2 Theoretical background and current research situation

Autism Spectrum Disorders are characterized by impairments regarding communication, interaction and behavior (APA, 2013). In the following the valid diagnostic criteria for ASD are introduced as well as a short overview concerning important therapy approaches and selected research findings, with the goal of integrating Neurofeedback into the current treatment and research situation. Subsequently, the procedure of Neurofeedback training is explained and important advantages of this treatment approach are discussed. Finally, results of empirical studies on the effectiveness of Neurofeedback training for Autism Spectrum Disorders are presented.

2.1 Autism Spectrum Disorder

According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; APA, 2013), the Autism Spectrum Disorder (299.00) belongs to the group of Neuro-developmental Disorders. The manifestation of an ASD begins early in the individual development and is characterized by deficits that typically remain persistent across the life-span. Unlike other disorders of that group, which only impact specific skills or functioning, the diagnosis of an ASD describes the existence of more extensive impairments regarding several functional aspects (ibid.). Individuals show restricted communication and interaction skills as well as linguistic impairments that can range up to a complete absence of language development. Additionally, distinctive behavioral features are characterized by repetitive motor mannerisms, restricted interests or the compulsive insistence on unchanging daily routines and environmental attributes (Sinzig, 2011).

The recently published DSM-5 contains an important revision of the previously valid diagnostic criteria of the DSM-IV-TR (APA, 2000). One of the most significant changes is that there is no longer any differentiation among four separate disorders. The former DSM-IV-TR diagnoses of Autistic Disorder (299.00), Asperger's Disorder (299.80), Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS, 299.80) and Childhood Disintegrative Disorder (299.10)

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are now integrated in the DSM-5 diagnosis of an Autism Spectrum Disorder. The main characteristics of the ASD are now described with two core symptom groups, with the requirement that attributes of both areas have to be present. Since the DSM-5 features some significant changes regarding the diagnosis of an Autism Spectrum Disorder, table 1 presents an overview of the current valid diagnostic criteria. This chart is also an explanation basis for the outcome measures used for the study. Independently of each other, both main symptom groups can vary in their severity, also referred to as the individual manifestations on the spectrum. To specify the extent of the particular impairments, both main diagnostic criteria need to be rated on a severity scale with three levels. These levels indicate if support (1), substantial support (2) or very substantial support (3) is required (APA, 2013). In addition, the diagnosis of an Autism Spectrum Disorder also includes further specifications, such as an accompanying language or intellectual impairment, the existence of other associating mental disorders or given genetic and medical conditions (ibid.).

Table 1: New diagnostic criteria for the Autism Spectrum Disorder (Excerpt from the Diagnostic and Statistical Manual of Mental Disorders (DSM-5); APA, 2013)

AUTISM SPECTRUM DISORDER 299.00 (F.84.0)

Diagnostic Criteria

A Persistent **deficits in social communication and social interaction** across multiple contexts, as manifested by the following, currently or by history:

1. Deficits in social-emotional reciprocity, ranging, for example, from abnormal social approach and failure of normal back-and-forth conversation; to reduced sharing of interests, emotions, or affect; to failure to initiate or respond to social interactions.
2. Deficits in nonverbal communicative behaviors used for social interaction, ranging, for example, from poorly integrated verbal and nonverbal communication; to abnormalities in eye contact and body language or deficits in understanding and use of gestures; to a total lack of facial expressions and nonverbal communication.
3. Deficits in developing, maintaining, and understanding relationships, ranging, for example, from difficulties adjusting behavior to suit various social contexts; to difficulties in sharing imaginative play or in making friends; to absence of interest in peers.

