Neurofeedback Treatment for Autism Spectrum Disorders � Scientific Foundations and Clinical Practice

Chapter · September 2011

4 authors, including:

Mirjam Kouijzer
GGz Breburg
11 PUBLICATIONS   **157** CITATIONS

Berrie Gerrits
Research Institute Brainclinics
10 PUBLICATIONS   **153** CITATIONS

Some of the authors of this publication are also working on these related projects:

Project Attentional Performance Related EEG-Cross-Frequency Coupling Components View project

Neurofeedback Treatment for Autism Spectrum Disorders – Scientific Foundations and Clinical Practice

Mirjam E.J. Kouijzer, Hein T. van Schie,
Berrie J.L. Gerrits, and Jan M.H. de Moor
Behavioural Science Institute, Radboud University Nijmegen
The Netherlands

1. Introduction

Neurofeedback is a technique to enable individuals to change their brain activity by using an instrument that provides information on the activity of the brain. The goal of neurofeedback is to improve behavioral or cognitive processes related to brain activity. The technique of neurofeedback, although available for some time, is rapidly gaining interest as a treatment of various disorders (Yucha & Montgomery, 2008). Recent evidence indicates that the technique may also be used beneficially for the treatment of autism spectrum disorders.

Currently, the most frequent application of neurofeedback lies in the treatment of epilepsy and attention deficit hyperactivity disorder (ADHD). Epilepsy has been treated with neurofeedback since the 70s of the previous century. Epilepsy is a chronic neurological disorder characterized by abnormal, excessive or synchronous neuronal activity in the brain resulting in seizures. The main focus of neurofeedback in epilepsy is to enhance the sensorimotor rhythm (SMR) originating from the sensorimotor cortex of the brain. This 12 to 15 Hz activity is involved in the inhibition and control of movement. Increased SMR is found to be related to improved movement inhibition and consequently offers protection to seizures in individuals with epilepsy (Sterman & Egner, 2006). Scientific studies that investigated the efficacy of neurofeedback in individuals with epilepsy were recently evaluated by Tan and colleagues (2009). They found that in a total of nine studies, neurofeedback was effective in reducing the number of seizures in 79% of participants with severe epilepsy who did not respond to medication. The number of sessions that was used in these studies varied from 24 to more than 200 sessions. It was concluded that neurofeedback is a promising treatment for individuals with severe epilepsy, but that future randomized, sham controlled studies are required to confirm the efficacy of neurofeedback (Tan et al., 2009).

Most research on neurofeedback has been conducted in individuals with ADHD. ADHD is a developmental disorder characterized by inattention, hyperactivity and impulsivity (American Psychiatric Association, 2000). The EEG profiles of 85 to 90% of the individuals with ADHD show elevated theta power and reduced beta power over frontal and central, midline cortical brain areas (Monastra et al., 2005). Neurofeedback in ADHD aims to inhibit

theta power and to elevate beta power in these cases. A recent meta-analysis on the efficacy of EEG-biofeedback in ADHD (Arns, de Ridder, Strehl, Breteler, & Coenen, 2009) demonstrated large effects on clinical symptoms of inattention and impulsivity and a medium effect on symptoms of hyperactivity. These conclusions, however, are mainly based on studies that were non-randomized and used no blinding of participants. Therefore, a conclusion on the efficacy of neurofeedback in ADHD is still preliminary at this point.

Neurofeedback has recently also been applied to individuals with autism. The term autism in this chapter refers to disorders of the entire autistic spectrum. The present chapter first provides an overview of the history of neurofeedback, followed by a detailed explanation of the practice of the technique as it is used in clinical practices. We furthermore describe what is known about working mechanisms that are involved in neurofeedback and provide an overview of the benefits of neurofeedback for individuals with autism. Finally, we review the existing literature on neurofeedback and autism and discuss several options for future research.

2. The origin of neurofeedback

The origin of neurofeedback goes back to the 1960s when Joseph Kamiya successfully trained human individuals to control alpha waves. Alpha waves are oscillations in the 8 to 12 Hz frequency range that are predominantly generated in occipital and parietal lobes and can be recorded during wakeful relaxation with eyes closed. In the experiment by Kamiya, participants were instructed to indicate whether they thought they were 'in alpha', i.e. whether their brain produced alpha as the dominant frequency, or not each time a tone sounded. They received feedback on whether the answer was correct or not. Initially the participants answered correct in about fifty percent of the trials. After alpha training was provided, some participants developed the ability to recognize the alpha state and to answer correctly in most of the trials. In a second experiment, the same participants were asked to go into the alpha state when a tone sounded once and not to go into the alpha state when the tone sounded twice. Interestingly, Kamiya found that some participants were able to enter the alpha state on command, whereas others were not (Kamiya, 1968).

Around the same time, Barry Sterman accidentally discovered the curative power of neurofeedback for patients with epilepsy. Sterman set up an experiment where he taught cats to produce 12 to 15 Hz oscillations along the sensorimotor cortex of the brain. He rewarded the cats with milk each time they produced 12 to 15 Hz oscillations and concluded that cats could learn to increase the sensorimotor rhythm (SMR). Increased SMR brought the motor suppression response under experimental control and helped to reduce muscle tone, reflex amplitudes, and cellular discharge in motor pathways. After this experiment ended, the cats were used for another experiment investigating the toxic symptoms of exposure to rocket fuel. Sterman's cats turned out to be more seizure resistant than cats that had not received SMR training (Wyricka & Sterman, 1968). It took only a few years before Sterman treated the first human patients with epilepsy. These patients showed a reduction of electroencephalographic and clinical epileptic manifestations after three months of SMR training (Sterman, Macdonald, & Stone, 1974).

Joel Lubar continued Sterman's work and used SMR training in patients with ADHD to reduce hyperactivity. Lubar and Shouse (1976) reported the results of 142 neurofeedback sessions in an 11-year old boy with ADHD who was trained to enhance SMR and to reduce theta power. After several months, the boy showed less undirected activities, less out-of-seat

behavior, and less oppositional behaviors. In addition, there was increased cooperation and improvement in school work. In the reversal phase of the study, the boy's behavior and school work were found to worsen and to improve again when the initial training was recommenced.

Margaret Ayers, fascinated by the outcomes of these experimental studies, opened the first neurofeedback practice in 1975. One of her patients was Brian, a boy with severe epilepsy whose severe epilepsy significantly reduced after neurofeedback treatment. The parents of Brian, Siegfried and Sue Othmer, were impressed by the results of neurofeedback in their son. They started to promote neurofeedback in the United States of America. In 1987 they introduced a computerized neurofeedback tool and subsequently started a clinical practice for neurofeedback.

After these initial cases, the application of neurofeedback in patients with epilepsy and ADHD further extended in the 90s of the previous century. Subsequently, neurofeedback has also been applied in healthy individuals and in patients with various other disorders like depression, learning disability, post traumatic stress disorder, traumatic brain injury, and autism spectrum disorders (see review in: Yucha & Montgommery, 2008).

3. The practice of neurofeedback

In a typical neurofeedback session, a client sits in front of a computer screen while his or her electroencephalographic (EEG) activity is recorded by one or more electrodes. Figure 1 shows an example of the set up of a neurofeedback session in which a Nexus-4 device (MindMedia, the Netherlands) was used.

Fig. 1. An example of the set up of a neurofeedback session.

Before a client can commence with neurofeedback treatment, a treatment plan needs to be determined specifying the frequency component (or components) that is to be altered and the exact locations on the scalp at which training will take place. In the field of neurofeedback, such a treatment plan is often referred to as a treatment protocol. The

components and locations for training of such a treatment protocol are typically determined by comparing a 19-channel EEG recording of the client with a normative database containing the EEG spectra of typically developing individuals of the same age.

