Neurofeedback treatment in autism. Preliminary findings in behavioral, cognitive, and neurophysiological functioning

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ABSTRACT

Effects of neurofeedback treatment were investigated in children with autism spectrum disorders (ASD). Sixty percent of the participants in the treatment group successfully reduced excessive theta power during neurofeedback treatment. Reduction of theta power was confirmed by pre- and post-QEEG measures. Parents of participants in the neurofeedback treatment group reported significant improvements in reciprocal social interactions and communication skills, relative to the parents of the control group. Set-shifting skills improved following neurofeedback treatment relative to the control group. The reduction of theta power is assumed to reflect modulation of activity in the anterior cingulate cortex (ACC), which is known to be involved in social and executive dysfunctions in autism.

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Autism spectrum disorders (ASD) have been defined as developmental disorders characterized by abnormalities in social interaction, communication skills, and behavioral flexibility (American Psychiatric Association, 1994). Although no evidence-based cure exists for ASD, psychosocial and pharmacologic interventions can improve the quality of life of children with ASD and their families. Psychosocial interventions in ASD include behavioral therapy, social skills training, and parental interventions. In general, psychosocial interventions appear to have limited effect sizes and maintenance of results over time. Recent research suggests that of all psychosocial interventions, intensive one-to-one behavioral therapy of at least 20 h per week at an early age is most effective (van Engeland & Buitelaar, 2008). Pharmacologic interventions such as atypical antipsychotics, serotonin reuptake inhibitors, and stimulants do not affect the core symptoms of ASD, but may be components of a comprehensive treatment program in temporarily reducing additional problem behavior. Both psychosocial and pharmacologic interventions provide no curative solution for the treatment of ASD, but might offer benefits for relieving ASD symptoms.

A relatively new form of treatment for ASD is neurofeedback. The goal of neurofeedback is to influence or change abnormal oscillatory activity by making clients aware of this activity and reward the inhibition or enhancement of desired oscillatory activity. In 2002, Jarusiewicz started research on the effects of neurofeedback in children with autism. She found a 26% decline in autistic behavior as reported by parents in 12 autistic children after inhibiting theta power and enhancing low beta power, compared to a 3% decline in a matched waiting list control group. Coben and Padolsky (2007) extended this...
research by comparing the outcomes of neurofeedback training in a treatment (n = 37) and control group (n = 12) on neuropsychological tests, behavior ratings, and neurophysiological measures. They showed improvement on all outcome measures for the treatment group but not for the control group. In our own study (Kouijzer, de Moor, Gerrits, Congedo, & van Schie, 2009) we evaluated neurofeedback treatment in seven children with ASD compared to a waiting list control group (n = 7) and found positive effects of inhibiting theta power and enhancing low beta power on behavioral, cognitive, and neurophysiological outcome measures. These results were maintained after one year, as was found in a follow-up study (Kouijzer, de Moor, Gerrits, Buitelaar, & van Schie, 2009). Compared to common psychosocial and pharmacological interventions, neurofeedback may be at an advantage with respect to shortened treatment duration, the absence of side effects, and long-term maintenance of treatment results. These advantages suggest that neurofeedback may be a promising tool for the treatment of children with ASD.

To further establish neurofeedback as an efficacious and specific treatment for ASD, the current study implemented several methodological improvements (cf. Heinrich, Gevensleben, & Strehl, 2007; Kouijzer, de Moor, Gerrits, Congedo, et al., 2009; LaVaque et al., 2002). First, our previous study reported positive results for children with pervasive developmental disorders – not otherwise specified (PDD-NOS), a relatively mild form of ASD. However, neurofeedback might also benefit children with more severe subtypes of ASD. The present study investigated neurofeedback treatment in children from the full autistic spectrum. Second, in contrast to the fixed treatment protocol that was used in our first study (Kouijzer, de Moor, Gerrits, Congedo, et al., 2009), i.e. reduction of 4–7 Hz power and increase of 12–15 Hz power at location C4, frequency bands and electrode placement for treatment in this study were adjusted to the individual quantitative electroencephalogram (QEEG) of each participant, which is referred to as individualized or QEEG-guided neurofeedback (Cohen & Padolsky, 2007; Heinrich et al., 2007; Walker & Kozlowski, 2005). Third, our first study found consistent changes in theta and low beta power over subsequent neurofeedback sessions, but no transfer of these changes in theta and low beta power to QEEG as measured during rest. In the present study, we extended analysis at the neurophysiological level by investigating transfer effects of neurofeedback on QEEG data during a variety of rest and task conditions. Fourth, evaluation of the procedure of the previous study revealed that the investment of time and energy of parents and children to visit the neurofeedback practice twice a week was extensive. In the present study, feasibility of neurofeedback treatment was increased by implementing neurofeedback treatment in the school programs of the participants. Finally, effects on behavior in our previous study were evaluated only by parents. However, behavior of children with ASD often is expressed differently across different contexts and improvement in behavior might vary across contexts as well. This study assessed behavioral effects of neurofeedback both at home and at school by enclosing parent and teacher questionnaires.

This paper describes and discusses the results of individualized neurofeedback in ASD by comparing treatment and control groups before and after treatment. Participants were randomly divided into treatment and control group. Six months after treatment ended there was a follow-up for both treatment and control group. The present study has three aims. First, the effects of neurofeedback treatment on social behavior were investigated. We evaluated social interactions, communication skills, and stereotyped and repetitive behavior in the neurofeedback treatment and control group with behavior questionnaires filled out by parents and teachers. Second, the effects of neurofeedback treatment on executive functioning, i.e. attentional control, cognitive flexibility, goal setting, and speed and efficiency, were investigated using a range of neuropsychological tasks. Finally, the effects of neurofeedback treatment on brain activity were examined by investigating session data that were gathered during neurofeedback treatment and pre- and post-measures of QEEG.

