Development of a semi-naturalistic QEEG guided neurofeedback protocol for treatment of young autistic children

L. Billeci[1], A. Narzisi[2], F. Apicella[2], K. Maharatna[3], F. Sicca[2], G. Pioggia[1], F. Muratori[2]
1 Institute of Clinical Physiology, National Council of Research (CNR), Pisa, Italy
2 IRCSS Stella Maris Scientific Institute, Pisa, Italy
3 University of Southampton, United Kingdom

Introduction

It's well established that ASDs are associated with brain connectivity abnormalities that are the basis of abnormal behaviours. Among all the methods developed to study connectivity underpinnings of ASDs, QEEG (Quantitative EEG) is able to identify dysfunction in various regions of brains of autistic individuals. Traditionally QEEG has been used to capture electrical patterns at the surface of the scalp, which primarily reflect cortical electrical activity or "brainwaves" – divided in "EEG bands": delta (1 – 4 Hz), theta (4 – 7 Hz), alpha (8 – 13 HZ), beta (16 – 35 HZ) and gamma (30 – 80 Hz). Each of these bands is uniquely related to different functionalities and their scalp distribution gives a clear indication of the brain functionalities and the brain's ability to respond under naturally occurring stimuli. Subsequently, QEEG has been employed widely to characterise the brain connectivity anomalies in autistic children. Typically QEEG signals are analysed with a power spectral analysis technique that allow computing the power spectral density (PSD) from which some quantitative features can be extracted. First of all the absolute total power of the signal and the absolute power of each bands computed for each electrode. Usually it is more correct to refer to the relative power of each band with the respect to the absolute power because relative measures have less variability among the different subjects. Moreover the brain symmetry index (BSI) between the two hemispheres and the coherence between two different signals of two different brain areas) can be computed. The BSI captures a particular asymmetry in spectral power between the two cerebral hemispheres, and is normalized between 0 (perfect symmetry) and 1 (maximal asymmetry). The coherence function gives an estimation of the linear correlation between two signals acquired from two different electrodes. Coherence is equal to the normalized cross-spectral density function and is a measure of phase locking. It is assumed to be an index of functional coupling between different brain areas. QEEG data are often used to develop an individually designed neurofeedback protocol. Neurofeedback is a non-medical intervention that has been used for a different types of brain dysfunction and recently it showed its effectiveness for treating ASD with results of improved eye contact, attention, communication, socialization, recall and a reduction of behavioural outburst. It provides auditory and visual feedback indicating when the brain has too much variability within the cortical activity. This process reinforces the two basic brain states of alert/focused and relaxed. Training these brain states allows the body to learn how to be relaxed and attentive. Typically neurofeedback process is initiated through the process of the patient watching some video/game on the computer screen. The reward band is set according to the observed brain activity during this process and the brain is "trained" to learn the appropriate "behaviour" through encouraging the patient to get reward and therefore training the patient to control his/her own brain waves. In recent years several studies have been published on the use of QEEG assessment and QEEG guided neurofeedback in autism. In the first study of QEEG in autism by Cantor et al. (1986), in which signals were acquired in an eyes open condition, the power spectral analysis of the different brainwaves of EEG signals revealed that autistic subjects have an increased delta and a reduced alpha power. Moreover the authors found an increased coherence and a decreased asymmetry with respect to controls. Similar results about power were obtained by following studies by Chan et al. (2007), Stregonova et al. (2007) and Sheikhani et al. (2010) where signals were acquired in the same condition. Moreover Stregonova et al. and Sheikhani et al. showed a leftward asymmetry in autistic subjects. In the study of Orekhova et al. (2007) a special attention was given to high frequencies (beta and gamma bands). The authors found an increase of high frequency in autistic subjects. In two studies performed acquiring signals in an open eyes condition different results were found (Murias et al., 2007; Coben et al., 2008). Murias et al. found an increased theta and beta powers and a decreased alpha power while Coben et al. found an increased beta power and a decreased delta and theta power. Most interesting some studies showed that QEEG is able to differentiate among different subgroups of autistic subjects. Dawson et al. (1995) showed that the ‘passive’ group of subjects had reduced EEG in delta and theta bands in all brain regions and reduced alpha power in the frontal regions with respect to the ‘active-but-odd’ group. Sutton at al. (2004) showed that subjects with greater social anxiety, greater general anxiety, greater social stress, and less satisfaction with interpersonal relations, had greater left-sided midfrontal activity. There are also some studies in which QEEG signals ere obtained while children perform specific tasks. For example in the study by Oberman et al. (2005) data were acquired while subjects observed a video of a moving hand and moving their own hand. The control group showed significant suppression from baseline in alpha during both the movement and observed movement conditions while the autistic group did not show significant suppression during the observed movement condition. In a recent study by Chan et al. (2011) EEG data were recorded while the child performed a memory task. In the autistic subjects a negative correlation was found between memory performance and the inter-hemispheric long-range coherence. The studies on the use of QEEG guided neurofeedcack in autism show controversial results. Some of these focused on the advantages of this method of treatment, while others have highlighted the ineffectiveness. In the first study, conducted by Cowan & Markham (1994), the authors showed a significant improvement in symptoms of autism in subjects who performed the treatment with neurofeedback. In 1995, Kaiser & Othmer reported improvements in attention, impulsivity and variability of response in 530 children with ASD treated with neurofeedback. Rossiter & La Vaque (1995) suggested the efficacy of neurofeedback just in case the pharmacological treatment was ineffective, or it caused serious side effects. Even Sichel, Fehmi & Goldstein (1995) concluded their research work indicating neurofeedback as an effective intervention in cases of mild autism. Jarusiewicz (2002) conducted a study of the effectiveness of neurofeedback in 24 subjects with autism among which 12 performed a neurofeedback training. The author showed that subjects submitted to neurofeedback had a better improvement in socialization, vocalization, anxiety, school and sleep, with respect to the control group. In 2007, Coben & Padolsky indicated a reduction in symptoms of inattention and a decrease of iper-connettivity in people with autism who received neurofeedback treatment. This is a very important finding because it shows that neurofeedback can lead to an improvement of brain connectivity that is usually increased in autistic subjects. Thompson & Thompson (1995) reached conclusions similar to those of Coben & Padolsky (2007). They suggest that the social deficits of people with autism may be associated with a connectivity problem and that neurofeedback treatment may improve social and emotional functions. In 2008 Coben proposed that neurofeedback could be used to remedy aberrant coherence patterns. Most recently, Holtmann (2011) suggested that neurofeedback is useful in reducing the symptoms of ADHD but not in autism. Nevertheless, in the same year, Legarda (2011) describing 'individual cases', recognize the effectiveness of neurofeedback in several diseases including autism. The studies reported above have some limits. First of all in the standard procedure for QEEG assessment and for neurofeedback treatment children interact of artificial stimuli like games or videos presented on a screen. The signals that are measured in these conditions may not correspond to the real signals that are generating in a naturalistic environment. In addition standard neurofeedback protocols require the participation of the subjects that need to perform some tasks in order to improve its brain connectivity. Usually neurofeedback processes consist in a passive cognitive activity without any mental stimulation. However if the children are very young it is almost impossible that they are able to perform these activities to train their brain. Our aim is to develop a QEEG guided neurofeedback protocol in a semi-naturalistic setting for young children with autism.

