiologies of autism. J. Autism Dev. Disord. 2001; 31:247–248.
37. Casanova MF, Buxhoeveden D, Gomez J. Disruption in the inhibitory architecture of the cell minicolumn: Implications for autism. The Neuroscientist. 2003; 9(6):496–507.
38. Yizhar O, Fenno LE, Prigge M, Schneider F, Davidson TJ, O'Shea DJ, Sohal VS, Goshen I, Finkelstein J, Paz JT, Stehfest K, Fudim R, Ramakrishnan C, Huguenard JR, Hegemann P, Deisseroth K. Neocortical excitation/inhibition balance in information processing and social dysfunction. Nature. 2011; 477(7363):171–78.
39. Williams JH, Whiten A, Suddendorf T, Perrett DI. Imitation, mirror neurons and autism. Neuroscience and biobehavioral reviews. 2001; 25(4):287-295.
40. Rizzolatti G, Craighero L. The mirror-neuron system. Annual review of neuroscience. 2004; 27:169–192.
41. Dapretto M, Iacoboni M. The mirror neuron system and the consequences of its dysfunction. Nat Rev Neurosci. 2006; 7(12):942–51.
42. Oberman LM, Ramachandran VS. The simulating social

mind: the role of the mirror neuron system and simulation in the social and communicative deficits of autism spectrum disorders. 2007; 133(2): 310–27.
43. Iacoboni M, Dapretto M. The mirror neuron system and the consequences of its dysfunction. Nature Reviews. 2006; 7(12):942–51.
44. Yamasaki S, Yamasue H, Abe O, Suga M, Yamada H, Inoue H, Kuwabara H, et al. Reduced gray matter volume of pars opercularis is associated with impaired social communication in high-functioning autism spectrum disorders. Biological psychiatry. 2010; 68(12):1141–7.
45. Hadjikhani N, Joseph RM, Snyder J, Tager-Flusberg H, Tager Flusberg H. Anatomical differences in the mirror neuron system and social cognition network in autism. Cereb Cortex. 2006; 16(9):1276–82.
46. Teitelbaum P, Teitelbaum O, Nye J, Fryman J, Maurer RG. Movement analysis in infancy may be useful for early diagnosis of autism. Proceedings of National Academy of Science USA. 1998;95(23):13982-87.
47. Mostofsky SH, Powell SK, Simmonds DJ, Goldberg MC, Caffo B, Pekar JJ. Decreased connectivity and cerebellar activity in autism during motor task performance. Brain. 2009; 132:2413–25.
48. Enticott PG, Bradshaw JL, Iansek R, Tonge BJ, Rinehart NJ. Electrophysiological signs of supplementary-motor-area deficits in high-functioning autism but not Asperger syndrome: an examination of internally cued movement-related potentials. Dev Med Child Neurol. 2009; 51:787–91.
49. Jung NH, Janzanik WG, Delvendahl I, Munchau A, Biscaldi M, Mainberger F, et al. Impaired induction of long-term potentiation-like plasticity in patients with high-functioning autism and Asperger syndrome. Dev Med Child Neurol. 2013; 55:83–89.
50. Fabbri-Destro M, Gizzonio V, Avanzini P. Autism, motor dysfunctions and mirror mechanism. Clinical Neuropsychiatry. 2013;10(5):177-187.
51. Dowell LR, Mahone EM, Mostofsky SH. Associations of postural knowledge and basic motor skill with dyspraxia in autism: Implication for abnormalities in distributed connectivity and motor learning. Neuropsychology. 2009; 23(5):563-70.
52. Dziuk MA, Gidley Larson JC, Apostu A, Mahone EM, Denckla MB, Mostofsky SH. Dyspraxia in autism: association with motor, social, and communicative deficits. Developmental Medicine and Child Neurology. 2007; 49:734-739.
53. Uzunova G, Pallanti S, Hollander E. Excitatory/inhibitory imbalance in autism spectrum disorders: implications for interventions and therapeutics. World J Biol Psychiatry. 2016;17(3):174-86.