1. Method

1.1. Participants

A total of 400 school files of two special education schools were screened to select participants for the present study. Inclusion criteria were an age between 8 and 12 years, an IQ-score of 80 and above, and the presence of autistic disorder. Asperger disorder or PDD-NOS according to the DSM-IV criteria as clinically diagnosed by a certified child psychiatrist or health care psychologist. Excluded were children using medication, children with a history of severe brain injury, and children with co-morbidity such as ADHD and epilepsy. Twenty children (17 males; 3 females) with a mean age of 9.3 years and a diagnosis of ASD were selected. Diagnoses were confirmed by an independent child psychiatrist who studied the files of the selected participants. Parents of all selected children signed informed consent. The protocol of the study was approved by the local medical ethics committee. Participants were randomly appointed to the neurofeedback treatment and the control group, although this resulted in uneven balanced diagnoses over groups. However, Social Communication Questionnaire (SCQ) data filled out by parents indicated that there were no initial differences in social interaction, communication, and limited and stereotyped behavior, $F(1,18) = 1.517, p = .251, \eta = .302$, between groups. An overview of the demographic characteristics of the treatment and the control group is given in Table 1.

1.2. Neurofeedback training

Neurofeedback shows the participant’s real time oscillatory brain activity on a computer screen and uses the principles of operant conditioning to influence or change this activity. During typical neurofeedback training, an electrode located at the scalp of the participant measures electroencephalographic (EEG) activity. This signal is amplified and filtered and
subsequently visualized on a computer screen via a bar graph, reflecting the amplitude of the particular frequency that is used for training. That is, the larger the amplitudes of the selected brain frequencies are, the higher the bar graph on the computer screen will be. While observing the amplitude of their own brain waves, the participant is instructed to “try to move down (or up) the brain activity using the feedback to guide you”. A criterion line is shown together with the bar graph reflecting a concrete goal during training, e.g. participants try to keep the bar graph beneath the criterion line. Visual and audio rewards fitting the participant’s individual age and interest are provided when the participant meets the criteria set by the criterion line. At first, changes in brain activity are short and mainly accidently, but after more training changes become more enduring and controlled.

The procedure within each of the 40 neurofeedback sessions comprised seven 3-min intervals of active neurofeedback training separated by 1-min rest intervals. During active training intervals, participants watched the computer screen while being motivated by the therapist to actively work on changes in the bar graph, i.e. their brain activity. Within each active training interval, criterion line placement was adapted to the participant’s ability to be rewarded 50–80% of the time. Fig. 1 illustrates the neurofeedback setting that was used in this study.

The neurofeedback treatment protocol of each participant aimed at decreasing excessive theta power at central and frontal brain areas. Frequency band and electrode placement on the scalp varied across participants and were based on the comparison between the participant’s individual QEEG and the Neuroguide database (Thatcher, Walker, Biver, North, & Curtin, 2003) that provides reliable descriptors of normative brain electrical activity and z-scores indicating deviances from normality per Hertz and per scalp location (John, Prichep, Fridman, & Easton, 1988). More information about the QEEG measures can be found under Neurophysiological measures in the Method section. Treatment protocols included Cz (n = 5), Fz (n = 2), and F4 (n = 3) as the main scalp locations that were used for neurofeedback training. The theta frequency bands that were used ranged from 3 to 7 Hz (n = 3), 3 to 8 Hz (n = 2), 3 to 6 Hz (n = 1), 4 to 7 Hz (n = 1), 4 to 8 Hz (n = 1), 5 to 7 Hz (n = 1), and 5 to 8 Hz (n = 1). All treatment protocols were evaluated at several times during treatment to accommodate participants’ reactions to the treatment such as tiredness and agitation.

### 1.3. Social behavior

Three questionnaires evaluating social interactions, communication skills, and stereotyped and repetitive behavior were filled out by parents and teachers, i.e. the Social Communication Questionnaire (SCQ), the Social Responsiveness Scale (SRS), and the Children’s Communication Checklist (CCC-2).
1.3.1. SCQ

The version ‘Current situation’ of the SCQ (Rutter, Bailey, & Lord, 2003; translated by Warreyn, Raymaekers, & Roeyers, 2004) generates a total score and sub-scores for social interaction, communication, and limited and stereotyped behavior based on behavior of the last three months. An example of a question is ‘Does he ever use your hand as a tool as it was part of his or her own body?’ and response categories are ‘yes’ and ‘no’. This questionnaire is based on items of the Autism Diagnostic Interview – Revised (ADI-R). The primary dependent measure for social behavior was the SCQ Total scale calculated by the sum of the three SCQ subscales.

1.3.2. SRS

The SRS (Constantino, 2002; translated by Roeyers, Thys, & Schittekatte, 2009) investigates whether 65 examples of behavior are ‘not true’, ‘sometimes true’, ‘often true’ or ‘always true’ during the last six months. An example of an item is ‘His or her facial expressions correspond with his or her verbal expressions’. A total score and sub-scores for Awareness, Cognition, Communication, Motivation, and Autistic mannerisms are calculated.

1.3.3. CCC-2

The CCC-2 (Bishop, 2003; translated by Geurts, 2007) assesses improvement in children’s language structure, pragmatics, and social interaction. Language structure includes the subscales speech production, syntax, semantics, and coherence. Pragmatics consists of the subscales inappropriate initiation, stereotyped conversation, use of context, and non-verbal communication. Social interaction includes the subscales social relations and interests. An example of an item is ‘Does not look at the person to whom he or she is talking’ and response categories for each question are ‘never or less than once a week’, ‘at least once a week, but not every day’, ‘once or twice a day’, and ‘more than twice a day or always’. An age-related standard score was calculated for each subscale, for pragmatics, and for the total score comprising language structure and social interaction.

