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Long-term effects of neurofeedback treatment in autism

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A B S T R A C T

Previously we demonstrated significant improvement of executive functions and social behavior in children with autism spectrum disorders (ASD) treated with 40 sessions of EEG neurofeedback in a nonrandomized waiting list control group design. In this paper we extend these findings by reporting the long-term results of neurofeedback treatment in the same group of children with ASD after 12 months. The present study indicates maintenance of improvement of executive functions and social behavior after 12 months in comparison with the immediate outcomes. Neurofeedback mediated suppression of theta power is supposed to promote more flexible functioning of the brain by enhancing activation in the medial prefrontal cortex and improving flexibility of activation in the default mode network supporting the improvement of executive functions and theory of mind in ASD.

In the evaluation of any treatment, it is extremely important to gather information about the long-lasting effects of treatment by collecting follow-up data. Follow-up research aims to measure effects of treatment over time to determine if the treatment has resulted in a structural improvement or if clients relapsed to pre-assessment levels. The importance of follow-up data for the evaluation of neurofeedback has been noted repeatedly. Heinrich, Gevensleben, and Strehl (2007), for example, suggest investigation of clinical outcomes, spectral EEG analysis, and neuromodulatory skills using at least a 6-month follow-up interval. Despite many recommendations, the use of follow-up in evaluating neurofeedback as a treatment for several disorders has been used only in a few studies. In

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ADHD, the population in which most of the neurofeedback research has been performed, follow-up data were only collected by Tansey (1993) in a case study and by Lubar (2003) in a retrospective study of 52 patients who ended neurofeedback treatment 1–10 years before. Recently, follow-up data after 6 months was reported by Leins et al. (2007).

In a recent study, we reported the results of neurofeedback treatment in children with autism spectrum disorders (ASD) as compared to a waiting list control group (Kouijzer, De Moor, Gerrits, Congedo, & Van Schie, 2009). Treatment consisted of 40 sessions of neurofeedback and included inhibition of theta activity (4–7 Hz) and rewarding low beta activity (12–15 Hz) over the right hemisphere. It was hypothesised that this induced change in EEG-power enhanced activation of the anterior cingulate cortex (ACC) that has been found to be underactivated in clients with ASD (Cherkassky, Kana, Keller, & Just, 2006), and improved ASD subjects' executive functioning and social behavior. Session data gathered during neurofeedback treatment revealed a clear and consistent linear decrease in theta power and an increase in low beta power over 40 sessions. On tasks taxing executive functioning, significant improvement in the treatment group was found for attention control, cognitive flexibility, and planning in comparison with the waiting list control group. Analysis of the CCC-2 and Auti-R questionnaires measuring social behavior of children with ASD revealed significant improvements in general communication and in non-verbal communication for children in the treatment group, but not for the waiting list control group. Furthermore, parents of children in the treatment group reported more improvement compared to parents of children in the control group on levels of social interaction, communication, and typical behavior. These parents also reported to be highly contented with the results. A follow-up after three months revealed maintenance of the described outcomes on both executive functioning and social behavior. See Kouijzer et al. (2009) for detailed explanation of the improvement in executive functioning and for an explanation of the tasks that were used.

The present study investigates maintained or increased performance in executive functioning and social behavior by comparing 12 months follow-up data (follow-up) with data gathered before (pre-assessment) and immediately after treatment (post-assessment). Maintenance of benefits of neurofeedback treatment would be demonstrated if, firstly, no significant decrease in performance is found between follow-up and post-assessment. Second, a comparison between follow-up and pre-assessment was made in order to confirm the significant effects of neurofeedback treatment in ASD in line with Kouijzer et al. (2009). No significant changes were expected in QEEG, since no significant differences between pre- and post-assessment were found in our earlier study.