54. Amassian VE, Stewart M, Quirk GJ, Rosenthal JL. Physiological basis of motor effects of a transient stimulus to cerebral cortex. Neurosurgery 1987; 20:74-93.
55. Wagner T, Valero-Cabre A, Pascual-Leone A: Non-invasive human brain stimulation. Annu Rev Biomed Eng. 2007; 9:527–565.
56. Merton PA, Morton HB: Stimulation of the cerebral cortex in the intact human subject. Nature. 1980; 285:227.
57. Barker AT. The history and basic principles of magnetic nerve stimulation. Electroencephalography and Clin Neurophysiology Supplement. 1999; 51:3–21.
58. Barker AT, Jalinous R, Freeston IL: Non-invasive magnetic stimulation of human motor cortex. Lancet. 1985;325:1106–07.
59. Oberman LM, Rotenberg A, Pascual-Leone A. Use of Transcranial Magnetic Stimulation in Autism Spectrum Disorders. J Autism Dev Disord. 2013.
60. Day BL, Dressler D, Maertens de Noordhout A, Marsden CD, Nakashima K, Rothwell JC, Thompson PD. Electric and magnetic stimulation of human motor cortex: surface EMG and single motor unit responses. Journal of Physiology. 1989; 412:449–473.
61. Kobayashi M, Pascual-Leone A. Transcranial magnetic stimulation in neurology. Lancet Neurology. 2003; 2(3):145–156.
62. Oberman LM, Rotenberg A, Pascual-Leone A. Use of transcranial magnetic stimulation in autism spectrum disorders. J Autism Dev Disord. 2015;45(2):524–536.
63. Garvey MA, Gilbert DL. Transcranial magnetic stimulation in children. European Journal of Paediatric Neurology. 2004; 8(1):7–19.
64. Lin, K. L., & Pascual-Leone, A. Transcranial magnetic stimulation and its applications in children. Chang Gung Medical Journal. 2002; 25(7):424–436.
65. Théoret H, Halligan E, Kobayashi M, Fregni F, Tager Flusberg H, Pascual-Leone A, Theoret H, et al. Impaired motor facilitation during action observation in individuals with autism spectrum disorder. Curr Biol. 2005; 15(3):R84–5.
66. Enticott PG, Kennedy HA, Rinehart N, Tonge BJ, Bradshaw JL, Taffe JR, Daskalakis ZJ, et al. Mirror Neuron Activity Associated with Social Impairments but not Age in Autism Spectrum Disorder. Society of Biological Psychiatry. 2011.
67. Fadiga L, Craighero L, Olivier E. Human motor cortex excitability during the perception of others' action. Current Opinion in Neurobiology. 2005.
68. Patuzzo S, Fiaschi A, Manganotti P. Modulation of motor cortex excitability in the left hemisphere during action observation: A single- and paired-pulse transcranial magnetic stimulation study of self- and non-self- action observation. Neuropsychologia, 200; 41(9):1272–78.
69. Strafella AP, Paus T. Modulation of cortical excitability during action observation: A transcranial magnetic stimulation study. Neuroreport. 2000; 11(10):2289–92.
70. Pedapati EV, Gilbert DL, Erickson CA, et al. Abnormal Cortical Plasticity in Youth with Autism Spectrum Disorder: A Transcranial Magnetic Stimulation Case-Control Pilot Study. J Child Adolesc Psychopharmacol. 2016;26(7):625–631
71. Dileone M. Enhanced human brain associative plasticity in Costello syndrome. J. Physiol. 2010; 588: 3445–56.
72. Murakami T, Sakuma K, Nomura T, Nakashima K. Short-interval intracortical inhibition is modulated by high-frequency peripheral mixed nerve stimulation. Neurosci. Lett. 2007; 420:72–75.
73. Balbi P, Perretti A, Sannino M, Marcantonio L, Santoro L. Postexercise facilitation of motor evoked potentials following transcranial magnetic stimulation:a study in normal subjects. Muscle Nerve. 2002; 25:448–452.