1.4. Executive functions

According to Anderson (2002), executive functions are typically divided into separate sub-domains, i.e. attentional control, cognitive flexibility, goal setting, and speed and efficiency. Each domain is represented by one or more executive function tasks. Selection of the tasks in this study was based on outcomes of our previous study (Kouijzer, de Moor, Gerrits, Congedo, et al., 2009).

1.4.1. Attentional control

Attentional control encompasses selective attention and response inhibition. Selective attention was measured by the Test of Sustained Selective Attention (TOSSA; Kovács, 2005b). In the TOSSA, participants have to respond to sets of 3 beeps while ignoring sets of 2 or 4 beeps. Beeps are presented during 8 min at variable speed. The test score reflects the percentage of correct answers, calculated by dividing the number of hits by the total amount of items, times 100. Response inhibition is divided in a verbal and a motor variant. Verbal response inhibition was assessed by the Stroop test (Stroop, 1935). In this test, participants have to read aloud as soon as possible (A) 100 words (green, red, yellow, and blue), (B) the color of 100 colored rectangles, and (C) the color of the ink of 100 written incongruent color names. The goal in part C is to pronounce the name of the color of the ink, while ignoring reading the word. The score on this test is the interferential time (time C minus time B) and represents the primary dependent measure of executive functioning in the present study. Motor response inhibition was assessed with the response inhibition score (RIS; range 0–100) of the TOSSA, based on the number of commission errors.

1.4.2. Cognitive flexibility

Cognitive flexibility covers set-shifting and concept generation. Set-shifting was examined by the Trail Making Test (TMT; Reitan, 1956). Participants have to (A) connect 26 numbers, (B) connect 26 characters, and (C) switch between the numerical mode and the alphabetic mode by connecting 26 numbers and characters in the 1-A-2-B-3-C – order. A score on the TMT is calculated by subtracting the time needed to finish part C and the time needed to finish part B in seconds. Concept generation was examined by the Milwaukee Card Sorting Test (MCST; Kovács, 2005a), a computerized version of the Wisconsin Card Sorting Test. The participant has to generate and apply a non-spoken rule for sorting cards (n = 60), based on feedback (e.g. ‘good’ or ‘fault’). These card sorting principles can be either color, shape or number and change after every 10 correct answers. An indicator for cognitive flexibility is the percentage (0–100%) of cases in which a participant gives the right answer.

1.4.3. Goal setting

Goal setting was assessed by the Tower of London (TOL; Kovács, 2005c). Participants have to copy a construction of blocks and bars by moving three prearranged different colored blocks along three bars of different lengths. The score on the TOL is a percentage calculated by dividing the participants’ score by the maximum score, times 100.

1.4.4. Speed and efficiency

Speed and efficiency was assessed by a computerized Stroop task that shows 90 words (red, blue or green) on a computer screen for 2 s, written with either congruent or incongruent color of ink. In case of corresponding ink color and word,
participants push the left mouse button, in case of non-corresponding ink color and word, participant push the right mouse button. Reaction times in seconds for incongruent items were used for analysis.

1.5. Neurophysiological measures

1.5.1. Session data

During all neurofeedback sessions, training equipment recorded oscillatory activity at the location where the electrode was pasted. Ground and reference electrodes were attached to the mastoids. Training equipment included a portable Nexus-4 amplifier and recording system (Mindmedia, the Netherlands). Ag/AgCl disposable snap-on sensors (MedCaT, the Netherlands) were used.

1.5.2. QEEG

A quantitative electroencephalogram (QEEG) is an assessment tool to determine individual differences in EEG oscillations along different frequency bands. A Mitsar EEG 201 System (Mitsar Medical Diagnostic Equipment, Russia) was used for recording and digitizing EEG. Data were acquired using a stretchable electrode cap containing 19 sensors at scalp locations Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, and O2, according to the International 10/20 System (Jasper, 1958). Two ear clips were used as reference electrodes. Impedance was kept below 5 kΩ, with a maximum difference of 1 kΩ between electrodes. Data were collected for 3 min in rest and task conditions. Rest conditions involved an Eyes open and an Eyes closed condition in which participants were instructed to sit quietly and relax, either with their eyes open, or closed, for 3 min. Task conditions involved a Stroop task as described under Executive functions, Speed and efficiency and a Movement task in which participants had to open and close their fist while watching their own movement. The Stroop task was included to investigate levels of theta activation during cognitively demanding conditions, considering the possibility that effects of neurofeedback training may become apparent during the actual conditions that require modulation of these components (i.e. Stroop performance is known to modulate theta; Hanslmayr et al., 2008). The Movement task was included because children with ASD may experience less agency over their movements resulting in difficulty in anticipating the consequences of their actions (Schmitz, Martineau, Barthélemy, & Assaiante, 2003). Impairments in agency may be reflected in theta activation accompanying deactivation of cortical midline structures in association with agency loss (Scheerina et al., 2008; Spengler, von Cramon, & Brass, 2009). QEEG data were collected during all four conditions, first before (Time1) and later after treatment (Time2).

