

Autism Spectrum Disorder: Main Problem Waiting for Solution in Kingdom of Saudi Arabia

Rana M. Zeina, Laila Al-Ayadhi, Shahid Bashir

Abstract—Autism Spectrum Disorders (ASDs) are characterized by abnormalities in social interaction and communication, as well as repetitive and stereotyped behaviors. Although various studies have been conducted in ASDs etiology across the world, it seems that they are still unknown in Middle East. Some scientific researches have been conducted on ASDs in Middle East (ME) especially in Kingdom of Saudi Arabia (KSA).

A systematic literature review was performed to identify the ASDs studies in KSA. Accordingly, PubMed, ISI web of Science and Google were searched to find KSA and ME studies in ASDs. The main focus of this review work is to outline an improved understanding of the underpinnings of ASD in order to achieve therapeutic interventions and we will discuss the main problem we waiting for solution with reference with role of Transcranial Magnetic Stimulation (TMS) to modulate cortical activity improve understanding ASD.

Keywords—Autism, Neurodevelopmental disorder.

I. INTRODUCTION

AUTISM SPECTRUM DISORDERS (ASD) are the most prevalent of the neurodevelopmental disorders, yet the epidemiology of these disorders remains largely puzzling. By the time the child is diagnosed, the resulting behavioral phenotype is likely the result of all of these multiple factors (restricted, repetitive, stereotyped patterns of behaviors, interests and deficits in social and communicative skills) so what is then observed is in fact the result of developmental and learning-related plasticity [1].

Although various studies have been conducted in ASDs etiology across the world, it seems that they are still unknown in developing and developed countries. In fact, ASDs have been introduced as multifactorial disorders; from ascendancy of genetic to environmental factors are involved in causing them [2]-[4].

Families with a child that has ASD experience considerable stress as they are confronted with extraordinary demands on their time, energy and financial resources. The lifetime per capita incremental societal cost of autism is estimated to be \$3.2 million [5].

Rana M Zeina was with the KSU-Autism Research and Treatment Center, Faculty of Medicine, King Saud University, Saudi Arabia (phone: 00966566977774, e-mail: ranazeinam@gmail.com)

Laila al Ayadh was with the KSU-Autism Research and Treatment Center, Faculty of Medicine, King Saud University, Saudi Arabia (e-mail: ayad@gmail.com).

Shahid Basher was with the KSU-Autism Research and Treatment Center, Department of Physiology, Faculty of Medicine, King Saud University, Saudi Arabia (e-mail: basher@gmail.com).

Based on some health organizations [6], 67 million individuals across the globe are afflicted with ASD, the need to conduct further studies and designing more effective treatments is even more apparent and considered as a national and international priority. The complexity of the biological aspects of this illness is the main culprit of this treatment failure. Different brain areas involved in different dimensions of this illness and complicate the execution of therapeutic interventions.

The diagnosis of autism is based on the Diagnostic and Statistical Manual for Mental Disorders (DSM-IV), Autism Diagnostic Interview- Revised (ADI-R), Autism Diagnostic Observation Schedule (ADOS), Childhood Autism Rating Scale (CARS) [7]. There is universal agreement in diagnostic criteria of ASDs; however the cultural differences influence their diagnosis and the age of noticing abnormality and starting intervention, developmental and parental problems tendency for neurodevelopment disorders. Culture also influences significantly the ways of investigating and treating autism [8].

With regards to obscure etiology of ASDs in KSA, they have not been specifically treated up to now. Nevertheless, several treatments have been performed to improve ASDs including behavioral, medical, biological, sensory-motor, hyperbaric oxygen therapy, camel milk, behavioral interventions as high functioning augmentative and alternative communication (AAC) and relationship development interventions have been performed in KSA [9].

II. ASDS PREVALENCE

Most studies about ASDs prevalence have been done in the western world [10]. Accordingly, diversity among prevalence estimations could be related to the age of participants, diagnostic criteria and geographical locations. In addition, less prevalence of ASDs can be explained by the less available services and lack of awareness about ASDs in developing countries [11]. While no advanced study have been conducted on the prevalence of ASDs in KSA [12].

III. ETIOLOGY OF ASDS

ASDs have multiple etiologies; genetic polymorphisms, epigenetics, convergent molecular abnormalities, mutations, chromosomal aberrations, disorders in mirror neuron system and central coherence, brain structure anomalies, cytogenetic abnormalities, single-gene defects, toxic exposures, teratogens, measles-mumps-rubella vaccines, some prenatal, obstetric and neonatal factors, etc.; that have been specified as

the contributing factors in the etiologies of ASDs in the different researches across the world [4], [13], [14].

