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Cognitive training modifies frequency EEG bands and neuropsychological measures in Rett syndrome



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ABSTRACT

Rett syndrome (RS) is a childhood neurodevelopmental disorder characterized by a primary disturbance in neuronal development. Neurological abnormalities in RS are reflected in several behavioral and cognitive impairments such as stereotypies, loss of speech and hand skills, gait apraxia, irregular breathing with hyperventilation while awake, and frequent seizures. Cognitive training can enhance both neuropsychological and neurophysiological parameters. The aim of this study was to investigate whether behaviors and brain activity were modified by training in RS. The modifications were assessed in two phases: (a) after a short-term training (STT) session, i.e., after 30 min of training and (b) after long-term training (LTT), i.e., after 5 days of training.

Thirty-four girls with RS were divided into two groups: a training group (21 girls) who underwent the LTT and a control group (13 girls) that did not undergo LTT. The gaze and quantitative EEG (QEEG) data were recorded during the administration of the tasks. A gold-standard eye-tracker and a wearable EEG equipment were used. Results suggest that the participants in the STT task showed a habituation effect, decreased beta activity and increased right asymmetry. The participants in the LTT task looked faster and longer at the target, and show increased beta activity and decreased theta activity, while a leftward asymmetry was re-established. The overall result of this study indicates a positive effect of long-term cognitive training on brain and behavioral parameters in subject with RS.

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1. Introduction

Rett syndrome (RS) is a childhood developmental disorder whose prevalence is estimated to be 1:8000 in females (Moretti & Zoghbi, 2006). Females are primarily affected, although a few cases of males have been reported in the literature (Leonard et al., 2001; Cohen et al., 2002). Its etiology involves the genetic mutation of gene MECP2 on the X-chromosome (Amir et al., 1999; Guy, Hendrich, Holmes, Martin, & Bird, 2001). RS was originally classified in the category of Pervasive Developmental Disorders according to the DSM-IV-TR (American Psychiatric Association, 2000) and has now been removed from the DSM-V because of its genetic etiology (APA, 2013).

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Its clinical features suggest that this disorder is the result of a primary disturbance of neuronal development (Johnston, Hohmann, & Blue, 1995), perhaps resulting in maturational arrest in selected brain regions (Armstrong, Dunn, Antalffy, & Trivedi, 1995). For example, the basis of this maturational arrest could be defective neurotransmitter systems that fail to provide normal trophic factors (Armstrong, Dunn, Antalffy, & Trivedi, 1995; Johnston et al., 1995).

Quantitative Electroencephalography (QEEG) is currently attracting great interest due to its characterization of brain functioning, and it is increasingly used in studies on neurodevelopmental disorders (Billeci et al., 2013; Blue Cross Blue Shield Association, 2014). It has been found to be a relevant aid in diagnosis, evaluating heterogeneity of behavioral disorders, treatment responses, and outcomes, among other issues.

Few studies have applied QEEG for the characterization of neurophysiological functioning in RS. In the study of Gorbachevskaya, Bashina, Gratchev & Iznak, (2001) QEEG revealed that RS girls were characterized by higher levels of theta activity and reduced levels of alpha and beta activity. Grachev (2001) showed that increased frontal theta activity in RT girls was significantly positively related with earlier onset of disease, reflecting more severe damage of the frontal lobes. Gorbachevskaya et al. (2006) successively confirmed the presence of significantly higher levels of theta activity and decreased alpha activity in RS patients with MECP2 mutations, and showed that this pattern was particularly evident when mutations were at the 3rd disease stage. Gorbachevskaya, Bashina, Gratchev, and Iznak (2001) also showed a modification of EEG parameters after Cerebrolysin treatment, in particular a decrease in theta activity over all cortical regions, an increase in beta activity, and some restoration of the occipital alpha rhythm.