Methods

The principal aim of our study is to develop a reliable tool for based neurofeedback therapy. In order to obtain a more naturalistic setting it is intended to present the neurofeedback not only in the form of computer games but also combining it with physical agents like toys, robots or other people. In this study we also intend to combine neurofeedback therapy with active mental stimulation or cognitive rehabilitation training to develop a comprehensive program with the goal of effective and individualized therapy. Particular attention will be devoted to specific tasks regarding imitation and joint attention. Another important aspect of our study is that we want to deal with very young autistic children (3 – 6 years). Special attention will be paid to the early treatment programs because several studies underline the importance of early intervention and treatment studies suggesting substantial gains achieved when treatment is provided at a very early age (Dawson et al., 2008; Altemeier et al., 2009). As a consequence of the very early age of the subjects, it is essential to develop neurofeedbck protocols with minimum involvement of these subjects. The first step of our study has been the development of a semi-naturalistic protocol based on imitation and joint attention tasks during which EEG data are acquired. A regards joint attention, a responding joint attention (RJA) condition was created. The RJA codes the child's response to the examiner's use of gaze and/or pointing in order to direct his/her attention to a distant object. The RJA task involves the child sitting at a table, the examiner sitting in front of the child and two more people at the sides. On the table there are some different shapes of different colours. One of the two people at the sides has half of the same shapes of the same colours while the other person has the second half. The child is instructed to look at the shape the examiner observes and take the corresponding shape on the table. Periodically the two people hold in their hand one shape each and the examiner decides to orient his gaze to one of the two pictures without moving his head. If the condition of RJA is verified the child looks at the same shape observed by the therapist so that they share the same target. In this case the child should take the right shape from the table. The imitation task is made up by two different paradigms. In the first one the child is instructed to imitate simple actions with real objects and with non-meaningful placeholders for the same objects. The actions used in this task are that coded in the ADOS-G (Lord et al., 2000) scale. In the second task the child has to imitate hand gestures realized by the examiner. In this case the gestures used are the ones indicated in NEPSY-II (Korkman et al., 2007) tests. We tested this two tasks in a semi-naturalistic setting in which the child could interact with the examiner and the people involved in the protocol. A 5 years old healthy child (male) was involved in the experiment. While the child was performing the tasks EEG signals were acquired using the 128 electrodes EGI system (Electrical Geodesic Inc.). Two sessions of joint attention task and one session for each of the two imitation tasks were performed. The EEG registration had a duration of about 14 minutes with each session lasted about 3:30 minutes. Data were digitized at the sampling frequency of 250 Hz. EEG data were segmented according to the behaviour of the examiner and of the child observed in the video registration. Data recorded in joint attention condition were divided in three segments: 1) from the beginning of the ocular deviation of the examiner to the beginning of the ocular deviation of the child, that corresponds to the observation phase, 2) ocular movement of the child, 3) from end of the ocular deviation of the child to the beginning of the deviation of the gaze of the child from the target, that corresponds to the actuation of the joint attention condition. Data recorded during the imitation task were segmented instead in two phases: 1) from the beginning of the observation of the action performed by the examiner to the end of the action 2) imitation task performed by the child. Moreover standard pre-processing steps like data filtering, baseline removal and data averaging as well as QEEG analysis in particular power spectral, coherence and asymmetry analyses were implemented.