In KSA, a country in the Middle East of about 23m people, which, despite its immense oil wealth, faces enormous problems of access to health care [15]. Although half of the population is below 15 years of age, services for children with developmental and psychiatric disorders are not well developed [16]. While exact figures are not available, anecdotal reports suggest an increase in the prevalence of autism in SA.

The relationships between ASDs and some effective factors have been investigated in KSA. The uninvestigated factor is the correlation between the paternal and maternal age and the risk of having ASD. Scientists in Riyadh, SA conducted a study "To investigate the link between autism disorders and engineering training of parents" and mentioned that there is a possibility of an association between autism and the engineering/math training of fathers [9].

IV. BEHAVIORAL AND SOCIAL THERAPIES OF ASDS

Educational provisions in SA still have a long way to go. In terms of the educational placements that are available in public schools that still are not able to conclude ASD students because of poor training and provisions from the responsible institutions. Therefore, autistic students are being referred to center for those severe learning difficulties, regardless of their intellectual ability or their different needs.

In addition, student with high functioning autism or Asperger Syndrome often remain undiagnosed because teachers are unable to recognize the symptoms of autism. In terms of the private sector, there are a few centers that specialize in autism in the major cities, (Riyadh, Dammam, and Jeddah) across the SA, there are three centers specialized in autism, Academy of Special Education, Jeddah Centre for Autism and Prince Faisal bin Fahd mother's Centre [9] and they seem capable of meeting the special needs of these students.

All of these centers adopt TEACCH (Treatment and Education of Autistic and Related Communication Handicapped Children) as a comprehensive. There are various intervention approaches for training children with ASDs. For instance, Applied Behavioral Analysis (ABA), Early Intensive Behavioral Intervention (EIBI), Hawaii Early Learning Profile (HELP), Psycho educational Profile: Third Edition (PEP-3) picture exchange communication system (PECS) and one to one support. Several studies indicated that these behavioral and social interventions can improve non-verbal IQ, expressive IQ, receptive language, adaptive behavior, verbal cognitive abilities, socialization, communication adaptive skills, reciprocal social interaction, intellectual and educational gains in children with ASDs [17]-[20].

V. MENTAL HEALTH OF ASDS PARENTS

Parents of children with ASDs are more likely to experience serious psychological distress than parents of children with other developmental disabilities [21], it seems raising a child with an ASD has often been associated with higher levels of parenting stress and psychological distress such as stigma, blame and insufficient social support in developing countries [22].

Several studies have been conducted to investigate parental problems, especially in mothers, in SA. Another study investigated personality characteristics and attachment style in mothers with autistic children in comparison with mothers who had normal children [11]. Some interventions were performed to reduce mental problems in mothers with autistic children. A preliminary investigation showed that the symptoms of stress, depression, and anxiety of mothers with autistic children were relatively reduced by guided imagery via music.

In another study, group counseling was administered to a group of mothers with autistic children. One study in SA used the cognitive behavior approach in reduce the degree of stress and the results indicated significant differences in family performance and marital satisfaction scores in mothers who had received the cognitive behavioral therapy compared with the control group [23], [24].

VI. PROBLEMS NEEDED TO BE ADDRESSED

Considering the presence of both biochemical and bioelectrical elements together in the brain, a goal oriented electrical intervention in brain functions along with behavioral interventions, has been considered as a theoretical possibility in recent years. There are significant questions and major limitations in areas of understanding the pathophysiology (course of the illness) and the treatment of ASD; and researches in TMS may provide answers and new solutions in this regard.

VII. THE LACK OF OBJECTIVE INSTRUMENTS FOR THE ACCURATE MEASUREMENT OF ASD

In the field of ASD studies, blood biomarkers, genetic indices, brain structural and functional changes, behavioural and cognitive functions are used in search for pathology as cited with the disorder. In addition, changes in physical and clinical conditions, and finally a vast range of subjective findings, are measured through biochemical tests, brain imaging, cognitive and behavioural experiments, clinical examination, and self-report inventories instruments are used for assessment.

However, despite the employment of all the mentioned instruments, the subtle changes in chemical molecules at synapses, which could lead to the formation of specific explicit or implicit mental processes are not measurable except in particular circumstances and using complex radioisotope imaging techniques (PET).

VIII. LACK OF APPROPRIATE MODELS REGARDING THE ROLE OF DIFFERENT BRAIN AREAS AND COGNITIVE PROCESSES IN ASD BEHAVIOR

One of the major limitations in the field of cognitive neuroscience is the use of correlation coefficients between external phenomena or cognitive processes with structural or functional guides in brain images, or other biomarkers instead of determining underlying relationships.

