

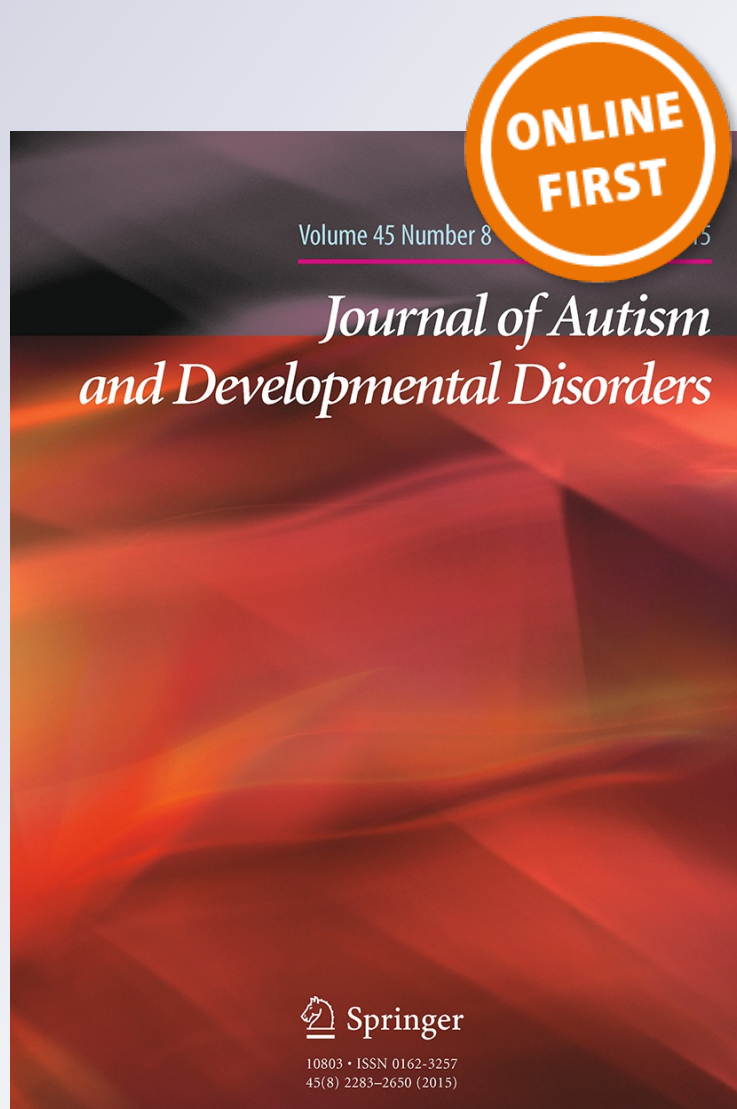
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An Effective Neurofeedback Intervention to Improve Social Interactions in Children with Autism Spectrum Disorder

Elisabeth V. C. Friedrich¹ · Aparajithan Sivanathan² · Theodore Lim² · Neil Suttie³ · Sandy Louchart^{3,4} · Steven Pillen¹ · Jaime A. Pineda¹

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Abstract Neurofeedback training (NFT) approaches were investigated to improve behavior, cognition and emotion regulation in children with autism spectrum disorder (ASD). Thirteen children with ASD completed pre-/post-assessments and 16 NFT-sessions. The NFT was based on a game that encouraged social interactions and provided feedback based on imitation and emotional responsiveness. Bidirectional training of EEG mu suppression and enhancement (8–12 Hz over somatosensory cortex) was compared to the standard method of enhancing mu. Children learned to control mu rhythm with both methods and showed improvements in (1) electrophysiology: increased mu suppression, (2) emotional responsiveness: improved emotion recognition and spontaneous imitation, and (3) behavior: significantly better behavior in every-day life. Thus, these NFT paradigms improve aspects of behavior necessary for successful social interactions.