B Restricted, repetitive patterns of behavior, interests, or activities, as manifested by at least two of the following, currently or by history:

1. Stereotyped or repetitive motor movements, use of objects, or speech (e.g., simple motorstereotypies, lining up toys or flipping objects, echolalia, idiosyncratic phrases).
2. Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior (e.g. extreme distress at small changes, difficulties with transitions, rigid thinking patterns, greeting rituals, need to take same route or eat same food every day).
3. Highly restricted, fixated interests that are abnormal in intensity or focus (e.g., strong attachment to or preoccupation with unusual objects, excessively circumscribed or perseverative interests).
4. Hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of the environment (e.g., apparent indifference to pain/temperature, adverse response to specific sounds or textures, excessive smelling or touching of objects, visual fascination with lights or movement).

C Symptoms must be present in the early developmental period (but may not become fully manifest until social demands exceed limited capacities, or may be masked by learned strategies in later life).

D Symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning.

E These disturbances are not better explained by intellectual disability (intellectual developmental disorder) or global developmental delay. Intellectual disability and autism spectrum disorder frequently co-occur; to make comorbid diagnoses of autism spectrum disorder and intellectual disability, social communication should be below that expected for general developmental level.

An important reason for considering and investigating Neurofeedback training as an effective treatment for ASD is the non-satisfying fact that numerous existing therapy approaches are not yet evidence-based. They also often cannot meet the needs of this heterogeneous patient group (Perry & Condillac, 2003). Currently there are only a few treatment approaches for ASD whose effectiveness has been empirically supported (level of evidence IIa), including the *Applied Behavior Analysis* (ABA), the *Treatment and Education of Autistic and related Communication handicapped Children (*TEACCH) and the *Picture Exchange Communication System* (PECS) (Bölte, 2009). The ABA (Lovaas, 1981, 1987) uses principles of classic and operant conditioning to modify behavior, basically by teaching and reinforcing desired behavior, as well as simultaneously reducing and fading out problem behavior. The TEACCH approach (Schopler et al., 1995) also aims at teaching behavioral and cognitive skills to enhance independency and decrease negative behavior. An important attribute of this treatment is the creation of an individually adapted and structured environment for the patients to facilitate the therapeutic work. The PECS method (Bondy & Frost, 1994) is especially helpful for nonverbal or minimally verbal children as it teaches the use of picture cards in order to express themselves and to communicate with others. This system can easily be combined with other treatments as an additional therapy component. As mentioned earlier, there are many more therapy methods, some more promising than others (Poustka, Bölte, Feineis-Matthews, & Schmötzer, 2004), whose effectiveness needs to be investigated in future research endeavors. Neurofeedback training certainly is an approach with a great potential. Initial support of successful implementations has already been established and will be cited later.

The finding of effective treatments is directly linked to the research regarding the actual causes of Autism Spectrum Disorders. Research studies have still not completely identified all possible sources. However, several scientific studies found that ASDs primarily have genetic causes (Meyer-Lindenberg, 2011). These genetic mutations can be high risk factors for an abnormal development of the brain, for example, by inhibiting the formation of important neuronal connections (ibid.) or by causing inadequate brain wave activity (Pop-Jordanova, Zorcec, Demerdzieva, & Gucev, 2010). These deviant patterns can lead to severe deficits in neuropsychological functions and abilities, such as executive functions, central coherence, theory of mind, language, intelligence and imitation abilities (Sinzig, 2011). Children usually begin to imitate gestures, facial expressions or actions including objects at a very young age. This is an important precondition for the development of the Theory of Mind, which is the ability to be aware of and comprehend internal thoughts and emotions, and those of others (ibid.). In children diagnosed with an ASD these abilities often are limitedly evolved (Rogers, Hepburn, Stackhouse, & Wehner, 2003). Therefore autistic individuals often show difficulties in planning and controlling their own behavior or in recognizing complex social situations. It can be very challenging to identify and understand emotions, thoughts or intentions (Sinzig, 2011). Numerous research studies investigated the neuropsychological functioning of people with autism (for a review see for example Dziobek & Köhne, 2011), and by now many experts agree that a dysfunctional mirror neuron system is one of the main causes for limited neurocognitive abilities (e.g. Poustka et al., 2004; Oberman et al., 2005; Pineda et al., 2008). This system controls perception and recognition of basic motor actions, but is presumably also involved in more complex cognitive processes and thereby may lead to the impairments described above (Rizzolatti, Fogassi, & Gallese, 2001; Oberman et al., 2005). Furthermore, scientists have detected that certain brain areas of people with an ASD are over- or under-aroused during cognitive processing, compared to normally functioning brains (Dziobek & Köhne, 2011). At times completely different areas become activated for cognitive performances, such as working memory or executive functions. This indicates the development of compensatory strategies in the autistic brain (ibid.). Another phenomenon often mentioned in the literature describes that cerebral functions are not sufficiently integrated and therefore different psychological functions cannot be coordinated correctly (Lautenbacher & Gauggel, 2010). This results in the often observable deficits in processing, integrating or reacting appropriately to perceptions, emotions or behaviors. Therefore it appears to be reasonable to research Neurofeedback as a form of intervention that is aimed at fundamentally changing the functioning of the brain.