Typically, an EEG recording is collected using a stretchable electrode cap that contains multiple electrodes to map the distribution of brain waves over multiple sites on the scalp. Each of the electrodes is connected to the client's scalp using a conductive electro gel. Figure 2 shows an example of the experimental setup of an EEG assessment using the Mitsar EEG 201 System (Mitsar Medical Diagnostic Equipment, Russia). Following the correct preparation of all electrodes in the cap, a client's EEG is recorded for several minutes in one or more conditions. The conditions eyes opened and eyes closed are usually included in the EEG assessment. In these conditions, the client is instructed to sit still on a comfortable chair while keeping the eyes opened or closed. Next to the recording of EEG in these rest conditions, the EEG may be recorded in task conditions like reading or math.

Fig. 2. An example of the set up of a 19-channel EEG assessment using the Mitsar EEG 201 System.

Raw EEG recordings are analyzed to construct a quantitative EEG (QEEG) containing the absolute and relative power spectra of the client's EEG per electrode. Relative power expresses the ratio of power in a particular frequency band relative to the total power across

frequencies. The client's absolute and relative QEEG data may be subsequently compared with a normative database containing EEG data of healthy individuals of the same age to estimate possible deviations from normality. Two databases that are often used are NxLink designed by John, Prischep, & Easton (NxLink, Ltd.) and NeuroGuide, designed by Thatcher (Applied Neuroscience, Inc.). These databases produce color-coded maps and data in digital format, providing information on a client's deviations from the norm group. The output of such a database comparison may be used to guide the selection of the frequency components and the location for the subsequent neurofeedback treatment.

Figure 3 shows part of the output of the NeuroGuide database revealed by comparing the QEEG of a 15-year old girl with Asperger disorder to this database. The maps indicate that, relative to the database, power in the theta range over central and frontal electrodes exceeds the population mean, i.e. a population of girls of the same age without an autism spectrum disorder, by more than one and a half standard deviations. As a consequence, neurofeedback might, in this case, target the inhibition of 3 to 7 Hz power over fronto-central scalp regions.
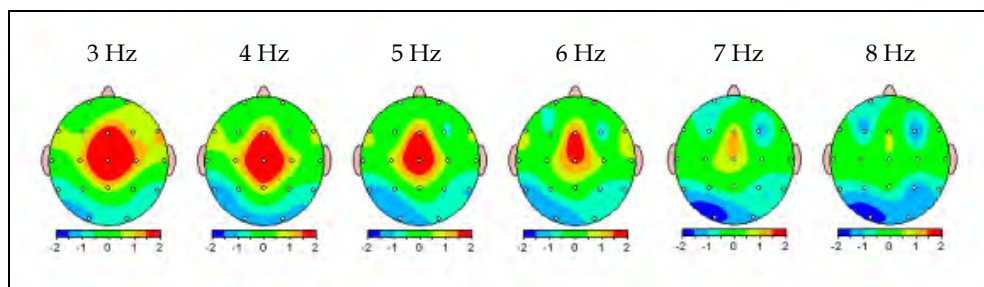

Fig. 3. An example of the output of a comparison between the QEEG of a 15-year old girl with Asperger disorder and the NeuroGuide database. Across fronto-central scalp sites a deviation of one and a half standard deviation is seen (color coded in red) of low frequency power in the 3-7 Hz frequency range compared to a norm group of girls with same age, without autism.

In addition to the method of using a database to determine possible frequency components and locations for training, a neurofeedback protocol may also be specified by visual inspection of the raw 19-channel EEG recording of the client. This procedure requires extensive knowledge of the raw EEG. A raw EEG signal is composed of separate brain waves with different frequencies and amplitudes, often arranged in separate frequency bands, i.e. delta (1-3 Hz) theta (4-7 Hz), alpha (8-12 Hz), beta (13-30 Hz), and gamma (above 30 Hz). These frequency bands can be identified in the raw EEG on the basis of the unique waveform patterns of each frequency band. Figure 4 shows an example of raw EEG data of a 10-year old boy with PDD-NOS in WinEEG software (Mitsar Medical Diagnostic Equipment, Russia). This example includes raw EEG activity measured by electrodes across several frontal sites. Visual inspection of this EEG fragment reveals clear theta activity at electrode Fz, which is indicated by the black arrow.

Instead of using individualized treatment plans wherein the frequency component and treatment location are determined on the basis of an individual's EEG characteristics, neurofeedback treatment may also be guided by predefined treatment protocols. Probably
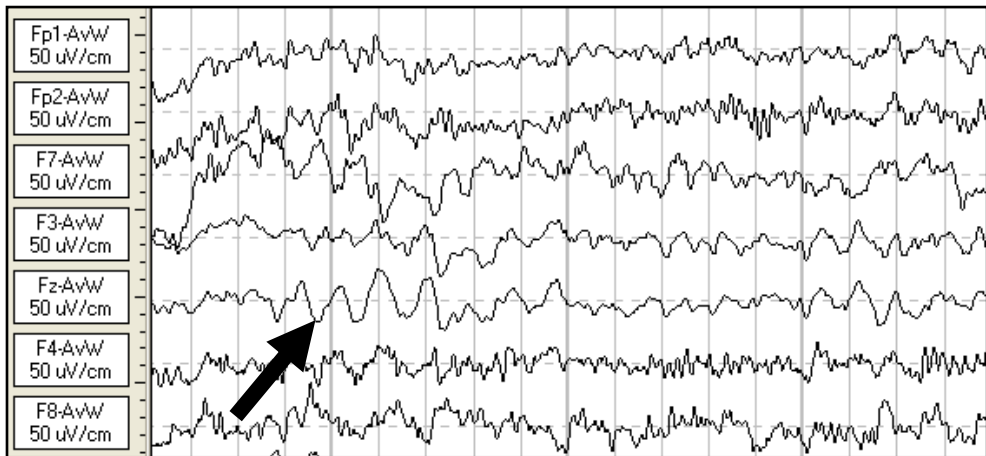
Fig. 4. Raw EEG data of a 10-year old boy with PDD-NOS in WinEEG software. The black arrow indicates the theta activity that is observed at electrode Fz.

the best known protocol is the theta/beta protocol that is used often in the treatment of ADHD. This protocol prescribes the decrease of theta power while beta power is increased at frontal or central, midline regions (Monastra et al., 2005). This protocol was developed after the finding that 85 to 90% of the individuals with ADHD have elevated theta power and reduced beta power over frontal and central, midline cortical regions of the brain (Monastra et al., 2005). Although the theta/beta protocol was originally applied to individuals with ADHD, this neurofeedback protocol has also been applied successfully to individuals with autism (Jarusiewicz, 2002; Kouijzer et al., 2009b; Scolnick, 2005; Sichel, Fehmi, & Goldstein, 1995; Thompson, Thompson, & Reid, 2010).

After a treatment plan has been established, the actual neurofeedback treatment may commence. In each neurofeedback session, an electrode needs to be attached to the selected treatment location by using conductive electrode paste. In addition, reference and ground electrodes are to be attached. Often the reference electrode is located somewhere on the head at a location where little or no of the frequency component that is selected for treatment is found, e.g. at an earlobe or at the bone behind one of the ears, i.e. the mastoid. The ground electrode is typically placed somewhere on the body, e.g. at the mastoid. Figure 5 provides an example of electrode configuration during a typical neurofeedback session, showing an EEG electrode that is used for feedback attached to the scalp (in red) and a reference electrode (in black) attached to the left mastoid.

During a neurofeedback session, information about the level of EEG activity in the frequency component that was selected for training is fed back to the client. Although in principle feedback may take any form or modality, most neurofeedback therapists use a bar graph on the computer screen to reflect the ongoing changes in EEG power over time. Figure 6 shows an example of such a computer screen created with BioTrace software (MindMedia, the Netherlands). The larger the amplitude of the recorded EEG activity is, the higher the orange bar graph on the computer screen will be presented. In this way, the bar graph informs the client about the amplitude of his or her EEG activity, almost immediately after it occurs. A criterion line is drawn together with the bar graph representing a concrete

Fig. 5. Electrodes attached to the scalp and the mastoid during neurofeedback.

goal for the trainee. That is, depending on the treatment plan (i.e. increase or decrease activation in a particular frequency range), the client may be directed at keeping the bar graph amplitude beneath or above the criterion line. At first, meeting the criterion is accidental, but over time participants may learn to maintain the bar graph below or above the indicated criterion.