1.6. Procedure

The study started with a baseline assessment (Time1) including a series of behavioral questionnaires completed by parents and teachers, a range of executive functions tasks, and QEEG recording. Participants were then randomly divided into treatment and control group. Individualized neurofeedback treatment protocols were developed for participants of the treatment group as described under Neurofeedback training. Shortly after, participants of the treatment group started neurofeedback training twice a week at their own schools and during school hours. After 40 sessions of neurofeedback (Time2) and a comparable time interval for the control group, data on social behavior, executive functions, and QEEG were re-collected. Six months after ending all neurofeedback sessions (Time3), the same measures were collected again in a follow-up. Teachers did not fill out behavioral questionnaires at Time3, because the summer holidays were in between Time2 and Time3 and pupils changed classes after the summer holidays.

1.7. Data analysis

1.7.1. Social behavior

Results of a one-sample Kolmogorov–Smirnov test showed that questionnaire data did not deviate significantly from normality. Besides, MANOVA demonstrated that treatment and control group showed no differences at any questionnaire scale at Time1. $F(1,18) = 3.334, p = .409, \eta = .983$. All outcome measures were analyzed with Time × Group repeated measures MANOVA. Follow-up data were analyzed by Time (Time2 vs Time3) × Group and Time (Time1 vs Time3) × Group repeated measures MANOVAs. The comparison between Time1 and Time3 could not be done for teacher questionnaires, since the summer holidays were in between Time2 and Time3 and participants changed classes after the summer holidays.

1.7.2. Executive functions

Results of a one-sample Kolmogorov–Smirnov test showed that data concerning attentional control, cognitive flexibility, goal setting, and speed and efficiency did not deviate significantly from normality. Besides, MANOVA demonstrated that treatment and control group showed no differences at any test for executive functions at Time1, $F(1,18) = .907, p = .544, \eta = .397$. All outcome measures were verified by Time × Group repeated measures MANOVAs. Follow-up data were analyzed by Time (Time2 vs Time3) × Group and Time (Time1 vs Time3) × Group repeated measures MANOVAs.

1.7.3. Session data

EEG data of all participants were recorded during 40 neurofeedback sessions at the scalp location where the electrode was placed for training. Eye blinks and other artifacts were manually removed. Data from a consecutive period of training at one
significant differences between treatment and control group,

\( F(1,18) = 9.874, p < .01, \eta = .367. \) Subsequent analyses revealed a main effect of Time indicating improvement in social behavior for the treatment group, \( F(1,9) = 24.962, p < .001, \eta = .735, \) but not for the control group, \( F(1,9) = .497, p = .501, \eta = .058. \) Other questionnaires were analyzed with a Time (2) x Group (2) x Questionnaire (2) repeated measures MANOVA revealing a significant three-way interaction, \( F(1,18) = 6.276, p < .05, \eta = .270. \) Subsequent analyses revealed a main effect of Time indicating improvement in social behavior for the treatment group, \( F(1,9) = 10.628, p < .01, \eta = .541, \) but not for the control group, \( F(1,9) = .007, p = .936, \eta = .001. \) Table 2 shows means and standard deviations of all questionnaire’s total and subscale scores of treatment and control group and corresponding \( p \)-values of univariate Time (2) x Group (2) interactions. Lower mean scores indicate less problematic behavior.

2.1.2. Teacher informant

Analysis of the primary dependent measure of social behavior, i.e. the SCQ Total score, with a Time (2) x Group (2) repeated measures MANOVA revealed no significant interaction effect, \( F(1,18) = .341, p = .566, \eta = .019. \) The other questionnaires were analyzed with a Time (2) x Group (2) x Questionnaire (2) repeated measures MANOVA and revealed no significant differences between treatment and control group, \( F(1,18) = 1.181, p = .292, \eta = .062. \) Means, standard deviations, and corresponding \( p \)-values can be found in Table 3, with lower scores indicating less problematic behavior.

2.2. Executive functions

Tasks taxing attentional control, cognitive flexibility, goal setting, and speed and efficiency before (Time1) and after treatment (Time2) were compared for treatment and control group using Time (2) x Group (2) repeated measures MANOVAs. Means, standard deviations, and \( p \)-values of Time x Group interactions can be found in Table 4. Higher scores indicate improvement of executive functions, except for inhibition of verbal responses, shifting, and speed and efficiency. Analysis of the primary dependent measure of executive functioning, i.e. the Stroop interferential time, with a Time (2) x Group (2) repeated measures MANOVA revealed no significant interaction effect, \( F(1,18) = 1.454, p = .243, \eta = .075. \) The other measures of cognitive performance were analyzed with a Time (2) x Group (2) x Executive function (6) repeated measures MANOVA revealing a significant three-way interaction, \( F(1,18) = 3.735, p < .05, \eta = .633. \) Further analysis revealed a significant Time x Group interaction for set-shifting, \( F(1,18) = 4.652, p < .05, \eta = .205. \) Subsequent analysis revealed a main effect of Time for the treatment group indicating significant improvement, \( F(1,18) = 3.555, p < .05, \eta = .221, \) but not for the control group, \( F(1,18) = .427, p = .530, \eta = .045. \) No significant effects were found for other domains of executive functioning, \( p > .05. \)

2.3. Session data

Reduction of theta power at central and frontal locations comprised the main part of treatment for all participants. Correlations between Time and theta power were calculated for all participants of the treatment group. Spearman’s correlation coefficients were calculated for the relation between EEG power and Time, i.e. the number of completed sessions.

1.7.4. QEEG

Eye blinks and other artifacts were manually removed from the raw EEG data, based on a screening of electrodes Fp1 and Fp2 for eye blinks, electrodes F7 and F8 for horizontal eye movement, and the full EEG for head movement and muscular interference. The artifactual raw data of the remaining 15 electrodes (F3, Fz, F4, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, and O2) were processed with fast Fourier transformations. Grand averages were calculated in each of four conditions (Eyes open, Eyes closed, Stroop, Movement) to determine individual location and frequency with maximum theta power. Data were analyzed in a Condition x Time x Group repeated measures MANOVA.