1. Methods

1.1. Participants

Participants of the present study were the same as in our earlier study (Kouijzer et al., 2009) and consist of fourteen children with ASD (12 males; 2 females) with a mean age of 10.1 years (range 8–12 years). All children had an IQ-score of 70 and above and a diagnosis of ASD (subtype pervasive developmental disorder—not otherwise specified, PDD-NOS), according to the criteria of DSM-IV conferred by a child psychiatrist or licensed psychologist. Each diagnosis was confirmed by a clinical psychologist and by results on the CCC questionnaire. None of the children used medication, had a history of severe brain injury, or had co-morbid diagnoses such as ADHD and epilepsy. The seven children who applied first, were assigned to the intervention group. The control group included seven children who were recruited out of a larger group of children who applied later and were selected to match children of the intervention group on age, sex, and intelligence scores. There were no significant differences between both groups with respect to the variables sex, mean age, total IQ, verbal IQ, and performal IQ. Most participants in the control group subscribed for neurofeedback treatment after ending participation in the waiting list control group.

1.2. Materials and procedure

Assessment of all participants during follow-up followed the same procedure and used the same materials, questionnaires and tests as in pre- and post-assessment. All participants performed tasks to

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assess four sub domains of executive functioning, i.e. attentional control, cognitive flexibility, goal setting, and speed and efficiency (Smidts, 2003). Parents of all children filled out two questionnaires about social interaction, communication, and typical behavior (CCC-2 and Auti-R). A detailed explanation of tasks and questionnaires can be found in Kouijzer et al. (2009).

2. Results

2.1. Executive functioning

For the comparison of results on executive functioning tasks between post-assessment and follow-up, a MANOVA with within-subject factor Time was performed. Table 1 reports means and standard deviations of all executive function tasks. Higher scores reflect better executive functioning, except on tasks evaluating visual selective attention and inhibition of verbal responses. On these tasks, lower scores indicate better results.

When post-assessment and follow-up data were compared, a significant improvement in auditory selective attention (F (1,6) = 16.248, $p < .010$, $\eta = .765$) between post-assessment and follow-up was found, indicating continuation of improvement of selective attention after 12 months. Furthermore, a marginal significant improvement was found for inhibition of motor responses (F (1,6) = 4.560, $p = .086$, $\eta = .477$). Non-significant improvement was found for inhibition of verbal responses (F (1,6) = .479, $p = .520$, $\eta = .087$), verbal memory (F (1,6) = 2.791, $p = .156$, $\eta = .358$), concept generation (F (1,6) = .152, $p = .713$, $\eta = .029$), and speed and efficiency (F (1,6) = .572, $p = .483$, $\eta = .103$). No significant decrease of performance was found between post-assessment and follow-up data on any aspect of executive functioning.

To compare follow-up data with pre-assessment data, a MANOVA with within-subject factor Time was conducted. Results confirmed the significant improvement of the treatment group for the same variables that were found improved in the previous comparison between pre- and post-assessments, i.e. sustained auditory selective attention (F (1,6) = 39.201, $p < .01$, $\eta = .887$), inhibition of verbal responses (F (1,6) = 15.458, $p < .05$, $\eta = .756$), inhibition of motor responses (F (1,6) = 10.696, $p < .05$, $\eta = .681$), set shifting (F (1,6) = 27.802, $p < .01$, $\eta = .848$), concept generation (F (1,6) = 18.540, $p < = .01$, $\eta = .788$), and planning ability (F (1,6) = 21.420, $p < .01$, $\eta = .811$). Consistent with the comparison between pre- and post-assessment data, none of the remaining scales showed a significant difference between pre-assessment and follow-up data (all F's < 1).

2.2. Behavior

For the comparison of communication skills assessed by the CCC-2 questionnaire between post-assessment and follow-up, a MANOVA with within-subject factor Time was conducted. In Table 2 the

Table 1
Mean (standard deviation) scores on tests for executive functions at pre-assessment, post-assessment, and follow-up.

	Pre-assessment	Post-assessment	Follow-up
Attentional control			
Visual selective attention[a]	4.33 (2.81)	4.17 (4.26)	4.71 (1.89)
Auditory selective attention	47.87 (14.21)	62.40 (14.18)	75.27 (13.79)
Inhibition of verbal responses[a]	68.17 (18.87)	30.00 (12.12)	26.50 (11.11)
Inhibition of motor responses	78.50 (13.16)	89.93 (9.20)	95.90 (4.13)
Cognitive flexibility			
Verbal memory	53.33 (3.62)	52.17 (4.07))	56.29 (2.14)
Visual memory	46.00 (3.74)	45.00 (4.34)	43.14 (4.10)
Shifting	30.00 (15.68)	47.00 (13.27)	47.86 (10.11)
Concept generation	2.55 (1.48)	4.96 (.45)	5.06 (.39)
Goal setting	55.45 (9.07)	75.85 (9.17)	72.83 (5.46)
Speed and efficiency	34.33 (7.06)	41.33 (5.13))	43.67 (10.86)

[a] Decrease in scores indicates improvement. For other scales, increase in scores indicates improvement.