Whenever the client manages to keep the bar graph below or above the criterion line for a minimal amount of time, visual and auditory rewards may be provided, often in the form of a film clip presented next to the bar graph. Film clips are usually presented with corresponding music or sound and are chosen according to to the age and interests of the client. Clients can also be rewarded by a counter that counts the number of seconds the criterion is met. If desired, the bar graph can change color when the EEG activity is not within the desired range, or the film clip can shrink to remove the reward. Some clients with autism show resistance to the combination of many different rewards, such as a shrinking film clip, music, a counter, and a color changing bar graph. Therefore, the exact form in which the reward is presented should reflect the preferences of the client.

A typical neurofeedback session consists of training and rest intervals. During training intervals, the client's goal is to move the bar graph below or above a criterion line. These

Fig. 6. An example of a computer screen where the mean amplitude of the EEG frequency of interest is fed back to the client via an orange bar graph with a white criterion line. In addition, a film clip and a counter are shown as rewards for the client.

training intervals are alternated with rest intervals, in which the client can relax for a short time. The length of the training intervals depends largely on the attention span of the client. Clients with a larger attention span may be presented with longer training intervals. A training interval of three minutes was chosen in several studies where neurofeedback was applied in children and adolescents with autism (e.g. Kouijzer et al., under review). If necessary, the length of training intervals may be adapted during the course of the training. Training and rest intervals are alternated manually or by predefined scripts. Clients with a high need for structure, like many clients within the autistic spectrum, might benefit from the accuracy that is provided by such a script.

Neurofeedback training is usually provided in psychological practices and typically takes place twice or thrice per week. Some neurofeedback therapists provide home training programs. The number of sessions is determined by the specific complaints of the client and on the progression of the client during the training. Neurofeedback for individuals with autism generally includes at least 40 sessions.

4. Cognitive and neuronal mechanisms underlying neurofeedback

Although the number of publications on the effects of neurofeedback is growing, little has been written about the actual functional and neuronal mechanisms that may be involved in its application and its resulting effects. In this paragraph we present an overview of several

functional and neuronal mechanisms that may play a role in changing brain activation via neurofeedback and discuss why some individuals are responsive to the application of neurofeedback whereas others are not. We end with a discussion on possible neural mechanisms in autism that may be targeted by neurofeedback.

4.1 Functional mechanisms underlying neurofeedback

Operant conditioning involves a process of behavior modification whereby the consequences of an action determine the likelihood that the same action will be expressed in the future. Positively reinforced actions will be performed more frequently, whereas negatively reinforced behavior will fade out (Gazzaniga & Heatherton, 2003). Closely related to operant conditioning is Thorndike's law of effect, stating that any behavior that leads to a satisfying state of affairs is more likely to occur again, and behavior that leads to an annoying state of affairs is less likely to occur again (Thorndike, 1933). The principles of operant conditioning are considered to be a major factor in the capacity of neurofeedback to effectuate changes in EEG. During a neurofeedback session, a client is rewarded each time he or she manages to move the bar graph on the computer screen below or above the criterion line. That is, a film clip turns on, music starts playing, or a counter starts running. Assuming that these rewards are satisfying to the client, chances increase that the patterns of EEG activity that preceded the reward are generated in the future. Vice-versa, brain activity that produces no rewarding effects will tend to fade away.

Following the principles of operant conditioning, the EEG activity of most clients who take part in neurofeedback is found to change during consecutive neurofeedback sessions. Notwithstanding the success of neurofeedback training in some clients, often however, there is also a second group of clients whose EEG activity is not found to change over time, and for whom neurofeedback does not seem to work. These two groups of clients are referred to as responders to neurofeedback and non-responders to neurofeedback, respectively. Responders to neurofeedback are clients whose EEG activity successfully changes during neurofeedback sessions. In non-responders there is no significant change in EEG activity observed during the course of the neurofeedback sessions. Figure 7 shows examples of EEG activity of a responder and a non-responder to neurofeedback. Both clients were trained to reduce theta power in 40 consecutive neurofeedback sessions. The responder to neurofeedback shows a clear decrease of average theta power, whereas the non-responder does not show such a decrease.

Response rates of neurofeedback in individuals with autism have been reported to vary between 54 and 76% (Coben & Padolsky, 2007; Kouijzer et al., 2009b; Kouijzer et al., 2010; Kouijzer et al., under review). This means that in more than half of the clients with autism who participated in a scientific study, EEG activity was successfully changed over the course of the neurofeedback treatment. At the same time, there is also a substantial group of clients that was unable to respond to neurofeedback over time. As such it may be interesting to speculate about the reasons why some individuals may turn out to be responsive to treatment with neurofeedback, whereas others may not.

Although the reason why some participants respond to neurofeedback whereas others do not is unclear at this time, it may be that responders and non-responders differ on certain psychological dimensions such as differences in attention span, cognitive flexibility or sensitivity to reward. Alternatively, there might be physiological differences between
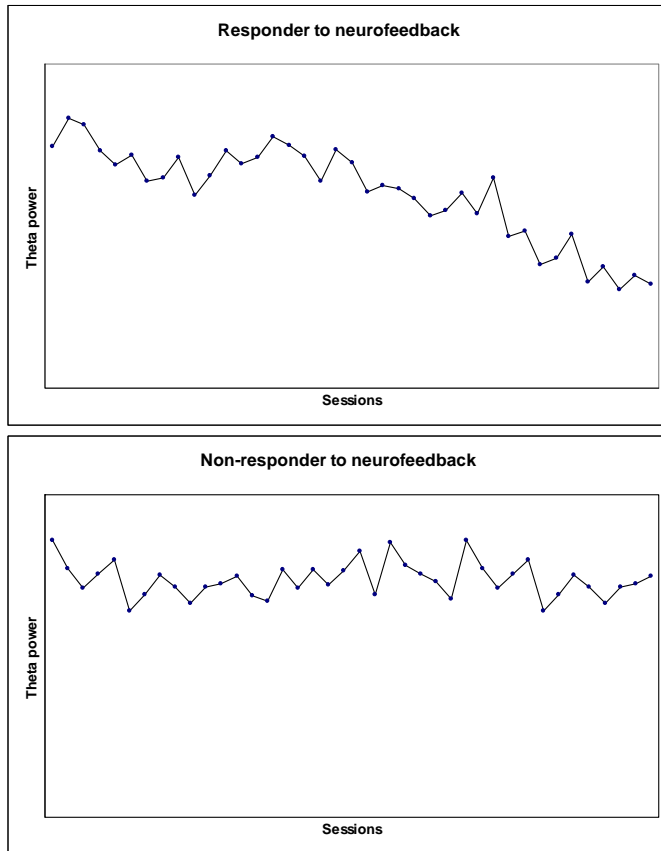
Fig. 7. Mean values of theta power of two clients who were trained to decrease theta power in 40 consecutive neurofeedback sessions. The upper part of the figure shows the mean values of theta power per session of a responder to neurofeedback; the lower part of the figure displays the mean values of theta power per session of a non-responder to neurofeedback.

responders and non-responders, for instance with regard to individual differences in QEEG profiles. Another possibility is that there may be differences between responders and non-responders in terms of the amount and the quality of the rewards they received during the neurofeedback treatment. That is, most therapists adapt the rewards to what they think works best for the individual client, which might introduce differences in both the quantity and quality of rewards between clients. For example, it may be that some clients respond best if they receive rewards in 80% of the time, whereas other clients may need more challenge and only respond to conditions in which rewards are provided in 50% of the time, or less. Similarly, some clients may be more responsive to exciting film clips, whereas others may benefit more from quiet and highly structured film clips. Inadequate choices of the therapist might influence a client's responsiveness to the treatment. A further understanding of individual preferences in both the amount and the type of rewards that are provided during neurofeedback is required to optimize the response rates of clients to neurofeedback

training. In addition, the application of neurofeedback as a treatment may benefit strongly from developing predictors, i.e. specific psychological or physiological differences between individuals that allow an early distinction between responders and non-responders, and thus to save time, effort, and money on treatment of non-responders.