For instance, it is known that the activation of different brain areas in functional brain imaging procedures such as fMRI is correlated with the behavioural outcome. However, the causal role of each of these areas in generating the behavioural issue seeking is hypothesized based on researchers' theorizing rather than direct findings of studies. Lesion studies are one of the rare chances to reach to a more causal model, but are almost impossible in human subjects, except having the chance to find cerebral infarction or localized traumatic brain injury cases.

IX. TMS AS A DIAGNOSIS TOOL

Transcranial Magnetic Stimulation (TMS) which uses localized alternating magnetic field over the scalp was introduced by Anthony Barker (University of Sheffield, UK) in 1985 [25]. Alvaro Pascual-Leone's study showed that more long-lasting effects could be achieved through repetitive TMS pulses (rTMS) and hence the dream of applying electrical stimulation in the brain with no need for open surgery and skull dissection was gradually realized [26]. Since its introduction, the use of TMS in clinical neurophysiology, neurology, neuroscience, and psychiatry has spread widely, mostly in research applications but increasingly with clinical aims in mind. A recent study in the field of ASD commenced and a new prospect was opened for the employment of this new technology in understanding and treating this disorder [27].

TMS has been used on over 800 typically developing children and 300 children with neurological disorders and an excellent safety profile [28]. Recently published safety guidelines, however, caution that children should not be used as subjects for repetitive TMS studies without compelling clinical reasons [29]. However, most of the potential of this technique is only hinted at by the work done to date, and despite this promise there haven't been any carefully designed clinical trials to back it up [30]. Studies carried out on the use of Single and Paired Pulse TMS for assessing the amount of brain excitability as well as the evaluation of speed of signal transfer (action potential conductance time) in intra and extra cerebral fibers between different brain regions that are mainly dependent on certain neurochemical agents, have raised the prospects for finding more objective standards to detect chemical changes, that are in-charge of subjective feelings or implicit cognitive processing at different levels of the nervous system synapses in different states. Using reversible TMS methods (low frequency or continuous theta burst stimulation) in human subjects, in a particular brain area, or making a "virtual lesion" in the course of a specific cognitive process, it is now hoped that relevant causal relationships could be determined.

X. CONCLUSION

Finally, the outline here is that we are not looking for a new miracle in ASD therapeutic, diagnosis out of TMS; the knowledge gained as a result of such studies may detect abnormalities in cortical functions that are subclinical, and identify as a marker used for ASD. Second, as we know psychiatric complications present such as depression and anxiety in patients with ASD. Considering the complexities of the illness of ASD and managing them via any intervention, along with ASD specific therapies, is very complicated and at times is ineffective. TMS interventions could provide efficient answers to this problem in the field of ASD.

ACKNOWLEDGMENT

Work on this study was supported by grants from the King Abdulaziz City for Science and Technology (A-L-11-0808 and A-V-34-60), and National Plane of Science and Technology Health Research program and Deanship of Scientific Research grant (RGP-VPP-216) from King Saud University, Saudi Arabia.

REFERENCES

- [1] Howlin P. *Autism and Asperger syndrome*, 2th ed. United States of America: Routledge; 2005
- [2] Mohammadi MR, Akhondzadeh S. *Autism Spectrum Disorders: Etiology and Pharmacotherapy*. *Curr Drug Ther* 2007; 2: 97-103
- [3] Gomez SL, Torres RMR, Ares EMT. *Reviews on Autism. Rev Latinoam Psicol* 2009; 41: 555-570
- [4] Grafodatskaya D, Chung B, Szatmari P, Weksberg R. *Autism spectrum disorders and epigenetics*. *J Am Acad Child Adolesc Psychiatry* 2010; 49: 794-809
- [5] Centers for Disease Control and Prevention 2009. *Prevalence of autism spectrum disorders—autism and developmental disabilities monitoring network, United States, 2006*. *MMWR Surveill. Summ.* 58:1–20.
- [6] World Health Organization (WHO), Fourth Conference, 2nd of October 2013.
- [7] Matson JL, Worley JA, Fodstad JC, Chung KM, Suh D, Jhin HK, et al. *A multinational study examining the cross cultural differences in reported symptoms of autism spectrum disorders: Israel, South Korea, the United Kingdom, and the United States of America*. *Res Autism Spectr Disord* 2011; 5: 1598-1604
- [8] Zaroff CM, Uhm SY. *Prevalence of autism spectrum disorders and influence of country of measurement and ethnicity*. *Soc Psychiatry Psychiatr Epidemiol* 2011; published online
- [9] Al Masoud Hanan. *The Education of Children with autism in Saudi Arabia: A Teaching Guide (2010)*. King Saud University Saudi Arabia Riyadh.
- [10] Williams JG, Higgins JP, Brayne CE. *Systematic review of prevalence studies of autism spectrum disorders*. *Arch Dis Child* 2006; 91: 8-15
- [11] Shamsi-pour M, Yonesian M, Mansouri A. *Epidemiology of autism: recent challenges in prevalence of autism and its risk factors*. *Journal of health and knowledge* 2010; 5: 133
- [12] Al-Salehi SM, Al-Hifthy EH, Ghaziuddin M. *Autism in Saudi Arabia: presentation, clinical correlates and comorbidity*. King Fahd Medical City Hospital 2009, Riyadh, Saudi Arabia.
- [13] Nickl-Jockschat T, Michel TM. *Genetic and brain structure anomalies in autism spectrum disorders. Towards an understanding of the aetiopathogenesis?*. *Nervenarzt* 2011; 82: 618-627
- [14] Dodds L, Fell DB, Shea S, Armson BA, Allen AC, Bryson S. *The role of prenatal, obstetric and neonatal factors in the development of autism*. *J Autism Dev Disord* 2011; 41: 891-902
- [15] Hussein H, Taha GR, Almanasef A. *Characteristics of autism spectrum disorders in a sample of Egyptian and Saudi patients: transcultural cross sectional study*. Okasha's Institute of Psychiatry, WHO Collaborative Center for Training and Research 2011, Ain Shams University Hospitals, Abbasia, Cairo, Egypt.