Keywords Neurofeedback training (NFT) · Autism spectrum disorder (ASD) · Mu rhythm · EEG

Introduction

Autism spectrum disorder (ASD) is an increasingly prevalent condition, with statistics changing rapidly. Currently, approximately 1 in 68 children and 1 in 42 boys are affected, with boys 4–5 times more likely to develop ASD than girls (Blumberg et al. 2013; American Psychiatric Association 2013; CDC 2014). Children with high functioning ASD show deficits primarily in social and communicative skills such as imitation, empathy, and shared attention, as well as restricted interests and repetitive patterns of behaviors (American Psychiatric Association 2013). These deficits substantially impair normal social interactions and prevent children from establishing adequate relations with their family or friends during development. The aim of the current study was to train and enhance normative brain responses and behaviors during social interactions and provide the basis for accepted emotional reactions for children with ASD.

The approach taken in the current study utilized neurofeedback training (NFT), an operant conditioning of brain electrical oscillations (Serman and Egner 2006). NFT allows real-time information of brain activity to be fed back visually to a user by means of a computer in a closed loop, enabling control and natural operation of brain oscillations across cortical networks in vivo and in near real-time (Nowlis and Kamiya 1970; Wolpaw et al. 2002; Neuper et al. 2009). The possibility of volitional control of brain electrical activity suggests, provided that they play a causal role in cognitive functions, that their modulation can have a functional impact. Previous studies have shown that children with ASD learn to regulate such brain activity and produce brain patterns similar to those of typically-developing (TD) children, resulting in behavioral improvements (Pineda et al. 2008; Thompson et al. 2010; Coben et al. 2010).

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In the current study, the NFT is based on modulating the mu rhythm, an 8–12 Hz oscillation scalp-recorded noninvasively over somatosensory cortex with electroencephalography (EEG). The rationale for training this rhythm is its sensitivity to motor, affective, and cognitive imagery (Pineda 2008; Hari et al. 1997; Klimesch et al. 1997; Pfurtscheller et al. 2000; Keuken et al. 2011). Furthermore, mu rhythm amplitude can be suppressed by object-directed actions and during self-initiated, observed, and even imagined movement (Muthukumaraswamy and Johnson 2004; Pineda 2005; Neuper et al. 2009). Moreover, mu suppression is prominent when TD participants engage in social coordination (Naeem et al. 2012) or have the desire to socially connect with others (Aragón et al. 2013). Hence, changes in mu rhythm amplitude are closely related to social interactions and a function of the level of social interactivity involved (Oberman et al. 2007). In individuals with ASD, mu rhythm suppression is a phenomenon observed during self-performed movements but absent during the observation of another person's actions (Oberman et al. 2005; Bernier et al. 2007). As the mu rhythm is purported to be functionally linked to mirror neuron activity [mirror neuron system (MNS), Rizzolatti and Craighero 2004; Pineda 2005; Keuken et al. 2011; Arnstein et al. 2011; Muthukumaraswamy et al. 2004], this has led to the hypothesis that a lack of MNS activation in social situations could be an underlying cause for the observed deficits in empathy and imitation behavior in individuals with ASD (Nishitani et al. 2004; Hadjikhani et al. 2006; Oberman et al. 2005; Bernier et al. 2007; Théoret et al. 2005; Dapretto et al. 2006). However, this hypothesis is the object of critical debates (Enticott et al. 2013; Mostofsky et al. 2006; Stieglitz Ham et al. 2011; Hamilton 2013). Although the extant literature shows that it is still unknown whether an altered MNS and mu rhythm are a common underlying cause for ASD, there is generally more agreement that the mu rhythm is linked to the MNS and that both are related to imitation behavior and social communication (Bernier et al. 2013; Keuken et al. 2011; Arnstein et al. 2011; Pineda 2008; Muthukumaraswamy et al. 2004; Braadbaart et al., 2013), which makes the mu rhythm a reasonable object of investigation for NFT.

Most studies using mu-based neurofeedback have trained increases in mu power (as quantitative measure) resulting in a reduction of autistic symptoms as measured by parental assessments, as well as in enhanced mu suppression during movement observation in post- compared to pre-tests (Pineda et al. 2008, 2014). High mu power indicates a synchronized, relaxed and yet focused state and is assumed to be a prerequisite for mu suppression (Nowlis and Kamiya 1970; Pineda 2005), which is suggestive of more activation of the MNS (Oberman et al. 2008). Additionally, in previous studies, training mu rhythm

enhancement usually involved feedback that was unrelated to the significance of the mu rhythm or the anticipated behavioral changes (e.g., using the speed of a car as feedback for training the mu rhythm to activate the MNS and thus improve imitation behavior) (Pineda et al. 2008, 2014; Coben et al. 2010; Thompson et al. 2010).