Whereas operant conditioning is generally considered to be a relatively passive process on which the trainee has little or no direct influence, learning processes during neurofeedback sessions might also be influenced by active processes. It is often reported that clients manage to develop deliberate control over their EEG activity, allowing them increase or decrease the height of the bar graph in a voluntary manner. There are also clients, however, who never gain deliberate control over their EEG activity. These clients might be responders to neurofeedback, but they can not intentionally act upon the EEG signal. Kamiya (1968) was to first to provide evidence for deliberate control over EEG activity. In his study, participants were first trained to produce alpha waves and some of them subsequently managed to recognize the state of these alpha waves on instruction. Nowadays, the deliberate control over EEG activity is used frequently in clinical settings where patients with neuromuscular impairments or locked-in syndrome use brain computer interfaces (BCI) to control external devices. Birbaumer and colleagues (1999), for example, showed that paralyzed patients who completely lack muscular control can learn to communicate with their environment by using an electronic spelling device that is controlled by EEG activity. By intentionally activating EEG activity in a specific frequency range, a computer cursor is controlled to point out and select different letters of the alphabet to construct a message.

The functional mechanisms that are used to control electrical activity of the brain in a deliberate way may not be so different from functional mechanisms that we use for controlling our body. A dominant theory in motor control is the Ideomotor Theory (Greenwald, 1970), which states that our actions are primarily controlled at the level of their sensory effects. For instance, when learning how to ride a bike, the motor system is attempting to match the anticipated visual and tactile consequences of the actions with an appropriate motor command. Development of new movement repertoire, e.g. in case children are learning how to drink from a cup without spilling its content, requires internal models that map the relation between sensory consequences and action output that need to be formed through experience. The ability to control one's own brain waves may well operate on similar principles, whereby the trainee's brain, over time, establishes the relationship between motor intentions and their sensory consequences, allowing an internal model to form and control the sensory effects that are provided by the neurofeedback. A simple experiment provides a convincing demonstration of this idea. Most people are unable to wiggle their ears but may easily learn to do so when the signal of the muscles controlling their ears is made explicit to them (Bair, 1901). You can try this yourself by putting your fingers behind your ears on the tendons that are controlling their movement. The direct sensory effect will make it much easier to establish control. In a sense, neurofeedback is no different from this example. All it does is make unconscious biological signals explicit to the client so that he or she may learn to control these signals in a deliberate manner.

4.2 Neuronal mechanisms behind neurofeedback

The exact cortical and subcortical mechanisms of the brain supporting neurofeedback training have received little or no attention so far, as have its neural effects. There is one

fMRI study that investigated the effects of neurofeedback on neural substrates in children with ADHD (Beauregard & Levesque, 2006). Fifteen children were trained to reduce 4 to 7 Hz power at Cz while enhancing power in the 12 to 15 Hz and 15 to 18 Hz frequency ranges. After neurofeedback training participants in the neurofeedback group showed significant loci of activation in brain systems mediating selective attention and response inhibition compared to the control group that had no neurofeedback training. The results of this study suggest that neurofeedback has the capacity to functionally normalize brain systems in children with ADHD.

Sterman theorized on possible neuronal mechanisms underlying the effects of neurofeedback targeting SMR (Sterman, 1996; Sterman & Egner, 2006). SMR is a 12 to 15 Hz rhythm that is found maximal over the sensorimotor cortex of the brain. SMR was found positively associated with control over excitation in the thalamocortical somatosensory and somatomotor pathways of the brain (Sterman, 1996; Sterman & Egner, 2006). By repeatedly producing increased amounts of SMR, postsynaptic cells may become more sensitive and consequently the probability of future activation of these cells may be increased. By increasing thresholds for excitation, neurofeedback may have beneficial effects on severity and frequency of seizures in clients with epilepsy. In ADHD, similarly increased thresholds for excitation are believed to be responsible for reductions in cortical and thalamocortical hyper-excitability and accompanying reductions in impulsive tendencies.

Less is known about the neuronal underpinnings of neurofeedback in individuals with autism. Although the autistic brain is an increasing topic of interest in scientific research (e.g. Brambilla, Hardan, Ucelli di Nemic, Perez, Soares, & Barale, 2008), little research has been conducted on the actual consequences of neurofeedback in autism. Studies investigating the EEGs of individuals with autism have revealed abnormal patterns of EEG activity as compared to healthy controls. For example, individuals with autism showed diminished frontal and occipital/parietal alpha power (e.g. Chan, Sze, & Cheung, 2007; Murias et al., 2007) and increased phase consistency between posterior-frontal and anterior-temporal brain areas as compared to healthy controls (e.g., Coben & Padolsky, 2007; Murias et al., 2007). Furthermore, elevated delta and theta power over frontal or fronto-central areas have been found in individuals with autism (e.g. Chan, Sze, & Cheung, 2007; Kouijzer et al., 2009b; Kouijzer et al., 2010; Kouijzer et al., under review; Murias, Webb, Greenson, & Dawson, 2007). Kouijzer and colleagues (2009b; 2010) found reductions in autistic symptoms and improvements in executive functions in accordance with reductions in frontomedial theta power following neurofeedback training. Theta is typically located to the medial prefrontal cortex (MPFC) including the anterior cingulate cortex (ACC; Tsujimoto, Shimazu, & Isomura, 2006) and is inversely related to BOLD (blood-oxygen-level dependence) activation in these structures (Meltzer, Negishi, Mayes, & Constable, 2007). As such, neurofeedback mediated reductions in frontomedial theta power may be directly responsible for improvement in executive functioning and social cognitive abilities, functions that are typically associated with activation of the MPFC (Bush, Luu, & Posner, 2000; Di Martino et al., 2009; Henderson et al., 2006; Mundy, 2003; Ohnishi et al., 2000).

5. Efficacy of neurofeedback in autism

Currently, about 10 scientific publications have reported on the efficacy of neurofeedback in autism. Table 1 provides an overview of the studies that investigated the effects of neurofeedback in autism. Some studies described the effects of neurofeedback in one or

more participants (Scolnick, 2005; Sichel, Fehmi, & Goldstein, 1995; Thompson, Thompson, & Reid, 2010), whereas other studies compared a group of participants that had neurofeedback with a group of participants that had no neurofeedback or another treatment (Coben & Padolsky, 2007; Jarusiewicz, 2002; Kouijzer et al., 2009b; Kouijzer et al., 2010; Kouijzer et al., under review). Furthermore, in all studies to date, the participants were either children or adolescents. No studies of neurofeedback in adults with autism have been published at this time. About 88% of the participants in all studies that have been published were male. In terms of the autistic spectrum, most studies included participants with a diagnosis autism, Asperger syndrome or PDD-NOS. One study focused on participants with PDD-NOS only (Kouijzer et al., 2009b), whereas two other studies mainly included individuals with Asperger syndrome (Scolnick, 2005; Thompson, Thompson, & Reid, 2010). This paragraph will provide a detailed description of the outcomes of studies investigating the effects of neurofeedback with a consecutive focus on (1) behavioral symptoms as reported by parents and teachers, (2) cognitive functions, and (3) the EEG. The paragraph ends with discussing the long-term maintenance of effects of neurofeedback.