Discussion and conclusions

The revision of the state-of-the-art on QEEG and neurofeedback in autism showed the importance of this technique for the assessment of brain connectivity and for the developing of an individualized therapeutic program. QEEG studies show how autistic children present several differences in power spectra, coherence and symmetry measures with respect to controls. This is true both when signals are acquired in resting condition, with open or closed eyes, and when specific tasks are performed. Moreover it is observed that it is possible to link a specific pattern of brain activation, characterized by specific features, to different behaviours. This means that it is possible to influence the connectivity of a child by acting on the behaviour. This is the fundamental base of neurofeedback in which autistic children are treated induced specific action that can train their brain to function in the right way. Although controversial, the results of the studies on neurofeedback in autism show that it is possible to reach good results in decreasing some symptoms of autism by using this approach. The aim of the study introduced here, is to overcome some limitation of the present applications of QEEG-guided neurofeedback in particular the artificial and constrained situations in which data are acquired and the need of an effort from the subjects that is difficult to obtain treating very young autistic children. In this pilot study we developed a semi-naturalistic paradigm of joint attention and imitation and we acquired EEG data with a high-density system while a healthy child performed these tasks. We observed that the young child of the study well accepted the EEG cap and the protocol and was able to perform the tasks without difficulties or constraints. The interaction with the examiner rather than with a screen is very important for recreating a more real situation with social interactions and cues. In this situation we can suppose that the signals acquired from the brain, are much more similar to that generated while the child interact in common life situations. Results of data analysis are not reported because it impossible to held to conclusion with a single subject. Some important issues emerged from this first experiment. First of all the importance of an eye-tracking, especially in the join attention task. The employment of an eye-tracking system is crucial in order to identify the moment of the beginning of the ocular deviation of the child, that is the starting point of joint attention, and the deviation of the gaze of the child from the target, which corresponds to the end of the joint attention. If these time points are correctly identified the segmentation of the EEG signals can be done in a proper way. Moreover it is important to have a clear distinction of the different phases of the tasks to have an appropriate segmentation of the signals. As emerge from the literature, QEEG features extracted in different conditions (for example during the observation of an action or the performing of an action) can be different. For this reason it is important to separate different conditions and analyse the corresponding signals distinctly. The next step of this study, that is just started, will be first of all the assessment of QEEG features during this conditions in a consistent group of young control children in order to characterize the "normal" brain pattern in the different phases of the different tasks. The same assessment will be done on autistic children to identify brain abnormalities. The analyses performed of QEEG data will be the standard spectral and coherence analysis already implemented as well as the application of more advanced techniques, such as multivariate techniques, that can be useful to extract from the signals information and features not yet characterized. The following step will be the development of a neurofeedback training mediated by the examiner who will train the child in order to bring its brain connectivity towards a normal pattern of activation.