1.7.5. Correlation analysis between social behavior, executive functions, and neurophysiological data

Spearman’s correlation coefficients between behavior, executive functions, and neurophysiological data in the treatment group were calculated using improvement scores of each level. The primary dependent measures for behavior (SCQ Total score) and executive functioning (Stroop interferential time) and theta power in QEEGs were used for calculating improvement scores by subtracting Time2 and Time1 scores. Improvement in session data was represented by the correlation coefficient between EEG power and Time.

2. Results

2.1. Social behavior

2.1.1. Parent informant

Three aspects of social behavior, i.e. social interactions, communication, and stereotyped and repetitive behavior, were compared before (Time1) and after treatment (Time2) for treatment and control group. Analysis of the primary dependent measure of social behavior, i.e. the SCQ Total score, with a Time (2) x Group (2) repeated measures MANOVA revealed a significant interaction effect, \( F(1,18) = 9.874, p < .01, \eta = .367. \) Subsequent analyses revealed a main effect of Time indicating improvement in social behavior for the treatment group, \( F(1,9) = 24.962, p < .001, \eta = .735, \) but not for the control group, \( F(1,9) = .497, p = .501, \eta = .058. \) Other questionnaires were analyzed with a Time (2) x Group (2) x Questionnaire (2) repeated measures MANOVA revealing a significant three-way interaction, \( F(1,18) = 6.276, p < .05, \eta = .270. \) Subsequent analyses revealed a main effect of Time indicating improvement in social behavior for the treatment group, \( F(1,9) = 10.628, p < .01, \eta = .541, \) but not for the control group, \( F(1,9) = .007, p = .936, \eta = .001. \) Table 2 shows means and standard deviations of all questionnaire’s total and subscale scores of treatment and control group and corresponding \( p \)-values of univariate Time (2) x Group (2) interactions. Lower mean scores indicate less problematic behavior.

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Tasks taxing attentional control, cognitive flexibility, goal setting, and speed and efficiency before (Time1) and after treatment (Time2) were compared for treatment and control group using Time (2) x Group (2) repeated measures MANOVAs. Means, standard deviations, and \( p \)-values of Time x Group interactions can be found in Table 4. Higher scores indicate improvement of executive functions, except for inhibition of verbal responses, shifting, and speed and efficiency. Analysis of the primary dependent measure of executive functioning, i.e. the Stroop interferential time, with a Time (2) x Group (2) repeated measures MANOVA revealed no significant interaction effect, \( F(1,18) = 1.454, p = .243, \eta = .075. \) The other measures of cognitive performance were analyzed with a Time (2) x Group (2) x Executive function (6) repeated measures MANOVA revealing a significant three-way interaction, \( F(1,18) = 3.735, p < .05, \eta = .633. \) Further analysis revealed a significant Time x Group interaction for set-shifting, \( F(1,18) = 4.652, p < .05, \eta = .205. \) Subsequent analysis revealed a main effect of Time for the treatment group indicating significant improvement, \( F(1,18) = 3.555, p < .05, \eta = .221, \) but not for the control group, \( F(1,18) = .427, p = .530, \eta = .045. \) No significant effects were found for other domains of executive functioning, \( p > .05. \)

2.3. Session data

Reduction of theta power at central and frontal locations comprised the main part of treatment for all participants. Correlations between Time and theta power were calculated for all participants of the treatment group. Spearman’s correlation coefficients were calculated for the relation between EEG power and Time, i.e. the number of completed sessions.
correlation coefficients showed significant reduction of theta power in six participants, ps < .05, rs = −.387 to −.832. Fig. 2 shows theta power of all participants of the treatment group.

2.4. QEEG

QEEG data were collected before (Time1) and after treatment (Time2). EEG data of both treatment and control group in the conditions Eyes open, Eyes closed, Stroop, and Movement were fast Fourier transformed. Time1 QEEG grand averages revealed maximal theta power in all participants and in all conditions at 5 Hz and at location Cz. Data in the 4–6 Hz band at Cz were therefore averaged for further analysis. Table 5 shows means and standard deviations of averaged 4–6 Hz power at Cz of participants that reduced theta power in session data and of the control group in each condition.

Time1 and Time2 theta power in each condition were compared for participants that successfully reduced theta power in session data and for the control group. Repeated measures MANOVA revealed a significant Time (2) × Group (2) × Condition (4) interaction, F(1,14) = 3.763, p < .05, η = .653. Further analysis showed decreases in theta power reflected by significant Time × Group interactions for the conditions Eyes closed, F(1,14) = 4.883, p < .05, η = .259, and Movement, F(1,14) = 7.856, p < .05, η = .359. Separate analysis of the two groups, however, revealed no main effects of Time for the condition Eyes closed for neither the treatment group, F(1,5) = 3.116, p = .138, η = .384, nor for the control group, F(1,9) = 1.340, p = .277, η = .130, suggesting that opposite directionality of effects in both groups contributed to the interaction. In the condition Movement there was an effect of Time for the treatment group, F(1,5) = 4.791, p < .05, η = .620, but not for the control group, F(1,9) = 2.433, p = .153, η = .213. The interaction between Time and Group for the condition Eyes open was not significant, F(1,14) = 1.828, p = .198, η = .115. No pre–post differences in theta power were found in the Stroop condition, F(1,14) = .018, p = .896, η = .001.