Neurofeedback was found to positively affect autistic symptoms, such as social interaction problems and communication deficits (Coben & Padolsky, 2007; Kouijzer et al., 2009b; Kouijzer et al., 2010; Sichel, Fehmi, & Goldstein, 1995). In addition, improvement in self-esteem, empathy, and flexibility were seen, as well as reductions of anxiety, temper tantrums, and mood changes (Scolnick, 2005). These positive effects of neurofeedback were all reported by parents who filled out questionnaires inquiring about their children's behavior (Coben & Padolsky, 2007; Jarusiewicz, 2002; Kouijzer et al., 2009b; Kouijzer et al., 2010; Thompson, Thompson, & Reid, 2010) or reflected the outcomes of parent interviews (Jarusiewicz, 2002; Scolnick, 2005; Sichel, Fehmi, & Goldstein, 1995). In one study, neurofeedback did not result in a reduction of autistic symptoms (Kouijzer et al., under review). The reason why some studies did find positive effects of neurofeedback on symptom reduction in autism while other studies did not is unclear at this time. Kouijzer and colleagues (under review) suggested that differences in neurofeedback protocols and in sample characteristics between studies may have been responsible for such varying study outcomes. Another possibility may be that variations in study design and thus in the degree of control for nonspecific effects (e.g. the attention that is received by trainees in addition to their training) are responsible. More information about the effects of nonspecific factors and related design issues is provided in the subsequent paragraph entitled 'Quality of neurofeedback research'.

In contrast to the reports of parents, teachers did not report as much improvement in social interactions and communication skills. At the same time, the observations of teachers were included in only three studies (Kouijzer et al., 2010; Kouijzer et al., under review; Scolnick, 2005). In one of these three studies, teachers reported improvement in behavior of adolescents with autism following neurofeedback (Scolnick, 2005). That is, in four out of five cases that were described in this paper, teachers noticed the same behavioral improvement as parents, such as improvement in self-esteem, flexibility, and empathy and reductions in anxiety and temper tantrums. In one case described in this paper, no changes in behavior were reported by the teacher, whereas the parents of that participant did report improvement. In two other studies that investigated teacher reports, teachers did not report any improvement in the behavior of children and adolescents following neurofeedback (Kouijzer et al., 2010; Kouijzer et al., under review).

Authors and year of publication	n	Study design	Age range (years)	Treatment	Number of sessions
Sichel, Fehmi, & Goldstein, 1995	1	Case study	8	Decrease 4-8 Hz; increase 12-15 Hz; P3, Pz, and P4	31
Jarusiewicz, 2002	24	Pretest posttest control group	4-13	Decrease 2-7 Hz and 22-30 Hz; increase 10-13 Hz; C4	20-69
Scolnick, 2005	5	Case study	12-16	Decrease 2-10 Hz and 22-30 Hz; increase 8-11 Hz, 12-15 Hz or 15-18 Hz; Fz, Cz, Pz, C4 or T6	24-31
Coben & Padolsky, 2007	49	Pretest posttest control group	3-14	Decrease hyperconnectivity	20
Kouijzer, de Moor, Gerrits, Congedo, & van Schie, 2009	14	Pretest posttest control group	8-12	Decrease 4-7 Hz; increase 12-15 Hz; C4	40
Kouijzer, van Schie, de Moor, Gerrits, & Buitelaar, 2010	20	Randomized pretest posttest control group	8-12	Decrease 3-7 Hz and slight variations; Fz, Cz or F4	40
Thompson, Thompson, & Reid, 2010	159	Case study	5-58	Decrease 3-7 Hz; increase 12-15 Hz; Cz or CFz	40-60
Kouijzer, van Schie, Gerrits, Buitelaar, & de Moor, under review	38	Randomized pretest posttest control group with blinded active comparator	12-18	Decrease 2-7 Hz and slight variations; Cz or CFz	23-40

Table 1. Overview of the studies that investigated the effects of neurofeedback in children and adolescents with autism.

Neurofeedback was demonstrated to have positive effects on cognitive functions of children and adolescents with autism (Coben & Padolsky, 2007; Kouijzer et al., 2009b; Kouijzer et al., 2010; Kouijzer et al., under review). These effects were measured by a series of neuropsychological tasks, which allow a more objective evaluation of the treatment effects than asking parents or teachers what they observed in the behavior of their child or student. A specific cognitive function that was found to be improved after neurofeedback treatment is cognitive flexibility. In three studies, improvement in cognitive flexibility was found in participants who received neurofeedback, whereas participants in the control groups showed no improvement in cognitive flexibility (Kouijzer et al., 2009b; Kouijzer et al., 2010; Kouijzer et al., under review). Cognitive flexibility is defined as the ability to shift to a different thought or action according to situational changes (Hill, 2004). Poor flexibility is one of the core characteristics of everyday behavior of individuals with autism and is often illustrated by a need for sameness. For example, many people with autism have difficulties in switching from one situation to the other or panic if an unexpected event occurs. The positive effects of neurofeedback on cognitive flexibility were found in studies that used the trail making task, which requires the participant to connect letters of the alphabet and numbers in an alternating manner (1-A-2-B-3-C, etc.) on paper. Whether neurofeedback also results in improvement in cognitive flexibility in real life is unknown at this time. Future studies may investigate if the effects of neurofeedback extend to real life conditions. For example by measuring the response of participants with autism in real life scenarios that require cognitive flexibility skills, e.g. a last minute change in schedule. In addition to

changes in cognitive flexibility, studies have reported improvements in other cognitive domains. Kouijzer and colleagues (2009b) noted additional improvements in attention, inhibition, and planning, suggesting a more general improvement in executive functions. This finding is supported by Coben and Padolsky (2007) who found a general improvement in executive functions accompanied by improvement in visual perceptual functioning and language skills following neurofeedback treatment.

Another relatively objective way to evaluate the effects of neurofeedback training is QEEG. Since neurofeedback focuses on the change of electrical brain activity, QEEG measures may be used to examine whether the treatment actually influenced the EEG in a structural manner or not. Most studies that examined the effects of neurofeedback in children and adolescents with autism compared pre- and post-treatment QEEGs and found that EEG activity changed after neurofeedback. The specific effects in EEG depended on the neurofeedback protocol that was used. After inhibiting theta power and rewarding beta power, the theta to beta ratios of participants decreased, i.e. changed in the direction of normality on a post treatment measurement (Sichel, Fehmi, & Goldstein, 1995; Scolnick, 2005; Thompson, Thompson, & Reid, 2010). Similarly, neurofeedback that focused on the inhibition of theta power resulted in decreased theta power (Kouijzer et al., 2010) and neurofeedback that aimed to decrease delta and theta power resulted in decreased delta power in subsequent QEEG measurements (Kouijzer et al., under review). A study by Coben and Padolsky (2007) was successful in reducing hyperconnectivity in most participants through the application of neurofeedback. Only one study failed to show effects in the EEGs of children and adolescents with autism who received neurofeedback (Kouijzer et al., 2009b).

