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Review article

Using neuroscience as an outcome measure for behavioral interventions in Autism spectrum disorders (ASD): A review



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ABSTRACT

Though medications have proven effective in improving associated symptoms of autism spectrum disorder (ASD), behavioral interventions remain the most effective method of improving core symptoms (e.g. social communication, restricted and repetitive behaviors) in this population. Although the cause remains unknown, research provides evidence that ASD is a neurologically based disorder, with differences in brain activity contributing to observed social difficulties. Given the above, along with recent publications underscoring the importance of utilizing neuroscience to measure changes associated with intervention in ASD, it is surprising that studies that measure neurological changes in response to behavioral interventions remain quite rare. Using systematic searches of the PsychINFO and MEDLINE databases, the current review summarizes the extant literature on neural changes in response to behavioral interventions in ASD, and compares the state of the literature in ASD with other disorders such as anxiety, depression, and schizophrenia. We conclude that research utilizing neuroscience to measure changes in response to behavioral interventions in ASD is lacking, and suggest that future research make integrating these two lines of research a priority.

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1. Introduction

Autism spectrum disorder (ASD) is a highly heterogeneous developmental disability characterized by persistent difficulties with social communication and interaction, along with restricted or repetitive behavior or interests (American Psychiatric Association, 2013). Given that social difficulties are among the core symptoms of ASD, many behavioral interventions have focused on improving social skills for children and adolescents with ASD (see Rao, Beidel, & Murray, 2008 and White, Keonig, & Scahill, 2007 for reviews). Although the causes of ASD remain unknown, a large body of research provides evidence that ASD is a neurologically based disorder, with disturbances of brain activity contributing to the social difficulties observed in ASD (Dawson, 2008; Mundy, 2003; Neuhaus, Beauchaine, & Bernier, 2010). Given the above, along with recent publications underscoring the importance of utilizing neuroscience to measure changes associated with intervention in ASD (e.g. McPartland & Pelphrey, 2012) it is surprising that studies that measure neurological changes in response to behavioral interventions remain quite rare.

The goal of the current review is to summarize the extant literature on neural changes in response to behavioral interventions in ASD. Though ASD is the primary focus of this review, for comparison purposes, we briefly review the literature on neural changes in response to behavioral interventions in other disorders.

2. Method

Systematic searches were conducted using the PsychINFO and MEDLINE databases with the search terms: "autism," "treatment," or "intervention," "outcome," and "fMRI" or "ERP" or "EEG" or "brain." We note that although Transcranial Magnetic Stimulation (TMS) is of potential interest in autism due to the ability to study cortical excitability and inhibition and the relevance of excitatory neurons in ASD (Rubenstein & Merzenich, 2003), a recent review of the literature concludes that the use of TMS in ASD remains preliminary (Oberman, Rotenberg, & Pascual-Leone, 2015), and no studies to our knowledge have utilized TMS before and after behavioral interventions. Thus, we do not discuss TMS as a methodology in the current review. The search was limited to empirical peer reviewed research publications on humans written in English. Upon completion of searches, articles were examined for the following inclusion criterion: 1. Use of an empirically supported behavioral intervention designed to improve core symptoms of ASD (e.g. studies using neurofeedback methods were not included), 2. Use of neuroscience methodology as an outcome measure. The reference section from included articles was also utilized to capture any articles that met criteria above but were missed in the initial searches. In total, four papers were identified that met the above criteria. Due to the small number of identified manuscripts, we broadened our search to include investigations of neural changes in response to behavioral training designed to enhance face "expertise" and emotion recognition in ASD. Three additional papers were identified using this broadened criteria, bringing the total number to seven.

In order to explore the extant literature on neural effects of behavioral interventions in other disorders (e.g. depression, anxiety), we completed the same search as above, but with the condition of interest's name in the search—"depression" or "anxiety" rather than "autism".

The current paper will review research utilizing a variety of neuroscience measures to quantify changes that occur in response to behavioral treatment such as functional magnetic resonance imaging (fMRI), and electrophysiology (EEG and ERP). We briefly review each of the techniques below.

Functional MRI (fMRI) is a neuroscience technique that measures and quantifies brain activity by measuring changes associated with blood flow. Due to the fact that blood flow in the brain and activity of neurons occur together, measuring changes in blood flow is an accurate method of assessing changes of brain activity in a given region. The most common form of fMRI utilizes blood-oxygen-level dependent (BOLD) contrast. This measures changes in hemodynamic response (e.g. blood flow), as these changes are related to energy use by neural cells. A significant strength of fMRI is its high spatial resolution, meaning it can accurately discriminate between nearby locations (at up to 1 mm accuracy). However, a drawback to this technique is its low temporal resolution, or the smallest time period of neural activity that can be reliably separated. For fMRI the smallest time period is typically 1–2 s. Therefore, fMRI is a technique best used when one is looking for reliable information about where in the brain changes are occurring, and also when the brain processes being studied last a few seconds.

Two electrophysiological methods will be discussed here: EEG and ERP. Electroencephalography (EEG) is a neuroscience method designed to record electrical activity of the brain. Electrodes are placed along the scalp, and voltage fluctuations within neurons of the brain are recorded. EEG data is often measured continuously while subjects are instructed to attend to a crosshair on the screen (known as "resting state" paradigms). In this case, data of interest is the type of neural oscillations that can be extracted from EEG recordings.

Although the preparation and equipment is often identical to EEG described above, a second electrophysiological technique utilizes event-related potentials (ERPs). This involves measuring EEG activity that is time-locked to the

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