2.5. Correlation analysis for social behavior, executive functions, and neurophysiological data

Correlation analyses were conducted to find relations between changes in behavior, executive functions, and neurophysiological data within the treatment group. Spearman’s correlation analyses showed a positive correlation between improvement on the primary outcome measure for social behavior (SCQ) rated by parents and improvement on the primary outcome measure for executive functions (Stroop), r = .701, p < .05 (see Fig. 3). No such significant correlation was found for
the control group, \( r = -0.328, p = 0.389 \). Average decreases in QEEG theta power correlated significantly with decreases in theta power in the session data that were shown by 60% of the participants, \( r = 0.943, p < 0.01 \) (see Fig. 4).

### 2.6. Follow-up data

Social behavior was evaluated by parents six months after treatment ended (Time3) to investigate maintenance of effects. Comparing Time2 and Time3 data with repeated measures MANOVA revealed no significant Time × Group interaction, \( F(1,18) = 1.099, p = 0.380, \eta = 0.180 \), nor an effect of Time, \( F(1,18) = 0.306, p = 0.820, \eta = 0.058 \), suggesting maintenance of post-treatment levels six months after treatment ended. The comparison between Time1 and Time3 with repeated measures MANOVA revealed a significant Time × Group interaction, \( F(1,18) = 4.871, p = 0.05, \eta = 0.223 \). Separate analysis of treatment and control group revealed significant improvement for the treatment group, \( F(1,9) = 8.988, p < 0.05, \eta = 0.794 \), but...
not for the control group, $F(1,9) = .306$, $p = .820$, $\eta = .058$. Within the treatment group, improvement was found on all questionnaires, e.g. the SCQ, $F(1,9) = 22.043$, $p < .05$, $\eta = .710$, the SRS, $F(1,9) = 6.355$, $p < .05$, $\eta = .414$, and the CCC, $F(1,9) = 7.892$, $p < .05$, $\eta = .467$.

Follow-up data (Time3) on executive functions was compared with Time2 data by Time x Group x Executive function repeated measures MANOVA and revealed no significant interaction, $F(1,18) = .186$, $p = .671$, $\eta = .010$, suggesting

![Fig. 2. Session data: theta power of 10 participants during neurofeedback sessions.](image)

![Fig. 3. Correlation between improvement in social behavior and improvement in executive functioning. Note. Improvement in Stroop interferential time is represented by the interferential time on the Stroop task at Time2 minus the interferential time on the Stroop task at Time1. Improvement in SCQ Total score is represented by the total score of the SCQ at Time2 minus the total score of the SCQ at Time1.](image)

**Table 5**

Means and standard deviations of the average of 4, 5, and 6 Hz power at Cz for treatment and control group before (Time1) and after treatment (Time2).

<table>
<thead>
<tr>
<th></th>
<th>Treatment group</th>
<th></th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Time1 M (SD)</td>
<td>Time2 M (SD)</td>
<td>Time1 M (SD)</td>
</tr>
<tr>
<td>Eyes closed</td>
<td>6.071 (3.357)</td>
<td>4.921 (1.972)</td>
<td>5.666 (2.019)</td>
</tr>
<tr>
<td>Eyes open</td>
<td>4.584 (1.835)</td>
<td>4.087 (1.155)</td>
<td>5.515 (2.462)</td>
</tr>
<tr>
<td>Stroop</td>
<td>5.476 (2.746)</td>
<td>5.125 (1.663)</td>
<td>6.414 (3.289)</td>
</tr>
<tr>
<td>Movement</td>
<td>4.810 (1.533)</td>
<td>3.547 (1.517)</td>
<td>4.894 (1.805)</td>
</tr>
</tbody>
</table>

Note. $M$ = mean, $SD$ = standard deviation.
maintenance of post-treatment levels six months after treatment ended. The comparison between Time1 and Time3 with Time x Group repeated measures MANOVA revealed a marginal interaction effect, $F(1,18) = 2.513$, $p = .077$, $\eta^2 = .594$. Further analysis revealed a significant Time x Group interaction for set-shifting, $F(1,18) = 5.499$, $p < .05$, $\eta^2 = .234$. Subsequent analysis revealed a main effect of Time for the treatment group indicating significant improvement six months after treatment ended compared to baseline, $F(1,18) = 17.249$, $p < .05$, $\eta^2 = .976$, but not for the control group, $F(1,18) = 2.302$, $p = .265$, $\eta^2 = .843$.

3. Discussion

The present study was successful in generating effects of neurofeedback training at behavioral, cognitive, and neurophysiological outcome measures in a group of children with ASD as compared to a control group who received no training.

3.1. Behavioral outcome measures

Parents of children in the treatment group reported improvement on questionnaire subscales measuring reciprocal social interactions and verbal and non-verbal communication skills, compared to parents of children in the control group who indicated little or no improvement. This result is in line with studies of Jarusiewicz (2002), Coben and Padolsky (2007), and Pineda et al. (2008), who found improvement in social behavioral and communication skills after neurofeedback training as well. Jarusiewicz (2002), for example, found improvement in social interactions and communication measured with Autism Treatment Evaluation Checklist (ATEC) subscales such as ‘sociability’ and ‘speech, language, and communication’ in the treatment group, but not in the control group. In our previous study (Kouijzer, de Moor, Gerrits, Congedo, et al., 2009), significant improvements in social interactions, communication, and stereotyped and repetitive behavior were reported by parents of the neurofeedback treatment group. These results were maintained for at least one year (Kouijzer, de Moor, Gerrits, Buitelaar, et al., 2009). In the present study, follow-up measures after six months indicated maintenance of the results in behavior as well.