74. Kim GW, Ko MH. Facilitation of corticospinal tract excitability by transcranial direct current stimulation combined with voluntary grip exercise. Neurosci. Lett. 2013; 548:181–4.
75. Chen X. Success rate of motor evoked potentials for intraoperative neurophysiologic monitoring: effects of age, lesion location, and preoperative neurologic deficits. J. Clin. Neurophysiol. 2007; 24:281–285.
76. Chipchase L, Schabrun S, Cohen L, Hodges P, Ridding M, Rothwell J, et al. A checklist for assessing the methodological quality of studies using transcranial magnetic stimulation to study the motor system: an international consensus study. Clinical Neurophysiology: Official Journal of the International Federation of Clinical Neurophysiology. 2012: 123(9):1698-704.
77. Bestmann S, Krakauer J. The uses and interpretations of the motor-evoked potential for understanding behaviour. Experimental Brain Research. 2015:233(3):679-89.

78. Abruzzese G, Trompetto C. Motor Evoked Potentials. Encyclopedia of Movement Disorders. 2010;194-195.
79. Bartholomeusz HH, Courchesne E, Karns CM. Relationship between head circumference and brain volume in healthy normal toddlers, children, and adults. Neuropediatrics. 2002; 33:239–241.
80. Mukherjee P, McKinstry RC. Diffusion Tensor Imaging and Tractography of Human Brain Development. Neuroimaging Clinics of North America Advanced Pediatric Imaging. 2006;16:19–43.
81. Yakovlev PI, Lecours AR. The myelogenetic cycles of regional maturation of the brain. In: Minkowski A, editor. Regional development of the brain in early life. Oxford: Blackwell. 1967;3-70.
82. Rajapakse T, Kirton A. Non-invasive brain stimulation in children: applications and future directions. Translational Neuroscience. 2013; 4(2):217–223.
83. Rossi S, Hallett M, Rossini PM, Pascual-Leone A. Safety of T.M.S. Consensus Group. Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. Clinical Neurophysiology. 2009; 120(12):2008–39.
84. Miyahara M, Tsujii M, Hori M, Nakanishi K, Kageyama H, Sugiyama, T. Briefreport: motor in coordination in children with Asperger syndrome and learning disabilities. J. Autism Dev.Disord. 1997; 27:595–603.
85. Ghaziuddin M, Butler E. Clumsiness in autism and Asperger syndrome: a further report. J. Intellect.Disabil. Res. 1998; 42:43–48.
86. Mari M, Castiello U, Marks D, Marraffa C, Prior M. The reach to grasp movement in children with autism spectrum disorder. Philos.Trans.RSoc. Lond.BBiol.Sci. 2003; 358: 393–403.
87. Noterdaeme M, Mildenberger K, Minow F, Amorosa H. Evaluation of neuro motor deficits in children with autism and children with a specific speech and language disorder. Eur.ChildAdolesc. Psychiatry. 2002; 11: 219–25.
88. Minshew NJ, Sung K, Jones BL, Furman JM. Under development of the postural control system in autism. Neurology. 2004; 63:2056–61.
89. Mattle HP, Edelman RR, Reis MA, et al. Flow quantification in the superior sagittal sinus using magnetic resonance. Neurology. 1990; 40:813–15.
90. Putranto T, Yusuf I, Murtala B, Wijaya A. IntraArterial Heparin Flushing Increases Manual Muscle Test – Medical Research Councils (MMT-MRC) Score in Chronic Ischemic Stroke Patient. Bali Medical Journal. 2016; 5(2):216-20.
91. Gilmore KL, Meyers JE. Using Surface Electromyography in Physiotherapy Research. Aust J Physiother. 1983; 29(1):3-9.
92. Yoon N.K, McNally S, Taussky P, Park MS. Imaging of cerebral aneurysms: a clinical perspective. Neurovascular Imaging. 2016;2(1):6.