2.2 Neurofeedback training

Neurofeedback, also called EEG biofeedback, is a computerized treatment approach for neurobiological dysfunctions that aims at modifying abnormal brain activity. By receiving immediate information about the neuronal patterns, individuals can learn to regulate the activity of their own brain waves based on operant conditioning (Thatcher, 2009). In the course of time, researchers developed several Neurofeedback training programs that partly differ in their recordings and possible training methods. A comprehensive description of these various programs would unfortunately exceed the framework of this paper. However, all approaches are based on the general principles of providing instantaneous feedback on recorded brain activity, with the objective of redirecting deviating brain waves to a designated range. This change is in turn "associated with positive changes in physical, emotional, and cognitive states" (International Society for Neurofeedback and Research, 2010). In the following a detailed explanation of the *Z-Score Neurofeedback Training* (Thatcher, 2009) is provided, as this is the form of training that was used in the present study.

The fundamental idea of this approach is the permanent comparison of the recorded brain activity to a normative database, therefore also referred to as QEEG (quantitative electro-encephalography). The QEEG signals deviations from normative metrics and thus can be used to identify the targets for the training (Larsen, 2012). Through 19 electrodes that are connected to the scalp (figure 1), the EEG activity of the brain is recorded. Figure 2 shows the positioning of all electrodes according to the International 10/20 System of electrode placement

(Jasper, 1958). Each electrode registers wave frequencies, this raw data is then divided into frequency bands via fast Fourier transformation. The power spectrum contains of the following known frequencies: delta (1-4 Hz), theta (4-8 Hz), alpha (8-12 Hz) beta (12-25 Hz) and high beta (25-30 Hz). Table 2 presents a short description of the different frequency bands and associated correlates, as well as consequences of abnormal occurrence.

Figure 1: Cap with 19 electrodes measuring brain wave activity
(Source: Jacob's Ladder Center)

Figure 2: Labeling of the 19 electrode positions on the scalp
(Note: A1 and A2 only serve as reference electrodes)
(Source: http://ionm.pro/2011/11/12/ american-clinical-neurophysiology-society-practice-guidelines-eeg-ep-iom/)

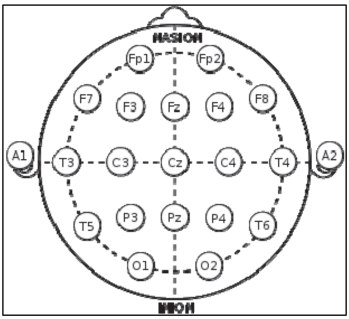


Table 2: Overview of the brain frequency bands and their occurrence (adapted from Robbins, 2008; Neurohealth Associates, 2004)