As the current study aimed to explore improvements in mu-based NFT methods and specifically to link appropriate brain response, behavior and emotions during social interactions to reduce symptoms of ASD, a social video game platform was developed (Social Mirroring Game, Fig. 1; Friedrich et al. 2014b). First, this game includes social interaction sequences as well as non-social gaming episodes in order to make modulation of mu power in relation to the situational context possible. A group of children with ASD was rewarded for decreasing mu power in the social interaction sequences (i.e. activation of MNS) while increasing it in the non-social gaming episodes (i.e. relaxed state). This 'bidirectional' group (Group 2) was compared to the standard 'unidirectional' uptraining group in which increased mu power was rewarded (Group 1). Second, the game itself provided functionally-significant feedback. For both groups, the rewarding feedback during the social interactions was based on imitation and emotional responsiveness and involved the child's avatar imitating the facial expressions of the game character (Fig. 1). This role-play mechanism is a powerful tool for intervention on deficient social behaviors and can be used to adapt learned social skills from the game to the real-world of children with ASD (Bernardini et al. 2014).

In the current study, it was expected that children with ASD in both training groups would learn to control the Social Mirroring Game via NFT and show modulation of mu rhythm from baseline activity. Furthermore, the implementation of functionally-significant feedback was expected to result in significant symptom reduction. Finally, it was hypothesized that the bidirectional Group 2 would result in greater mu suppression to movement observation, social or emotional stimuli and more imitation behavior after NFT than the unidirectional Group 1 due to the bidirectional nature of the training.

Methods

Participants

Fifteen children with ASD participated in the current study, with two participants dropping out prior to completion. The remaining thirteen children completed pre- and post-tests and sixteen 1-h NFT sessions 2–3 times a week for 6–10 weeks (average 8 weeks duration). The participants had not participated in NFT previously and were