Neurological abnormalities in RS are reflected in several behavioral and cognitive impairments. Cross-disciplinary studies have been performed with the aim of defining the RS phenotype and behavioral condition (Mount, Hastings, Reilly, Cass, & Charman, 2001, 2002; Berger-Sweeney, 2011; Gadalla, Bailey, & Cobb, 2011; Matsushita, Yamashita, Takahashi, & Nagamitsu, 2011). Recently, technology has improved the possibility of assessing behavior and cognitive processes in girls with RS. Baptista, Mercadante, Macedo, and Schwartzman (2006) were among the first to use eye-tracking technology during various cognitive tasks in which the subject was asked to choose the target stimulus between a target and a distractor. Girls with RS reported high rates of correct answers, thus suggesting that intentional gaze in girls with RS is measurable and can be used as a way to explore their cognitive performances. Other recent studies have focused on the relationship between cognitive and neurophysiological factors, showing that the age of onset of epilepsy and seizure frequency were strongly correlated with neuropsychological outcomes and that the age of onset of epilepsy was inversely correlated with the ability to recognize stimuli (Vignoli et al., 2010). Girls with RS were also found to have longer event-related potential latencies and smaller event-related potential amplitudes than controls, suggesting slowed information processing and reduced brain activation with advancing years (Stauder, Smeets, van Mil, & Curfs, 2006).

Although the overview of cognitive deficit in RS is not yet exhaustive or clear, girls with RS show intention and preference regarding social and cognitive stimuli, and also seem to have the potential for learning in an intentional way (Fabio, Giannatiempo, Antonietti, & Budden, 2009a; Fabio, Antonietti, Marchetti, & Castelli, 2009b; Fabio, Giannatiempo, Oliva, & Murdaca, 2011). Cognitive rehabilitation in RS in the form of behavioral training based on operant conditioning principles (Lovaas & Leaf, 1981; Smith, Klevstrand, & Lovaas, 1995), as well as in the form of intervention in the communication (Sigafoos, Laurie, & Pennell, 1995; Watson, Umansky, Marcy, & Repacholi, 1996), have been implemented. Other interventions have been focused on the role of the environment and of the caregiver (Burford & Trevarthen, 1997; Evans & Meyer, 1999, 2001; Koppenhaver et al., 2001; Tortora, 2001; Ryan et al., 2004; Skoto, Koppenhaver, & Erickson, 2004) and on the use of special programs and devices (Hettroni, Rubin, & Konkol, 2002; Lotan, Isakov, & Merrick, 2004), including non-verbal training aimed at teaching basic and complex emotion recognition (Antonietti, Castelli, Fabio, & Marchetti 2008) in order to understand other people's behavior on the basis of mental state reasoning (Antonietti, Castelli, Fabio, & Marchetti, 2002).

The underlying process of rehabilitation is linked to modifiability. Cognitive modifiability through the impact of external conditions show previously non-existent capacities (Feuerstein, Rand, & Rynders, 1988). In a recent study Fabio, Castelli, Antonietti, and Marchetti (2013) applied cognitive training in a single case of RS. The girl achieved adequate reading-writing abilities, proving the validity of cognitive intervention.

Cognitive training or rehabilitation can enhance both neuropsychological and neurophysiological parameters. Extensive research has been dedicated to understanding the neurophysiological mechanisms of cortical plasticity (Buonomano & Merzenich, 1998; Jagadeesh et al., 2006). Several authors have shown the ability of long-term training or behavioral intervention to alter cortical connectivity in neuropsychiatric and neuropsychological disorders using EEG. For example Spironelli, Penolazzi, Vio, and Angrilli (2010) suggested that 6 months of phonological training might reorganize cortical areas in dyslexic children. In another study the effect of a 3-month cognitive behavioral therapy program, performed with children with clinical levels of externalizing behavior, was analyzed on EEGs recorded during a go/no-go task requiring inhibitory control (Woltering, Granic, Lamm, & Lewis, 2011). More recently, Faja et al. (2012) investigated the effect on EEG activity of expertise training with faces in adults with ASD who showed initial impairment in face recognition.

A few studies have also demonstrated that learning or repetitive activity leaves local traces that can be detected immediately after the performance, using EEG. For example, after 24 h of continuous performance, theta activity increases in parieto-occipital areas after a driving video game (Hung et al., 2013), and over language-related areas after listening to audio-books (Landsness et al., 2011). Similar traces in the spontaneous EEG could also be detected after tasks of shorter duration. Landsness et al. (2011) showed significant changes in alpha power in resting-state EEG after a 40-min motor task

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