The positive effects of neurofeedback on reciprocal social interactions and communication skills reported by parents were not observed by teachers. There might be several reasons why this was the case. First, agreements on the rating of behavioral traits between different informants, i.e. parents and teachers, are often only moderate (Achenbach, McConaughy, & Howell, 1987; Ronald, Happé, & Plomin, 2008) and might explain different outcomes on parent and teacher questionnaires in the present study. Second, from behavioral analyses we know that context characteristics may influence behavior (Achenbach et al., 1987). That is, because the child’s home and classroom provide largely different contexts, this might have affected the behavior of the children and subsequent estimations of parents and teachers. Finally, autistic children may not automatically transfer newly acquired skills from one situation, for example at home, to other situations, for example the school. This generativity problem, which is often seen in autism (Hill, 2004), may have enhanced the variation of ASD subjects’ behavior across contexts.

![Fig. 4. Correlation between theta reduction in QEEG and theta reduction in session data for participants that were successful in using neurofeedback to decrease theta power. Note. Mean session data theta decrease is represented by the correlation coefficient between theta power measured during training and time, i.e. over the course of the training. Mean QEEG theta decrease is represented by the mean theta power at Time2 minus the mean theta power at Time1.](image-url)
3.2. Cognitive outcome measures

At the cognitive level, executive function tasks before and after neurofeedback treatment revealed improvement on set-shifting for the treatment group as compared to the control group who improved less. Additionally, there was a positive correlation between cognitive and behavioral task improvement; the more participants improved on the primary outcome measure for executive functioning, i.e. the Stroop task, the more improvement in behavior parents reported on the primary outcome measure for behavior, i.e. the SCQ questionnaire. Follow-up measures revealed that improvement in set-shifting was maintained for at least six months after neurofeedback treatment ended. Similar results were found in our previous study (Kouijzer, de Moor, Gerrits, Congedo, et al., 2009) where improvements on several executive function tasks including set-shifting were found after neurofeedback treatment. These results were maintained for at least one year.

3.3. Neurophysiological outcome measures

In addition to improvement at behavioral and cognitive levels, neurophysiological changes were found both during and after neurofeedback treatment, i.e. in EEG activity. Sixty percent of the participants in the present study succeeded to linearly decrease excessive theta activity over fronto-central scalp locations during neurofeedback training. Similar percentages were reported in previous studies (65%; Kouijzer, de Moor, Gerrits, Congedo, et al., 2009, 60–70%; Monastra et al., 2005). Furthermore, neurofeedback treatment was found to have an effect on theta power in participants’ QEEG that was recorded during post-treatment measures, in particular in the conditions Eyes closed and Movement, whereas no such effects were found in the control group. No differences between groups were found for the Stroop task and the Eyes open condition. Interestingly, decreases of theta power in session data and in QEEG were highly correlated, suggesting that the treatment induced reduction in theta power was sustained after neurofeedback treatment ended. It is however unclear at this point why reductions in theta activation were found selectively during Eyes closed and Movement conditions and not during Eyes open and the Stroop task.

Results of the present study indicate that autistic subjects were able to reduce slow wave brain activity and that neurofeedback caused changes in QEEG and improvement in set-shifting, reciprocal social interactions, and communication skills. It is interesting to speculate about the possible neurophysiological mechanisms underlying these outcomes. Neurofeedback treatment aimed at decreasing theta power, which is known to be generated in the medial prefrontal brain regions including the anterior cingulate cortex (ACC; Tsujimoto, Shimazu, & Isomura, 2006). The medial prefrontal cortex (MPFC) has been associated with executive functions and social cognitive ability and is likely involved in executive dysfunctioning and behavioral disturbances in autism (Bush, Luu, & Posner, 2000; Di Martino et al., 2009; Henderson et al., 2006; Mundy, 2003; Ohnishi et al., 2000). Ohnishi et al. (2000), for example, found that abnormal ACC activity was related to behavioral symptoms measured with the Childhood Autism Rating Scale (CARS).

Medial frontal theta power is inversely related to activation of medial prefrontal areas. The reduction of excessive theta power by neurofeedback in the present study thus might have enhanced activation of the MPFC and may thus have contributed to positive changes in set-shifting, reciprocal social interactions, and communication skills. Activation of the ACC by neurofeedback treatment was already demonstrated by Levesque, Beuregard, and Mensour (2006) who showed significant activation of the right ACC during a Stroop task in participants with ADHD after 40 neurofeedback sessions inhibiting theta power (4–7 Hz) and enhancing SMR (12–15 Hz) and beta power (15–18 Hz).

Parts of the ACC belong to the default mode network (DMN), which is found activated mainly during rest and tasks requiring self-reflection (Northoff et al., 2006; Raichle et al., 2001). The rostral ACC and posterior cingulate cortices are mainly found to activate during rest and self-reflective, social tasks, whereas the dorsal ACC typically deactivates in these conditions (Di Martino et al., 2009; Kennedy & Courchesne, 2008; Raichle et al., 2001; Scheeringa et al., 2008). In reverse, the dorsal ACC becomes activated during cognitive demanding tasks, whereas the rostral ACC and posterior cingulate cortices will deactivate (Bush et al., 2000; Raichle et al., 2001). In autistic subjects, both dorsal and rostral ACC and posterior cingulate cortices were found to be functionally and structurally abnormal (Cherkassky, Kana, Keller, & Just, 2006; Di Martino et al., 2009; Kennedy & Courchesne, 2008). A recent meta study of DiMartino et al. (2009), for example, reported hypoactivation of the dorsal and perigenual ACC during cognitive and social tasks respectively.