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Table 2
Mean (standard deviation) scores on the CCC-2 at pre-assessment, post-assessment, and follow-up.

	Pre-assessment	Post-assessment	Follow-up
General communication	115.14 (10.45)	101.29 (12.09)	101.83 (16.34)
Pragmatics	60.57 (7.00)	54.14 (5.579)	53.00 (7.48)
Speech production	12.86 (2.54)	10.86 (2.96)	11.71 (3.50)
Syntax	12.71 (1.89)	11.29 (2.69)	11.28 (3.45)
Semantics	12.29 (2.29)	12.00 (2.08)	11.43 (2.64)
Coherence	15.43 (1.81)	14.28 (1.50)	13.29 (4.57)
Inappropriate initialization	14.29 (1.89)	13.86 (1.57)	11.86 (3.76)
Stereotyped conversation	15.14 (2.27)	13.57 (1.81)	13.14 (1.95)
Context use	15.14 (1.77)	13.71 (1.80)	13.83 (2.14)
Non-verbal communication	15.86 (2.34)	13.71 (2.50)	13.00 (3.41)
Social relations	15.57 (1.90)	14.57 (2.07)	13.86 (3.76)
Interests	13.57 (1.90)	12.14 (3.67)	12.57 (3.31)

Note: Decrease in scores indicates improvement.

Table 3
Mean (standard deviation) scores on the Auti-R at post-assessment and follow-up.

	Post-assessment	Follow-up
Total score	113.83 (7.17)	109.67 (9.63)
Social interaction	36.50 (3.51)	35.00 (5.62)
Communication	29.00 (1.79)	29.17 (3.43)
Typical behavior	48.33 (3.44)	45.50 (2.17)

average ratings of children's communication skills are reported for sub- and compound-scales of the CCC-2. Lower values reflect better communication skills.

Subscales that significantly improved previously in the comparison between pre- and post-assessment data, maintained at the same level when post-assessment and follow-up were compared, i.e. general communication (F (1,6) = .016, p = .904, η = .003) and non-verbal communication (F (1,6) = .578, p = .476, η = .088). Subscales that were not significant in the previous analysis did not show significant changes either (range of F-values = .000–3.111, p's > .05, range of η's = .000–.341). This finding confirmed the hypothesis that behavioral improvement after neurofeedback treatment was continued after 12 months. Next, follow-up data was compared with pre-assessment data. Similar to the previous analysis, a MANOVA with within-subject factor Time showed significant improvement for the treatment group for non-verbal communication (F (1,6) = 7.125, p < .05, η = .543), but no longer for general communication (F (1,6) = 2.745, p = .149, η = .314). Consistent with the comparison between pre- and post-assessment data, none of the remaining scales showed a significant difference between pre-assessment and follow-up data.

Results of the Auti-R questionnaire were analyzed by comparing post-assessment and follow-up data in a paired sample t-test for each of the scales on social interaction, communication, and typical behavior and for the complete questionnaire. Mean score's of each scale can be found in Table 3. Higher scores indicate better results. Post-assessment results already revealed increases of the treatment group on all scales of the questionnaire, i.e. social interaction, communication, and typical behavior. The comparison between post-assessment and follow-up data revealed no significant differences (range of t-scores: −.123 to 1.647, p's > .05), indicating maintenance of the results after 12 months.

3. Discussion

In our previous paper (Kouijzer et al., 2009), the results of 40 sessions of neurofeedback treatment in seven children with ASD as compared to a waiting list control group were described. Treatment comprised inhibition of theta activity (4–7 Hz) and rewarding low beta activity (12–15 Hz) over the right hemisphere. Session data gathered during neurofeedback treatment revealed a clear and consistent linear decrease in theta power and an increase in low beta power over 40 sessions. It was hypothesised that this induced change in EEG-power enhances activation of the anterior cingulate cortex (ACC) and improves ASD subjects' executive functioning and social behavior. Pre- and post-assessment revealed significant improvement in the treatment group for attention control, cognitive flexibility, and planning in comparison with the waiting list control group. Analysis of the CCC-2 and Auti-R questionnaires revealed significant improvement in social interaction, verbal and non-verbal communication skills, and typical behavior.