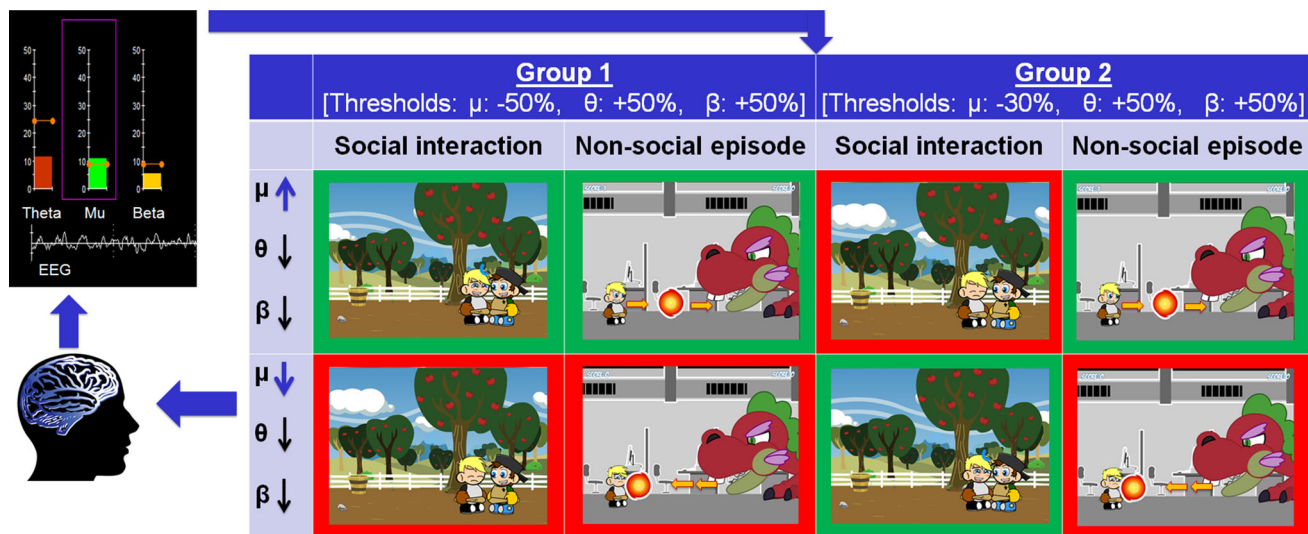


Fig. 1 Closed feedback loop of the Social Mirroring Game. The user's EEG was recorded and fed into the Social Mirroring Game, which gives the user visual feedback. Positive feedback (*green frame*) is provided by the child's avatar (i.e. child with the blond hair) imitating the non-player characters (NPC) facial emotions in the social interaction sequences and by winning in the non-social gaming episodes (e.g. hitting the dragon with a fireball). For negative feedback (*red frame*), no imitation behavior is shown in the social interaction sequences and the child's avatar loses in the non-social

gaming episodes (e.g. is getting hit by a fireball). Group 1 received positive feedback for enhancing mu power (μV^2) above the threshold in the social interaction as well as in the non-social gaming parts (for more details on the threshold settings, please see the section Study Design and Threshold Settings). Group 2 received positive feedback for decreasing mu power during the social interaction sequences and for enhancing mu power during the non-social gaming parts. Both groups had to decrease theta (θ) and beta (β) below the threshold in order to receive the reward (Color figure online)

6–17 years old (mean = 11.5 ± 3 years). Their diagnosis of ASD was verified by a clinician within a year prior to training and all of the children were able to understand the tasks and were compliant (Table 1). Participants were pseudo-randomly assigned to one of two training groups, Group 1 (unidirectional) or Group 2 (bidirectional). The mean age, cognitive skills and severity of autistic symptoms were comparable between groups (Table 1). The University of California, San Diego's Institutional Review Board approved the current study and participants and parents gave informed consent in accordance with the Helsinki Declaration.

Neurofeedback Training

EEG as well as peripheral physiological measurements were recorded during NFT using Thought Technology Ltd. (Canada) bioamplifiers and proprietary software. EEG was recorded from one electrode over right sensorimotor cortex (C4), sampled at 256 Hz and filtered for mu (8–12 Hz), theta (3–8 Hz) and high beta (18–30 Hz) frequency bands. The children were trained to modulate the frequency bands in the EEG. To increase mu power, children were asked to relax, while to decrease mu power, children were asked to imagine socially interacting with their friends. The beta and theta frequency bands, typically associated with blinks and overall muscle movements, were inhibitors of positive

feedback on the NFT when the amplitudes in these frequency bands exceeded a specified threshold (Fig. 1). Electromyography (EMG) was recorded from the superficial flexor muscles of the left forearm, sampled at 2048 Hz and filtered between 100 and 200 Hz. If a movement exceeded 10 μV , the positive feedback was inhibited in order to avoid children receiving positive feedback while moving, or learning to modulate mu activity over the right sensorimotor cortex by moving the left hand.

Social Mirroring Game

The children sat in front of a computer screen playing the Social Mirroring Game while physiological measures were recorded (Fig. 1; Friedrich et al. 2014b). The story plot of this game involves a treasure hunt to which the child's avatar gets invited by a friend (i.e. a non-player character, NPC). In the non-social gaming episodes, both characters pick apples to carry on their journey, fly a balloon over mountains to collect coins, and try to outmaneuver a dragon in order to get the treasure. During these episodes children can control the game by enhancing mu power. That is, a positive feedback, triggered by mu power exceeding a threshold, is translated into apples flying towards the bucket, coins streaming towards the child's balloon, and the dragon getting hit by a fireball. Negative feedback is indicated by the apples avoiding the bucket, the