The positive effects on autistic symptoms, cognitive flexibility, and EEG activity that were found after neurofeedback are only clinically significant if they are maintained after treatment has ended. That is, if participants would return to pre-treatment levels after the last neurofeedback session, they should continue neurofeedback training for the rest of their lives in order to benefit from its effects. This would be comparable with the structural use of medication for reducing behavioral problems that are co-occurring with autism. Aggressive behavior, for example, can be reduced by the use of atypical antipsychotics (McCracken et al., 2002) and overactivity or disruptive behavior has been decreased with stimulants (Research Units on Pediatric Psychopharmacology, 2005). When the intake of such medication is interrupted, the beneficial effects typically disappear and symptoms return to earlier levels. On the basis of current evidence, however, it appears that neurofeedback in individuals with autism has long term effects on autistic symptoms and leads to long term improvement in cognitive functions. Kouijzer and colleagues used follow-up measures of autistic symptoms and cognitive functions either six months (Kouijzer et al., 2010; Kouijzer et al., under review) or twelve months (Kouijzer et al., 2009a) after the last neurofeedback session was completed. In one study, the effects in EEG theta activity were found to be maintained six months after neurofeedback treatment had ended (Kouijzer et al., 2010), whereas another study found that the initial changes in EEG delta activity that were found directly after the treatment had returned to baseline after six months (Kouijzer et al., under review). The reason why EEG changes were long lasting in one study but not in the other study might be related to the different samples that were used in these studies. The former study included participants of 8 to 12 years old and a broad range of behavioral problems, whereas the latter study included participants of 12 to 18 years old with mainly internalizing problems. Perhaps EEG changes in younger participants or in participants

with both externalizing and internalizing behavior problems are more likely to remain over time as compared to EEG changes in older participants or in participants with internalizing behavior problems. Although the changes in EEG activity were not maintained after six months in the study of Kouijzer and colleagues (under review), the positive effects on cognitive flexibility skills that co-occurred after neurofeedback were found to be maintained six months later. This suggests that long term changes in EEG are no requirement for structural improvements in cognitive flexibility. Perhaps a reduction of slow wave power is required for the initiation of cognitive flexibility improvement, whereas continuation of the ability for task switching relies on other mechanisms.

6. Quality of neurofeedback research

The efficacy of any treatment program in any specific population can be investigated by experimental research. Such experimental research should meet a number of criteria in order to prevent the study outcomes from being influenced by other factors than the treatment itself. Campbell and Stanley (1963) recommended the use of a pretest-posttest control group design to control for factors that might produce effects confounded with the effects of the experimental treatment such as maturation. In such a randomized pretest-posttest control group design, participants are randomly allocated in two research groups: a treatment group that receives the treatment of interest and a control group that does not receive the treatment. Participants of both groups are assessed at comparable times before and after treatment. The results of the two groups at both times are compared in order to find effects of the treatment. Of the studies that investigated the effects of neurofeedback in individuals with autism, only two studies used random allocation of participants in treatment and control groups (Kouijzer et al., 2010; Kouijzer et al., under review), compared to six studies that did not.

Several authors have suggested that the outcomes of previous studies that investigated the effects of neurofeedback were not a result of neurofeedback per se, but rather reflected nonspecific effects of neurofeedback. Nonspecific treatment effects are positive effects that are caused by other factors than the treatment of interest. In the case of neurofeedback, implicit attention training and intensive one-to-one contact with the therapist might positively affect the results of the treatment. Neurofeedback is a treatment that includes many sessions that are provided twice or thrice a week. In each of these sessions, the client is instructed to focus his or her attention on the computer screen in front of him or her. Several authors have suggested that participants might be positively affected by being involved in such an intensive treatment that requires paying sustained attention to a computer screen (Gevensleben et al., 2009; Heinrich, Gevensleben, & Strehl, 2007; Kouijzer et al., 2010). Furthermore, the long-duration of neurofeedback typically implies intensive one-to-one contact between client and therapist. Therapists pay individual attention to the client and provide warmth, empathy, and acceptance. Furthermore, the contact between client and therapist in neurofeedback sessions has a highly structured character because it often follows a fixed program of alternating training and rest intervals. These factors might be especially important in individuals with autism, who often have difficulties in building a relationship with unfamiliar others. Because neurofeedback offers so many opportunities for the development of the relationship between client and therapist in a structured and predictable environment, there is a good chance for the client with autism to successfully participate in a reciprocal relationship with the therapist. This experience might cause

improvement in the social behavior of participants that is unrelated to improvement as a result of neurofeedback training (Gevensleben et al., 2009; Heinrich, Gevensleben, & Strehl, 2007; Kouijzer et al., 2010). In order to control for such nonspecific effects of neurofeedback, a control condition in which participants receive similar amounts of attention training and one-to-one contact with the therapist should be included in the research design.

Another factor that might have played a role in studies that investigated the effects of neurofeedback is treatment expectancy of participants and their parents. The notion of receiving therapy is known to generate expectancy for improvement in participants and their parents (Borkovec & Nau, 1972). Especially if parents have invested time and money in the treatment of their child, these parents may have been inclined towards a positivity bias that matches their investments. Several authors have suggested that the outcomes of previous studies that measured behavioral improvement with parent questionnaires could have been affected by expectancy biases of parents (Gevensleben et al., 2009; Heinrich, Gevensleben, & Strehl, 2007; Kouijzer et al., 2010). In order to control for the effects of expectancy, the expectancy of parents and participants should be measured in each study that evaluates the effects of neurofeedback.

Only one study fully controlled for the nonspecific effects of implicit attention training, one-to-one contact between client and therapist, and treatment expectancy (Kouijzer et al., under review). In this study, an alternative treatment group was created next to the neurofeedback group and the waiting list control group. This alternative treatment was almost identical to neurofeedback training, except for the signal that was fed back to the participants. In the neurofeedback group, the EEG signal was fed back to the client, whereas in the alternative treatment group another bodily signal, i.e. the skin conductance (SC) signal, was fed back. Participants and their parents were blinded and thus not informed about the signal that was used during their training. The participants of the SC group were expected to improve in relaxation and calmness as an effect of the SC training, but not to show reductions in symptoms of autism and to improve in cognitive functions and EEG as much as the participants in the neurofeedback group.

Another option to control for the nonspecific effects of neurofeedback is to use a double-blind placebo controlled study design. Such a study includes one group that receives the treatment of interest and one group that receives a placebo treatment. In the case of neurofeedback, the placebo treatment could include fake feedback that is unrelated to the participants' brain activity. Neither participants nor therapists are aware of the type of feedback that is provided to the participants. For neurofeedback, however, such a design is hard to realize for three reasons. First of all, both the therapist and the participants in the placebo group are likely to discover that the fake feedback is unrelated to the participants' EEG activity. Secondly, high drop-out rates have been found in placebo groups where participants were unable to gain any control over the EEG signal (Orlandi & Greco, 2005). Finally, patients often do not want to take the risk of receiving placebo training for so many sessions and therefore it is hard to include large numbers of participants in double-blind controlled studies. An alternative for placebo feedback is mock-feedback. This training method takes care of extreme situations in which the participant produces extreme muscle activity or in which the electrode detaches from the scalp. The use of mock-feedback dramatically increases the reliability of the feedback and is thus more appropriate to apply in studies evaluating the effects of neurofeedback.

Because most studies that investigated the effects of neurofeedback in children and adolescents with autism did not fully control for the nonspecific effects of neurofeedback,

there is a high need for further research that does control for such effects. Therefore, conclusions on the efficacy of neurofeedback for individuals with autism can only be drawn after several such studies have been conducted. Until then, the conclusions of the studies that investigated the effects of neurofeedback should be taken cautiously.

Another aspect that needs attention in future research concerns the treatment protocols that are used in neurofeedback. So far, most neurofeedback studies focused on the reduction of theta power with or without the reward of low beta power (Jarusiewicz, 2002; Kouijzer et al., 2009b; Kouijzer et al., 2010; Kouijzer et al., under review; Scolnick, 2005; Sichel, Fehmi, & Goldstein, 1995; Thompson, Thompson, & Reid, 2010). Furthermore, Coben and Padolsky (2007) used an original approach to use a neurofeedback protocol directed at the normalization of coherence between two or more brain areas. The different treatment outcomes of these and other neurofeedback protocols have not been investigated systematically. It might turn out that some treatment protocols work best for a specific group of individuals with autism, whereas other treatment protocols are most effective for a group of individuals with other characteristics.

A final challenge for future research concerns the identification of responders to neurofeedback. As mentioned earlier in this chapter, some individuals with autism respond well to neurofeedback and are able to change EEG activity during neurofeedback sessions, whereas other individuals do not respond and elicit no EEG changes. Importantly, a recent study (Kouijzer et al., under review) demonstrated that the benefits of neurofeedback only take place in individuals with autism who respond to neurofeedback. It is therefore of crucial importance to identify responders to neurofeedback in an early stage or even better, before treatment starts. Future research should identify demographic, psychological or physiological characteristics of individuals who respond to neurofeedback.