The present paper describes 12-month follow-up data that was compared with pre- and post-assessment data. First, analysis of follow-up data concerning executive functions revealed that effects that were found immediately after treatment were maintained or increased 12 months after ending neurofeedback. Second, follow-up data assessing social behavior revealed that children's immediate improvement on social interaction skills, communicative abilities, and typical behavior were maintained as well. Improvement in communication skills were long lasting as measured by the Auti-R questionnaire, and partly sustained according to the CCC-2 questionnaire. It can be concluded that neurofeedback resulted in long lasting improvement in executive functions and social behavior of children with ASD.

In line with our previous paper we suggest one particular mechanism to underlie the effects of neurofeedback on both executive functions and social behavior levels. This network comprises the default mode network (DMN) including the ACC. The ACC is one of the main generators of theta activity in the brain (Meltzer, Negishi, Mayes, & Constable, 2007; Onton, Delorme, & Makeig, 2005; Tsujimoto, Shimazu, & Isomura, 2006) and is well known for its role in regulating cognitive and emotional processes contributing to cognitive control and executive function (review in Bush, Luu, & Posner, 2000). As part of the DMN, the ACC is characterized by a high default metabolism during rest and inversely related to other areas that are activated during cognitive tasks. Kennedy, Redcay, and Courchesne (2006) found that autistic subjects, as compared with controls, did not deactivate their ACC in order to allow activation of other task relevant brain areas. By learning to reduce theta activity in the ACC by neurofeedback, structural hypo-activation of the ACC in subjects with ASD might have increased towards normal levels to allow functional activations and deactivations of the ACC in line with cognitive and executive demands. This increased flexibility of the DMN might allow other brain areas supporting cognitive functions to activate more effectively during cognitive tasks and therefore improve performance.

In contrast to the attenuation of activation in the DMN during tasks requiring cognitive control, the DMN is typically found to be activated during tasks requiring Theory of Mind (ToM). ToM is the ability to ascribe mental states, such as desires, beliefs, feelings, and intentions to oneself and to other people (Baron-Cohen, 2001). Carlson and Moses (2001) found ToM performance and executive functions to be closely interwoven in terms of developmental timetable (substantial growth in the preschool period), brain region (prefrontal cortex), and affected appearance in ASD. Because of this close relation between development and manifestation of ToM and executive functions, improved flexibility of the ACC of autistic individuals might support both executive functions and ToM performance. Where executive functions demand a decrease of ACC activation, optimal performance of ToM tasks requires activation in this area (Kennedy et al., 2006). Analysis of the present study cautiously confirms this hypothesis by revealing significant improvement in executive functions, social interaction, and communication skills for participants who received neurofeedback treatment.

The hypothesis that neurofeedback increases flexibility of the brain is supported by the results of the comparison between pre- and post-assessment of QEEG data in the previous study. QEEG data of participants in the treatment and the control group were not significantly different (Kouijzer et al., 2009), in contrast to the session data of the treatment group that showed a clear decrease of theta power and an increase in low beta power. A possible explanation for this apparently paradoxical finding is that neurofeedback allows the brain to function in a more flexible way and enables the brain to switch between different cognitive states more easily. The QEEGs used for this study were recorded during rest and therefore do not demonstrate changes in flexibility of the brain. Session data, however, were gathered during neurofeedback sessions when participants had a clear task to fulfil. A hypothesis to be tested in future research is the effect of neurofeedback on QEEGs collected during the performance of cognitive tasks, where theta activity has to be modulated.

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The present study revealed that in addition to the immediate effects of inhibiting theta power in combination with rewarding low beta power over the right hemisphere of the brain, neurofeedback improved executive functions and social performance over a prolonged period of time. Considering the above explanation, these results confirm the hypothesis that enhancement of activation in the ACC may have helped children with ASD to improve executive functions and ToM abilities structurally and long lasting.

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