Table 1 Participants

	Cut-offs	Group 1	Group 2
Number of Participants		6	7
Age		M = 11.8, SD = 3.9	M = 11.1, SD = 2.3
Gender		5 male, 1 female	7 male
Handiness		6 right-handed	6 right-handed, 1 ambidextrous
Intelligence test: full score		M = 93.3, SD = 22.6	M = 91.3, SD = 30.1
Verbal IQ		M = 90.5, SD = 18.4	M = 89.2, SD = 36.5
Performance IQ		M = 92.5, SD = 23.7	M = 95.3, SD = 25.3
Pre-test diagnosis			
VABS Composite score		M = 79.2, SD = 12.1	M = 81.7, SD = 12.4
SRS total score		M = 68.3, SD = 9.8	M = 77.0, SD = 16.3
ATEC total score		M = 28.8, SD = 23.6	M = 36.4, SD = 20.2
ADOS			
Communication	2	M = 4.8, SD = 1.5	M = 5.8, SD = 3.5
Reciprocal social interaction	4	M = 8.3, SD = 4.3	M = 9.8, SD = 3.0
Interaction and communication	7	M = 13.0, SD = 5.7	M = 15.5, SD = 6.1
Stereotyped behaviors	–	M = 2.3, SD = 3.2	M = 3.5, SD = 2.6
ADI-R			
Qualitative abnormalities in reciprocal social interaction	10	M = 24.3, SD = 2.1	M = 19.3, SD = 7.6
Qualitative Abnormalities in communication (verbal)	8	M = 21.3, SD = 1.5	M = 12.7, SD = 10.3
Qualitative abnormalities in communication (non-verbal)	7	M = 11.0, SD = 2.0	M = 8.0, SD = 6.6
Restricted, repetitive and stereotyped behaviors	3	M = 9.0, SD = 4.4	M = 8.3, SD = 4.0
Abnormality of develop evidence before 36 months	1	M = 3.0, SD = 1.7	M = 4.0, SD = 1.0

The participants were pseudo-randomly assigned to one of two mu training groups (Group 1 or Group 2)

The groups were comparable concerning the mean age, cognitive abilities and severity of autistic symptoms, which were examined within the last year by a psychologist or physician. All of the children underwent extensive diagnostic assessment, however, due to difficulties in recruitment not all diagnosis were evaluated with the same diagnostic tools (see limitation of the study in the discussion section)

To assess cognitive abilities, an intelligence test with a mean (M) of 100 and a standard deviation (SD) of 15 was applied (i.e., Wechsler Abbreviated Scale of Intelligence, Wechsler Intelligence Scale for children, Wechsler Preschool and Primary Scales of Intelligence or Stanford Binet Intelligence Scale). There was no difference between the two groups in IQ scores ($p > .1$)

For the comparison of autistic symptoms, the total scores of the Vineland Adaptive Behavior Scale (VABS), the Social Responsiveness Scale (SRS) and the Autism Evaluation Checklist (ATEC), which were completed for every participant before the first NFT sessions, were used. No significant differences between the groups in these tests were found in the pre-test ($p > .1$). Moreover, most of the children received the Autism Diagnostic Observation Schedule (ADOS) (Lord et al. 2000) and the revised Autism Diagnostic Interview (ADI-R) (Lord et al. 1994). The scores on these tests were comparable between the groups ($p > .1$). Other tests applied included the Asperger's Syndrome Diagnostic Scale (ASDS), Autism Spectrum Rating Scale (ARS), Gilliam Autism Rating Scale, Gilliam Aspergers Disorder Scale and the Childhood Rating Scale (CARS)

coins avoiding the balloon, and the child's avatar getting hit from the fireball. Unique to this game is the occurrence of a social interaction sequence before each non-social game episode. During these social interactions, the child's avatar approaches the NPC while the child presses the arrow keys with the right hand. Then, while facing the NPC, the child participant must modulate mu power [either increase (Group 1) or decrease (Group 2) it relative to a set threshold level] in order to get rewarded. The positive feedback involves the child's avatar imitating the facial expression of the NPC in real-time. For negative feedback, a sad face without any imitation behavior is shown. The game proceeds if the child's avatar has a positive interaction with the NPC for at least 30 s (i.e., he/she is successful

at modulating mu power and causing imitation of the facial expression). Then, the NPC tells the child's avatar how to proceed with the game. The story plot requires the participants to approach and successfully interact with the NPC twice before the game proceeds to the next gaming episode.