- [16] Al-Eithan MH, Balkhi SH, Al-Bluwi AM. *Autism and parents' education. New data from the developing world*. Psychology Department & Research Center, Sultan Bin Abdulaziz Humanitarian City 2010, Riyadh, Kingdom of Saudi Arabia .
- [17] Zachor DA, Ben-Itzhak E, Rabinovich AL, Lahat E. *Change in autism core symptoms with intervention*. Res Autism Spectr Disord 2007; 1: 304-317
- [18] Callahan K, Shukla-Mehta S, Magee S, W ie M. *ABA versus TEACCH: the case for defining and validating comprehensive treatment models in autism*. J Autism DevDisord 2010; 40: 74-88
- [19] Gould E, Dixon DR, Najdowski AC, Smith MN, Tarbox J. *A review of assessments for determining the content of early intensive behavioral intervention programs for autism spectrum disorders*. Res Autism Spectr Disord 2011; 5: 990-1002,
- [20] Peters-Scheffer N, Didden R, Korzilius H, Sturm ey P. *A meta-analytic study on the effectiveness of comprehensive ABA-based early intervention programs for children with Autism Spectrum Disorders*. Res Autism Spectr Disord 2011; 5: 60-69,
- [21] Chimeh N, Pouretamad HR, Khoramabadi R. *Need assessment of mothers with autistic children*. Journal of family research 2007; 3: 697-707
- [22] Mohammadi A, Pouretamad HR, Khosravi G. *An initial examination of the effect of guided imagery via music on reduction of stress, depression, and anxiety of mothers with autistic children*. Journal of family research 2005; 1: 289-303
- [23] Al faisal fahda, *The effectiveness of cognitive behavioral program to reduce the degree of psychological stress among a sample of mothers of children with autism*. King Saud University Saudi Arabia Riyadh 2010.
- [24] Bromley J, Hare DJ, Davison K, Emerson E. *Mothers supporting children with autistic spectrum disorders: social support, mental health status and satisfaction with services*. Central Manchester and Manchester Children's University Hospitals NHS Trust 2004, UK.
- [25] Barker AT, Jalinous R, Freeston IL. *Non-invasive magnetic stimulation of human motor cortex*. Lancet 1985; 1: 1106-07.
- [26] Pascual-Leone, A., Valls-Solé, J., Wassermann, E.M., Hallett, M. *Responses to rapid-rate transcranial magnetic stimulation of the human motor cortex*. Brain 1994, 117, 847-58.
- [27] Oberman L, Ifert-Miller F, Najib U, Bashir S, Woollacott I, Gonzalez-Heydrich J, Picker J, Rotenberg A, Pascual-Leone A. *Transcranial magnetic stimulation provides means to assess cortical plasticity and excitability in humans with fragile x syndrome and autism spectrum disorder*. Front Synaptic Neurosci 2010 2:26
- [28] Frye, R.E., Rotenberg, A., Ousley, M., Pascual-Leone, A. *Transcranial magnetic stimulation in child neurology: current and future directions*. J. Child Neurol 2008., 23, 79-96.
- [29] Johnson, C.P. *Early Clinical Characteristics of Children with Autism*. In: Gupta, V.B. ed: Autistic Spectrum Disorders in Children. New York: Marcel Dekker, Inc., 2004:85-123
- [30] Ganz ML. *The lifetime distribution of the incremental societal costs of autism*. Arch Pediatr Adolesc Med. 2007;161(4):343-34