It is presently unclear which midline cortical structures were influenced by the current neurofeedback treatment. In both our previous and present studies, effects in theta power were most clearly visible at the central scalp location Cz. Luu and Tucker (2001) suggest that different parts of the ACC may contribute to theta activity at Cz. One explanation might be that neurofeedback treatment targeted dorsal ACC activity. This would mean that the neurofeedback treatment directly enhanced activation of areas in the ACC supporting executive functions, which may have contributed to the improvement in set-shifting that was found. Set-shifting refers to the ability to reflect on more than one set of rules and to shift rapidly between different actions or thoughts in reaction to changes in the context (Hill, 2004). Dealing with changes in schedules and procedures in daily life requires set-shifting and is crucial in showing socially adjusted behavior (Anderson, 2002). Set-shifting might be a basic skill for a variety of daily pursuits, such as reciprocal social interactions and communication skills. The improvements in set-shifting skills that were found in the present study might arise from enhancing activation in the dorsal ACC and may have contributed indirectly to the improvements in reciprocal social interactions and communication skills that were observed by parents. Another possibility is that neurofeedback treatment affected theta power in the rostral ACC and the posterior cingulate cortex. Enhancing activation in the rostral ACC and the posterior cingulate cortex would be...
expected to support social interactions and self-reflection, which could underlie the reported improvements in subjects’ reciprocal social interactions and communication skills indicated by parents. Furthermore, enhancing subjects’ ability to modulate activity in rostral ACC and posterior parts of the DMN might positively affect operation of these areas. This is, during cognitive tasks, enhanced activation of the dorsal ACC is typically supported by lowering activation in the DMN. The clear correlation between improvement in behavior measured with the SCQ and improvement on the cognitive Stroop task supports the hypothesized relation between social and executive functions of the ACC.

Interestingly, compared to other studies that found theta power maximal at electrode site Fz (Ishii et al., 1999; Meltzer, Negishi, Mayes, & Constable, 2007; Onton, Delorme, & Makeig, 2005), the current study found maximal effects of theta power at Cz. The most likely explanation is that our study included children who typically show enhanced theta power more posterior than adults (Yordanova & Kolev, 1997). Future research should clarify the involvement of the rostral and dorsal ACC and posterior cingulate cortices in neurofeedback treatment to further elaborate the neurophysiological basics underlying the efficacy of neurofeedback treatment.

### 3.4. Limitations

Randomized, controlled research should disentangle specific and unspecific effects of neurofeedback treatment (Heinrich et al., 2007). Although participants in the present study were randomly appointed to treatment and control conditions, we cannot exclude effects of parents’ expectations on the questionnaire data. Nevertheless, a positive correlation between behavioral improvements as indicated by parents and improvements on a non-biased executive functioning task suggests that parents’ evaluations were in line with the more objective measures of cognitive performance. Besides expectations of parents, teachers filling out behavioral questionnaires before and after treatment were also expected to have expectations of the behavior of their pupils who had neurofeedback treatment, especially because treatment was carried out at school and during their classes. However, no effect of expectation was found in the teacher questionnaires.

In addition to expectation biases, results at behavioral, cognitive, and neurophysiological levels could be biased by differences in attention that were given to both groups. Providing high amounts of time and attention to a group of participants might have positively affected these participants, rather than the treatment was truly effective. Providing an attention placebo to the control group would control for possible attention differences between groups and thereby helps to disentangle specific and unspecific effects of neurofeedback treatment.

### 3.5. Recommendations

Intervention programs should control for unspecific effects that might affect the outcomes of the study by carefully designing adequate research designs. As was mentioned earlier, parents’ expectations of the treatment and the provision of time and attention to the treatment group could have influenced the data. Future research should disentangle these biases.

As indicated by Heinrich et al. (2007), investigating the optimal neurofeedback protocol for each participant is necessary in further developing neurofeedback as an intervention for children with ASD. First, attention has to be paid to the frequency of training. In both our previous and present studies, neurofeedback sessions were successfully conducted twice a week until 40 sessions were completed. Whether this is the optimal composition of a neurofeedback treatment for children with ASD, however, is unknown. Second, procedures for determining scalp locations for electrode placement and frequency bands to be used for training have to be investigated. Autism has been referred to as a spectrum disorder ranging from a relatively mild to severe disorder and encompasses a broad range of symptoms. Therefore, it has been recommended to adapt interventions for autistic children to the individual needs of each participant (Howlin, 1998). In contrast to our previous study (Kouijzer, de Moor, Gerrits, Congedo, et al., 2009) where one single treatment protocol was applied to all participants, i.e. inhibition of 4–7 Hz and stimulation of 12–15 Hz at C4, frequency bands and scalp locations in the present study were based on outcomes of QEEG comparisons with a normative database and therefore optimally adapted to each participant. In all cases, treatment protocols comprised the inhibition of a frequency range within the theta band between 3 and 8 Hz. Scalp locations varied between Cz, Fz, and F4. Both neurofeedback treatments using fixed (Kouijzer, de Moor, Gerrits, Congedo, et al., 2009) and individualized treatment protocols thus appeared to be successful. The added value of individualized neurofeedback over fixed treatment protocols should be studied more directly in a single study.

### 3.6. Conclusion

Children with ASD that participated in the present neurofeedback study were able to reduce excessive theta power by neurofeedback, as was demonstrated by 60% of the participants. QEEG measures indicated significant decreases of theta power over medial frontal brain regions, suggesting a structural enhancement of activation of the ACC. Furthermore, reciprocal social interactions, communication skills, and set-shifting skills improved after neurofeedback treatment. Although there were biases in the study design concerning parents’ expectations and time and attention provided to both groups, these results suggest that neurofeedback treatment has the potential to become an important and prominent intervention for children with ASD.
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References