Study Design and Threshold Settings

Participants were divided into two groups: Group 1 received a reward for enhancing mu power in the non-social gaming episodes as well as in the social interaction sequences. Group 2 was trained to increase mu power during the non-social gaming episodes but to decrease mu

power during the social interaction sequences of the game (Fig. 1). The thresholds for EEG were set as a function of an initial preceding period of baseline activity. In Group 1, mu values were set to -50% of the baseline value in the first session. Since participants were rewarded if their mu levels were above this threshold in social and non-social episodes, this setting made it initially easier to exceed the threshold. Threshold values subsequently were set higher in continuing sessions to shape behavior. In Group 2, mu threshold values were set to -30% of the baseline value in the first session and were then increased in the same way as in Group 1. This setting was chosen to make a decrease of mu power below the threshold possible in the bidirectional training condition. In the non-social gaming episodes, participants in Group 2 were rewarded if they exceeded the threshold. In the social interaction parts, participants were rewarded if they were below the threshold. For both groups, the threshold for theta and beta were set to $+50\%$ of the baseline value in the first session. Since users only received a reward if they were below the beta and theta thresholds, this setting made it initially easier to get below the threshold. Beta and theta values were subsequently lowered in continuing sessions.

Pre- and Post-Tests: Evaluation of Training Success

Training success was evaluated by a series of EEG, facial EMG, and behavioral outcome measures before and after the 16 training sessions (Fig. 2). Children were asked to sit silently and motionless in a comfortable chair inside an electrically- and acoustically-shielded chamber and to focus on a computer screen in front of them. The pre- and post-tests were conducted by two experimenters, one constantly checking the physiological signals and the other making sure the child followed the instructions.

EEG was recorded from 32 channels with a Biosemi system (BioSemi B.V., Netherlands) and sampled at 2048 Hz. Artifacts from muscle movement were visually identified and removed with the assistance of a tool that identified data sections with peak amplitudes in the highest 20% of a given data file. Trials as well as channels were excluded individually, whereas C3 and C4 never had to be excluded. All data were referenced to a common average.

Facial EMG was recorded from two electrodes on the left cheek (zygomaticus major) and two above the left eyebrow (corrugator supercilii) and sampled at 2048 Hz in order to measure imitation behavior (smiling and frowning, respectively) (Van Boxtel 2010). Artifacts were removed with the assistance of a tool which identified data sections with peak amplitudes outside the limits of ± 3 standard deviations of a given data file. EMG recordings were bipolar.

The various outcome measures included the following (Fig. 2):

- a. *Resting state EEG* Participants were asked to sit relaxed for each of 6 min with either closed or open eyes. The data were cut into 2 s epochs, resampled at 512 Hz, and log transformed. Mu power values from 8 to 12 Hz were computed in channel and component space [i.e. independent component analysis (ICA)]. To make mu power changes comparable between sessions and groups, a ratio between the mu and the general power level was used:

$$\text{MU} = \text{Mu Power} / \text{Mean Power (6–8 Hz + 12–14 Hz)}$$
- b. *Mu Suppression Index (MSI) task* The MSI was developed and used as evaluation for NFT in previous studies (Oberman et al. 2005; Pineda et al. 2008). Participants were asked to watch six 1-min videos twice in random order. The videos included movement observations as well as real movement (i.e. experimental conditions) and a baseline video (see Fig. 2b). The data from the same conditions were appended, resampled to 256 Hz, and mu power was extracted. To control for individual differences in scalp thickness and electrode impedance, a ratio was used:

$$\text{MSI} = \text{Log} [\text{Mu Power (experimental/baseline)}]$$
- c. *Reading the Mind in the Eyes Test (RMET)* The RMET was developed by Baron-Cohen et al. (2001) and assesses social cognition and emotion recognition. Children were shown pictures of the eye region of a face for 10 s and afterwards they had to determine the emotional expression or, as a control, the gender of the individual. The percentage of correct responses and reaction times were calculated. For the EEG analyses, the data were resampled to 256 Hz and mu power was extracted. The fifty-two 10-s trials of picture presentations (i.e. 26 for emotion and 26 for gender tasks) without any motor response were cut to .5–9.5 s and appended. Then the MSI was calculated in order to find specific changes in emotion recognition independent from general EEG effects:

$$\text{MSI} = \text{Log} [\text{Mu Power (emotion/gender)}]$$
- d. *Emotion Imitation Task* Participants were asked to watch 2-s videos of smiling (i.e. positive emotions) and angry or fearful (i.e. negative emotions) faces (Beall et al. 2008). The stimuli were from the MMI Facial Expression Database (Pantic et al. 2005; Valstar and Pantic 2010). Each of the 68 trials (i.e. 34 for positive and 34 for negative emotions) was cut into 4-s segments (i.e. 2 s before and 2 s after the start of the video). The 1.5-s segments after onset of the video were related to the baseline of 1.5–.5 s before the onset of the video for the EEG and facial EMG time–frequency analyses. The EEG data were resampled to