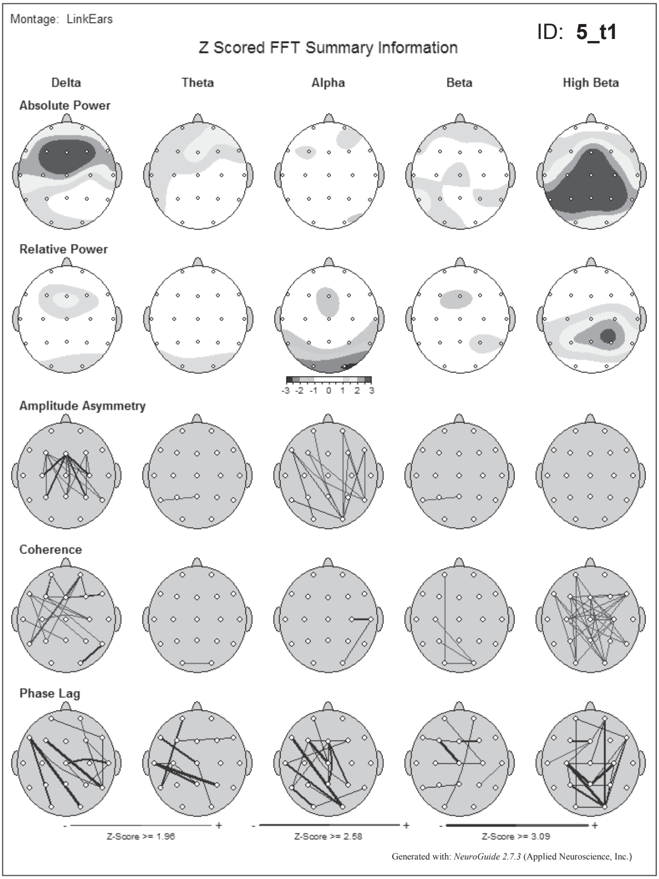
<table>
<tr><th>Frequency Band</th><th>Related Brain States</th><th>Associated Behavior</th><th>Physiological Correlates</th><th>Possible effects of abnormal occurrence</th></tr>
<tr><td>Delta (1-4 Hz)</td><td>deep, dreamless sleep, trance, unconscious</td><td>lethargic, not attentive</td><td>low level of arousal</td><td rowspan="2">too much delta and/or theta can limit the ability to focus, concentrate and maintain attention; can interfere with learning and memory</td></tr>
<tr><td>Theta (4-8 Hz)</td><td>hypnogogic state, consciousness between sleep and deep relaxation</td><td>daydreaming, creativity, internal focus</td><td>integration of mind and body</td></tr>
<tr><td>Alpha (8-12 Hz)</td><td>relaxed, but awake</td><td>no action, mental resourcefulness, resting</td><td>relaxed, calm, alert, but not actively processing information</td><td>more/less alpha can cause abnormal sensations, deficiencies in self-control</td></tr>
<tr><td>Beta (12-25 Hz)</td><td>normal waking consciousness</td><td>mental activity: listening, thinking, decision making</td><td>alert, active, but not agitated</td><td rowspan="2">too much beta and/or high beta can increase alertness, tension, mental stress or anxiety; less beta/high beta can cause a lack of focused attention, emotional instability</td></tr>
<tr><td>High Beta (25-30 Hz)</td><td>alertness, high concentration</td><td>mental activity: math, planning, analytical problem solving</td><td>general activation of mind and body functions</td></tr>
</table>

The fragmented data is quantitatively compared to a matching normative group, featuring the same age, gender and handedness as the patient, in order to identify abnormalities (Larsen, 2012). The values are then converted into z-scores, facilitating the estimation of deviations. Previously to the beginning of the actual

Neurofeedback training, the data is merged to a brain map, summarizing the data visually and numerically. Figure 3 shows an example of a brain map (topographic presentation). The electrodes record information about the following dimensions: absolute power of the frequency bands (voltage, measured in microvolt), the relative power (represented amount of each frequency band), as well as the amplitude asymmetry (balance of the brain activity between the different areas), the coherence (connection and communication between the different areas) as well as the phase lag (timing of the energy transfer) (Thatcher, 2009). Taking into account all this information, considerable abnormalities can be identified easily and, consequentially, the goals for the Neurofeedback training can be defined.