7. Future developments in neurofeedback

Neurofeedback as a treatment for clients with various disorders has rapidly expanded in the past years, due to increasing technological developments which made the registration of EEG activity more accurate and available for therapists. Next to the traditional neurofeedback as described previously in this chapter, several other modalities of neurofeedback have been developed. In the next section three of these recent developments are discussed, i.e. LORETA-neurofeedback, ICA-neurofeedback, and fMRI-neurofeedback.

LORETA refers to low resolution tomography and is an inverse technique for reconstructing the source of EEG activity in the three-dimensional brain by electrophysiological models. In LORETA-neurofeedback, feedback reflects EEG activity that is generated by a specific source, which deviates from traditional neurofeedback approaches where feedback reflects spatially nonspecific EEG activity at the sensor level (Congedo, 2003). LORETA-neurofeedback can not be applied in real time, because of time and capacity consuming calculations of the computer. Therefore, LORETA-neurofeedback is applied by using a spatial filter after the EEG activity is recorded. LORETA-neurofeedback can be used to alter EEG activity generated in deep brain structures that can not be recorded accurately by traditional neurofeedback. In a study by Congedo, Lubar, and Joffe (2004) the application of LORETA-neurofeedback was investigated in six healthy students. These participants were trained to decrease beta power and to concurrently increase alpha power generated in the ACC. The results of this study show an increased beta/alpha ratio in the regions of the ACC that were involved in the LORETA-neurofeedback (Congedo, Lubar, & Joffe, 2004). These

findings suggest that EEG activity in specific brain areas may be altered by LORETA-neurofeedback.

Related to LORETA-neurofeedback is ICA-neurofeedback. ICA refers to independent component analysis and is a mathematical approach that separates a multivariate signal in independent components. In the case of ICA-neurofeedback, ICA separates the raw EEG signal in separate sources of the signal. This technique can be applied in cases where neurofeedback focuses on specific EEG components that can not be detected easily from the raw EEG signal by traditional neurofeedback devices. ICA- and LORETA-neurofeedback can be used interchangeably, but are not similar. ICA-neurofeedback uses mathematical models to calculate the solutions of the EEG signal, whereas LORETA-neurofeedback is based on electrophysiological models.

A third modality of neurofeedback is fMRI-neurofeedback. FMRI-neurofeedback is an advanced method that uses the BOLD response of regions in the brain. FMRI is a technique that allows measurements of brain activity with a high spatial resolution, but low temporal resolution, as compared to EEG which has a high temporal resolution, but is limited in the spatial domain. At this time, fMRI-neurofeedback is mainly used in research settings and is hardly applied in the treatment of clinical populations. The main reason for this is that fMRI is an expensive technique and that any treatment application will suffer from a long time delay, which lies in the order of several seconds, resulting from the sluggishness of the BOLD response. This delay in feedback makes it especially hard for individuals to relate the feedback to the actual brain activity. Nevertheless, DeCharms and colleagues (2004) successfully applied fMRI-neurofeedback in six healthy participants. They were instructed to imagine hand movements while trying to optimize their strategy to increase activation in a brain area involved in this cognitive process, i.e. the sensorimotor cortex. The participants received continuous information about the strength of activation they were producing in their sensorimotor cortex. After three sessions, participants succeeded in controlling task-specific activation in the sensorimotor cortex.

LORETA-neurofeedback, ICA-neurofeedback, and fMRI-neurofeedback are examples of recent developments in the field of neurofeedback that are expected to gain further scientific interest over the coming years. These techniques hold the potential for changing activation in specific neural regions using neurofeedback. As such, it is more than likely that the clinical application of EEG neurofeedback in the coming years will develop in the direction of EEG source modeling techniques (such as LORETA- and ICA-neurofeedback) to allow the activation or deactivation of specific neural structures that are implicated in neurological conditions such as autism. FMRI-neurofeedback on the other hand may prove a valuable experimental technique for assisting cognitive neuroscience in its aim to uncover the functional organization of the brain.

8. Conclusion

Neurofeedback is a technique that is used to alter activity of the brain that deviates from normality in a variety of clinical disorders, such as autism. Recent findings suggest that neurofeedback may provide a beneficial treatment for individuals in the autism spectrum. Indeed several studies have shown that individuals with autism are able to alter their brain activity in specific frequency bands through the use of neurofeedback and that neurofeedback training may be accompanied by prolonged changes in autism symptoms, cognitive functioning and long-term changes in EEG. Although the prospects for the

application of neurofeedback in autism spectrum disorders certainly look promising, the scientific evidence for its effectiveness to date is still rather thin. Future studies will have to be conducted using larger samples and appropriate control conditions to allow reliable measures of the efficacy of neurofeedback treatment in autism both in the lab and in clinical practice.

9. References

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders, text revision* (4th ed.). Washington, DC: American Psychiatric Association.

Arns, M., de Ridder, S., Strehl, U., Breteler, M., & Coenen, A. (2009). Efficacy of neurofeedback treatment in ADHD: the effects on inattention, hyperactivity, and impulsivity: a meta-analysis. *Clinical EEG and Neuroscience, 40* (3), 179- 189.

Bair, J.H. (1901). Development of voluntary control. *Psychological review, 8,* 474-510.

Beauregard, M & Lévesque, J. (2006). Functional Magnetic Resonance Imaging Investigation of the Effects of Neurofeedback Training on the Neural Bases of Selective Attention and Response Inhibition in Children with Attention-Deficit/Hyperactivity Disorder. *Applied Psychophysiology and Biofeedback, 31,*(1), 3-20.

Birbaumer, N., Ghanayim, N., Hinterberger, T., Iversen, I., Kotchoubey, B., Kübler, A., Perelmouter, J., Taub, E., & Flor, H. (1999). A spelling device for the paralysed. *Nature, 398,* 297-298.

Borkovec, T.D. & Nau, S.D. (1972). Credibility of analogue therapy rationales. *Journal of Behavior Therapy & Experimental Psychiatry, 3,* 257-260.

Brambilla, P., Hardan, A., Ucelli di Nemic, S., Perez, J., Soares, J.C., & Barale, F. (2008). Brain anatomy and development in autism: review of structural MRI studies. *Brain research bulletin, 61,* 557-569.

Bush, G., Luu, P., & Posner, M. I. (2000). Cognitive and emotional influences in anterior cingulate cortex. *Trends in Cognitive Science, 4,* 215–222.

Campbell, D.T. & Stanley, J.C. (1963). *Experimental and quasi-experimental designs for research.* Chicago, llinois: Rand McNally.

Chan, A.S., Sze, S.L., & Cheung, M. (2007). Quantitative Electroencephalographic Profiles for Children With Autistic Spectrum Disorder. *Neuropsychology, 21* (1), 74-81.

Cherkassky, V. L., Kana, R. K., Keller, T. A., & Just, M. A. (2006). Functional connectivity in a baseline resting-state network in autism. *Neuroreport, 17,* 1687–1690.

Coben, R. & Padolsky, I. (2007). Assessment-guided neurofeedback for autistic spectrum disorders. *Journal of Neurotherapy, 11,* 5-23.

Congedo, M. (2003). *Tomographic neurofeedback; a new technique for the self-regulation of brain electrical activity.* Thesis, Knoxville, TN: The university of Tennessee, Knoxville.

Congedo, M. Lubar, J.F., & Joffe, D. (2004). Low-resolution electromagnetic tomography neurofeedback. *Neural systems and rehabilitation engineering, 12* (4), 387-397.

DeCharms, R.C., Christoff, K., Glover, G.H., Pauly, J.M., Whitfield, S., & Gabrieli, J.D.E. (2004). Learned regulation of spatially localized brain activity using real-time fmri. *Neuroimage, 21*(1), 436-443.