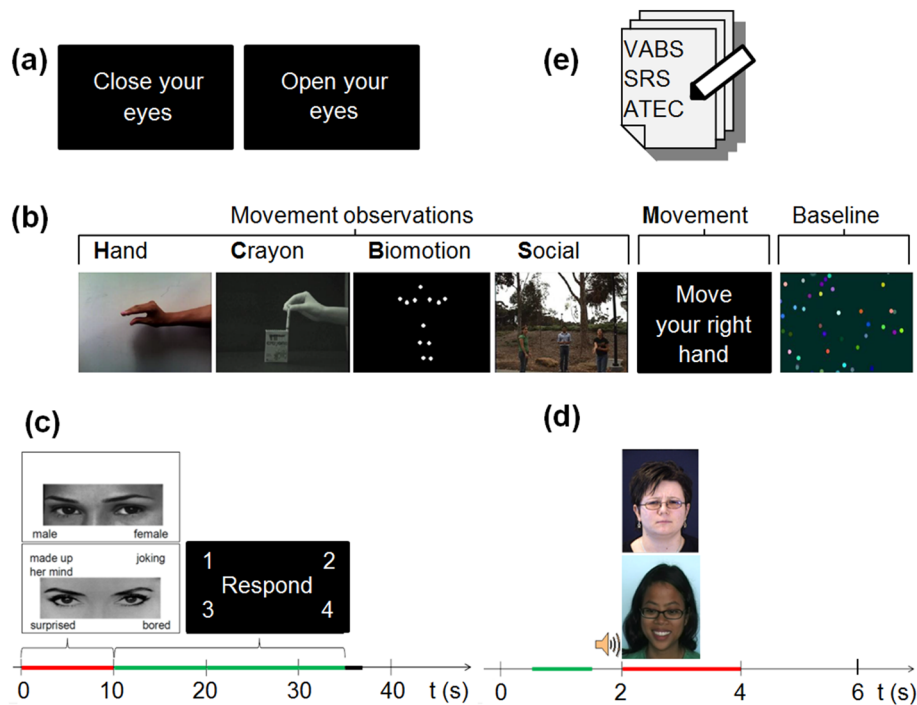


Fig. 2 Outcome measures before and after the Neurofeedback training. A resting state EEG was always administered first and then the other tasks occurred in pseudo-random order. **a** *Resting state EEG*. Participants were asked to sit relaxed for 6 min with closed eyes and 6 min with open eyes. **b** *Mu Suppression Index (MSI) task*. Participants watched six 1-min videos twice in random order. The videos included movement observations, such as watching a hand opening and closing (Hand), a hand pulling a crayon from a crayon box using a precision grip (Crayon), dots representing a moving human (Biomotion) and three people playing catch with a ball (Social). In the fifth experimental condition, participants were asked to make a movement with their right hand (Movement). In the baseline condition, randomly moving dots were presented. **c** *Reading the Mind in the Eyes Test (RMET)*. Participants were shown pictures of individuals' eye regions for 10 s. At the corners of the screen either

the gender (male or female) or four possible emotions were presented. After 10 s, the children were asked to press a button corresponding to their choice (i.e. in the above example, the child was instructed to press button “1” if he/she thinks the person has “made up her mind”, button “2” if the person is “joking”, etc.). As soon as they pressed a button, the next picture appeared with a 2 s break in-between. The maximum amount of time for the response was 25 s. **d** *Emotion Imitation Task*. Participants were asked to watch 2-s videos of smiling (i.e. positive emotion) and angry or fearful (i.e. negative emotion) faces. 120 ms before the onset of the video, a tone was presented. The baseline was between 1.5 and .5 s before the onset of the video. The break between trials varied randomly between 4 and 5 s. **e** *Parental assessment*. One parent rated the child on the Vineland Adaptive Behavioral Scale (VABS), Social Responsiveness Scale (SRS) and Autism Treatment Evaluation Checklist (ATEC)

256 Hz, mu power for statistical analyses was extracted from 8 to 12 Hz. The EMG was analyzed from 12 to 216 Hz with a notch filter from 55 to 65 Hz. Only significant changes in relation to the baseline according to bootstrap .01 alpha level are shown in the EEG and EMG time frequency plots.