For the actual training, the threshold for the target frequency and dimension needs to be set. Several target frequencies, dimensions and electrode positions can be selected at the same time, but this increases the difficulty of the training as several activity patterns need to be adapted simultaneously in order to be rewarded. At the beginning of the training the threshold value is usually set at a relatively low level, in order to have the subject experience successful participation. This process can be seen as a form of operant conditioning, since the reinforcement is only obtained when the desired brain wave activity is shown (Larsen, 2012). In the course of the training, the threshold value is raised to higher levels, aiming at a movement towards a low z-score that indicates no or only minimal deviations from the norm. With the help of a special computer program the permanently recorded raw data can be converted to auditory and visual signals, simultaneously representing the brain signals (Congedo et al., 2004). This apparent feedback can help to increase the patient's awareness of his or her own brain activity and to learn how to modify it. To enhance the success and Neurofeedback experience for younger patients – as the ones in the present research project – the feedback can be displayed in an age-appropriate way, for example in the form of a movie or video game that only plays when the brain wave activity appears as desired.

Figure 3: Topographic brain maps representing the QEEG data
The dots symbolize the 19 electrodes on the scalp; the colors illustrate the severity of the deviation (indicated in z-scores, see legends for details). A clear image would represent normal functioning concerning the particular frequency and target dimension.



In this example the absolute power (voltage) of delta and theta is distinctively increased, especially in the frontal and left temporal area. The absolute power of high beta is expansively highly increased. Alpha frequencies are significantly underrepresented in the occipital area, while high beta frequencies are overrepresented in the central, parietal and temporal areas. (During the recording of the EEG data the subject was awake, but relaxed, no instruction for a mental activity was given.)

Besides the previously described standard surface Neurofeedback, researchers developed another, more advanced approach in the last years that can analyze deeper into the brain. With the help of LORETA (Low Resolution Electromagnetic Tomography) a 3-dimensional localization of problem areas in cortical and subcortical regions is possible. Specific brain areas and functional systems can be identified more precisely and thereby an even better targeted training is possible (Robbins, 2008; Larsen, 2012).

Neurofeedback training is a cost-intensive method that still needs further systematic empirical evidence of its effectiveness. However, there are several advantages that should be considered as they depict Neurofeedback as a promising approach for numerous disorders, such as Attention Deficit Hyperactivity Disorder, Autism Spectrum Disorder, anxiety, brain injuries or Post-Traumatic Stress Disorder (e.g. Peniston & Kulkolsky, 1991; Gevensleben et al., 2009; Larsen, 2012). In contrast to many other therapies, Neurofeedback training aims at changing the individual's brain activity fundamentally, instead of only treating the symptoms of a disorder. It is a noninvasive approach, thus the brain cannot become dependent on outside influences like medication or electric impulses (Niv, 2013). For these reasons it is likely that Neurofeedback can create long-term effects, which can remain persistent even after the termination of the training. First studies found evidence for long-term effects of positive changes in the brain wave activity (e.g. Abarbanel, 1995; Kouijzer, de Moor, Gerrits, & Buitelaar, 2009b). Moreover, Neurofeed-back training sessions are completely individualized, based on the subject's recorded brain activity and the accompanying symptoms, which is an important requirement especially concerning treatment approaches for ASD (Bölte, 2009). In addition, Neurofeedback training is adjustable at any time, for example in case of the worsening of symptoms or similar occurrences. Moreover, to date no side effects from Neurofeedback training have been reported (Coben, Linden, & Myers, 2010). Another important benefit is the possibility of combining Neurofeedback training with other treatment approaches to potentially increase the therapy progress. Thatcher (2009) describes several specific advantages of the real-time z-score training, including a simplification of the data analyses as different metrics (power, coherence etc.) are converted into common z-scores. He also states that this form of training provides a definite threshold ($z = 0$) and a clear direction of change, as the goal of this treatment is a movement of the EEG towards a healthy reference group (ibid.).

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