Di Martino, A., Ross, K., Uddin, L. Q., Sklar, A. B., Castellanos, F. X., & Milham, M. P. (2009). Functional brain correlates of social and nonsocial processes in autism spectrum disorders: An activation likelihood estimation meta-analysis. *Biological Psychiatry, 65,* 63–74.

Gazzaniga, M.S. & Heatherton, T.F. (2003). *Psychological Science*. New York: W.W. Norton & Company.

Gevensleben, H., Holl, B., Albrecht, B., Vogel, C., Schlamp, D., Kratz, O., Studer, P., Rothenberger, A., Moll, G.H., & Heinrich, H.. (2009). Is neurofeedback an efficacious treatment for ADHD? A randomised controlled clinical trial. *Journal of Child Psychology and Psychiatry, 50* (7), 780-789.

Greenwald, A.G. (1970). A choice reaction time test of ideomotor theory. *Journal of Experimental Psychology, 86*, 20-25.

Heinrich, H., Gevensleben, H., & Strehl, U. (2007). Annotation: Neurofeedback—train your brain to train behavior. *Journal of Child Psychology and Psychiatry, 48*(1), 3–16.

Henderson, H., Schwartz, C., Mundy, P., Burnette, C., Sutton, S., Zahka, N., et al. (2006). Response monitoring, the error-related negativity, and differences in social behavior in autism. *Brain and Cognition, 61*, 96–109.

Hill, E.L. (2004). Executive dysfunctions in autism. *Trends in cognitive sciences, 8* (1), 26-32.

Jarusiewicz, B. (2002). Efficacy of neurofeedback for children in the autistic spectrum: A pilot study. *Journal of Neurotherapy, 6*, 39–49.

Kamiya, J. (1968). Conscious control of brain waves. *Psychology Today, 1*, 57-60.

Kennedy, D. P., & Courchesne, E. (2008). The intrinsic functional organization of the brain is altered in autism. *NeuroImage, 39*, 1877–1885.

Kouijzer, M.E.J., de Moor, J.M.H., Gerrits, B.J.L., Buitelaar, J.K., & van Schie, H.T. (2009b). Long-term effects of neurofeedback treatment in autism. *Research in Autism Spectrum Disorders, 3*, 496-501.

Kouijzer, M.E.J., de Moor, J.M.H., Gerrits, B.J.L., Congedo, M., & van Schie, H.T. (2009a). Neurofeedback improves executive functioning in children with autism spectrum disorders. *Research in Autism Spectrum Disorders, 3*, 145- 162.

Kouijzer, M.E.J., van Schie, H.T., de Moor, J.M.H., Gerrits, B.J.L., & Buitelaar, J.K. (2010). Neurofeedback treatment in autism. Preliminary findings in behavioral, cognitive, and neurophysiological functioning. *Research in Autism Spectrum Disorders, 4*, 386-399.

Kouijzer, M.E.J., van Schie, H.T., Gerrits, B.J.L, Buitelaar, J.K., & de Moor, J.M.H. (under review). Is EEG-biofeedback an Effective Treatment For Autism? A Randomized Controlled Trial.

Kropotov, J.D., Grin-Yatsenko, V.A., Ponomarev, V.A., Chutko, L.S., Yakovenko, E.A., & Nikishena, I.S. (2005). ERPs correlates of EEG relative beta training in ADHD children. *International journal of psychophysiology, 55*, 23-34.

Lubar, J. F., & Shouse, M. N. (1976). EEG and behavioral changes in a hyperkinetic child concurrent with training of the sensorimotor rhythm (SMR): A preliminary report. *Biofeedback and Self Regulation, 3*, 293-306.

McCracken, J.T., McGough, J., Shah, B. Cronin, P., Hong, D., Aman, M.G., et al. (2002). Risperdone in children with autism and serious behavioral problems. *New England journal of medicine, 5*, 314-321.

Meltzer, J. A., Negishi, M., Mayes, L. C., & Constable, R. T. (2007). Individual differences in EEG theta and alpha dynamics during working memory correlate with fMRI responses across subjects. *Clinical Neurophysiology, 118*, 2419–2436.

Monastra, V.J., Lynn, S., Linden, M., Lubar, J.F., Gruzelier, J., & LaVaque, T.J. (2005). Electroencephalographic Biofeedback in the Treatment of Attention-

Deficit/Hyperactivity Disorder. *Applied Psychophysiology and Biofeedback, 30* (2), 95-114.

Mundy, P. (2003). Annotation: The neural basis of social impairments in autism: The role of the dorsal medial-frontal cortex and anterior cingulate system. *Journal of Child Psychology and Psychiatry, 44*, 793–809.

Murias, M., Webb, S. J., Greenson, J., & Dawson, G. (2007). Resting state cortical connectivity reflected in EEG coherence in individuals with autism. *Biological Psychiatry, 62*, 270–273.

Ohnishi, T., Matsuda, H., Hashimoto, T., Kunihiro, T., Nishikawa, M., Uema, T., et al. (2000). Abnormal regional cerebral blood flow in childhood autism. *Brain, 123*, 1838–1844.

Orlandi, M.A. & Greco, D. (2005). *A randomized, double-blind clinical trial of EEG neurofeedback treatment for attention deficit/hyperactivity disorder (ADHD)*. In ISNR conference.

Raichle, M. E., MacLeod, A. M., Snyder, A. Z., Powers, W. J., Gusnard, D. A., & Shulman, G. L. (2001). A default mode of brain function. *Proceedings of the National Academy of Sciences, 98*, 676–682.

Research Units on Pediatric Psychopharmacology (2005). Randomized, controlled, crossover trial of methylphenidate in pervasive developmental disorders with hyperactivity. *Archives of general psychiatry, 62*, 1266-1274.

Scolnick, B. (2005). Effects of electroencephalogram biofeedback with Asperger's syndrome. *International Journal of Rehabilitation Research, 28*, 159–163.

Sichel, A. G., Fehmi, L. G., & Goldstein, D. M. (1995). Positive outcome with neurofeedback treatment in a case of mild autism. *Journal of Neurotherapy,* 1 (1), 60-64.

Sterman, M. B. (1996). Physiological origins and functional correlates of EEG rhythmic activities: Implications for self- regulation. *Biofeedback and Self Regulation, 21*, 3–33.

Sterman, M.B. & Egner, T. (2006). Foundations and practice of neurofeedback for the treatment of epilepsy. Applied *Psychophysiology and Biofeedback, 31* (1), 21-35.

Sterman, M. B., Macdonald, L. R. and Stone, R. K. (1974). Biofeedback Training of the Sensorimotor Electroencephalogram Rhythm in Man: Effects on Epilepsy. *Epilepsia, 15*, 395–416.

Tan, G., Thornby, J., Hammond, D.C., Strehl, U., Canady, B., Arnemann, K., & Kaiser, D.A. (2009). Meta-analysis of EEG-biofeedback in treating epilepsy. *Clinical EEG and Neuroscience, 40* (3), 1-7.

Thompson, L., Thompson, M., & Reid, A. (2010). Neurofeedback Outcomes in Clients with Asperger's Syndrome. *Applied Psychophysiology and Biofeedback, 35*, 63-81.

Thorndike, E.L. (1933). A proof of the law of effect. *Science, 77*, 173.

Tsujimoto, T., Shimazu, H., & Isomura, Y. (2006). Direct recording of theta oscillations in primate prefrontal and anterior cingulate cortices. *Journal of Neurophysiology, 95*, 2987–3000.

Wyricka, W. & Sterman, M.B. (1968). Instrumental conditioning of sensorimotor cortex EEG spindles in the waking cat. *Physiology and Behavior, 3*, 703-707.

Yucha, C. & Montgomery, D. (2008).*Evidence-Based Practice in Biofeedback and Neurofeedback*. Wheat Ridge, CO: Association for Applied Psychophysiology and Biofeedback.