References

1. Cantor DS, Thatcher RW, Hrybyk M, Kaye H. (1986) Computerized EEG Analyses of Autistic Children, *Journal of Autism and Developmental Disorders, 16(2)*.
2. Chan AS, Sze SL, Cheung M (2007) Quantitative Electroencephalographic Profiles for Children With Autistic Spectrum Disorder, *Neuropsychology, 21(1):74-81*.
3. Stroganova TA, Nygren G, Tsetlin MM, Posikera IN, Gillberg C, Elam M, Orekhova EV, Abnormal EEG lateralization in boys with autism, *Clinical Neurophysiology,118:1842–1854*.
4. Sheikhani A, Behnam H, Mohammadi MR, Noroozian M, Mohammadi M (2010) Detection of Abnormalities for Diagnosing of Children with Autism Disorders Using of Quantitative Electroencephalography Analysis, *J Med Syst*.
5. Orekhova EV, Stroganova TA, Nygren G, Tsetlin MM, Posikera IN, Gillberg C, and Elam M, (2007) Excess of High Frequency Electroencephalogram Oscillations in Boys with Autism, *Biol Psychiatry, 62:1022–1029*.
6. Coben R, Clarke AR, Hudspeth W, Barry RJ(2008) EEG power and coherence in autistic spectrum disorder, *Clinical Neurophysiology 119:1002–1009*.

7. Murias M, Webb SJ, Greenson J, Dawson G (2007) Resting state cortical connectivity reflected in EEG coherence in individuals with autism, Biol Psychiatry. 2007; 62(3): 270–273.
8. Dawson G., Grofer Klinger L., Panagiotides H., Lewy A., Castelloe P. (1995) Subgroups of Autistic Children Based on Social Behavior Display Distinct Patterns of Brain Activity, Journal of Abnormal Child Psychology, 23:5.
9. Sutton SK, Burnette CP, Mundy PC, Meyer J, Vaughan A, Sanders C, Yale M. (2004) Resting cortical brain activity and social behavior in higher functioning children with autism, *Journal of Child Psychology and Psychiatry, 45:0,1–12*.
10. Oberman LM, Hubbard EM, McCleeryb JP, Altschulera EL, Ramachandrana VS, Pinedad JA (2005) EEG evidence for mirror neuron dysfunction in autism spectrum disorders, Cognitive Brain Research, 24 190–198.
11. Chan AS, Han YM, Sze SL, Cheung M, Leung WW, Chan RCK, To CY, (2011) Disordered connectivity associated with memory deficits in children with autism spectrum disorders, Research in Autism Spectrum Disorders 5 237–245.
12. Coben R., Padolsky I. (2007) Assessment-Guided Neurofeedback for Autistic Spectrum Disorder Journal of Neurotherapy, vol. 11(1).
13. Cowan J., Markham L. (1994) EEG biofeedback for the attention problems of autism: A case study. Presented at the 25th Annual Meeting of the Association for Applied Psychophysiology and Biofeedback..
14. Holtmann M, Steiner S, Hohmann S, Poustka L, Banaschewski T, Bölte S. (2011) Neurofeedback in autism spectrum disorders. *Dev Med Child Neurol. 53(11):986-93*.
15. Kaiser D. (1995) Efficacy of neurofeedback on adults with attentional deficit and related disorders. *Available from EEG Spectrum, Inc., 16100 Ventura*. Blvd, Suite 10, Encino, CA 91436.
16. Korkman, M., Kirk, U., Kemp, S. (2007) NEPSY-II: A developmental neuropsychological assessment. San Antonio, TX: The Psychological Corporation.
17. Jarusiewicz B. (2002) Efficacy of neurofeedback for children in the Autistic Spectrum: A pilot study. *Journal of Neurotherapy, 6 (4); 39-49.*
18. Lord C, Risi S, Lambrecht L, Cook EH Jr, Leventhal BL, DiLavore PC, Pickles A, Rutter M. (2000) The autism diagnostic observation schedule-generic: a standard measure of social and communication deficits associated with the spectrum of autism. *J Autism Dev Disord. 30(3):205-23.*
19. Rossiter T. R., La Vaque T. J. (1995) A comparison of EEG biofeedback and psychostimulants in treating attention deficit/hyperactivity disorders. *Journal of Neurotherapy, 1, 48-59.*
20. Sichel A. G., Fehmi L. G., Goldstein D. M. (1995). Positive outcome with neurofeedback treatment of a case of mild autism. *Journal of Neurotherapy, 1 (1), 60-64.*
21. Thompson L., Thompson M. (1995) Autism/asperger's/obnoxious child, 3 case histories: How we get positive results with complex ADD clients. *Presented at the Annual Conference of the Society for Neuronal Regulation.*
22. Dawson G. (2008). Early behavioral intervention, brain plasticity, and the prevention of autism spectrum disorder. *Dev* Psychopathol, 20: 775-804.
23. Altemeier WA., Altemeier LE. (2009), How can early, intensive training help a genetic disorder? *Pediatr Ann, 38: 167-170*.