- e. *Parental assessment* One parent rated the child on (1) the Vineland Adaptive Behavior Scale (VABS) (Sparrow and Cicchetti 1985) which is a well-known, well-standardized, interview that measures developmental and behavioral skills; (2) the Social Responsiveness Scale (SRS) (Constantino et al. 2003) which provides a quantitative metric of the type and severity of impairments in social functioning that are characteristic of ASD children and (3) the Autism Treatment Evaluation Checklist (ATEC) (Magiati et al. 2011; Rimland

and Edelson 1999) which is used to measure changes in ASD symptomology in response to treatment.

Analyses

All physiological data were analyzed with Matlab (The MathWorks, Inc., USA) and EEGLab (Delorme and Makeig 2004). For statistical analyses, repeated-measures analyses of variance (rANOVAs) were computed to evaluate differences between the within-subject factors of session, condition, electrode, time, subscale and the between-subject factor of group [Group 1 (unidirectional)/ Group 2 (bidirectional)]. Additionally, the effect size was calculated by partial Eta-squared (η^2). The Kolmogorov–Smirnov-Test proved all variables to be normally

distributed with one exception in the EMG analyses of the Emotion Imitation Task. However, this variable did not reveal any differences. If sphericity was not found, Greenhouse-Geisser epsilon was taken for correction. For the Post-hoc tests, Unequal N HSD was used.

Results

Neurofeedback Training

To address the first hypothesis and determine whether children learned to control the game, the success of the NFT to produce increases in baseline mu and in the performance during the Social Mirroring Game over the 16 training sessions was examined. As shown in Fig. 1, a performance increase indicates that Group 1 was able to increase mu during the entire game and Group 2 was able to increase mu in non-social gaming episodes and decrease mu in social interactions while keeping the theta and beta frequency bands low.

Control of EEG Frequency Bands

For mu power, baseline values were significantly higher than the threshold values ($F_{1,11} = 52.6, p < .01, \eta^2 = .83$) which was true especially for Group 1 ($F_{1,11} = 10.9, p < .01, \eta^2 = .5$; Fig. 3a). This is in line with the study design (Fig. 1). Mu power also increased across sessions ($F_{2.2, 24.7} = 3.2, p = .05, \eta^2 = .22$). For theta and beta, the baseline values were significantly lower than the threshold values ($F_{1,11} = 57.4/38.3, p < .01, \eta^2 = .84/.77$), which is also in line with the study design (Fig. 1). The threshold values (but not the baseline values) decreased significantly across sessions ($F_{7,77} = 5.5, p < .01, \eta^2 = .34$; $F_{2.7,30.0} = 3.6, p < .05, \eta^2 = .25$).

Performance Adjusted for Difficulty

Because thresholds were changed in order to induce learning, the level of task difficulty changed. The previously described results and Fig. 3a indicate that the baseline and threshold values converged in the course of sessions for the theta and beta band, which made it more difficult for the participant to be below threshold. Thus, in order to correct the performance of the participants in the NFT for the increasing level of difficulty over sessions, performance was computed as follows (Friedrich et al. 2014a):

$$\text{Performance} = \text{Hitrate} \times \text{Difficulty}$$

A hit was defined as fulfilling all threshold criteria (e.g. above mu and below beta, theta) and thus triggering positive feedback in the game (increasing performance). In

order to make non-social gaming episodes and social interactions comparable, the hitrate itself was defined as:

$$\text{Hitrate} = \text{Hits} / \text{Minutes}$$

To adjust the hitrate for the level of difficulty, the distances (Δ_{obs}) between the shaped threshold and the preceding baseline were considered. Distances were calculated so that positive numbers reflect the threshold being set easier than the baseline values and negative numbers reflect the threshold being set as more difficult than the baseline values. The observed distances were then normalized (Δ_{norm}) to the defined standard distance (Δ_{std}). The standard distance was set such that the mu (μ) threshold was 50 % lower and the beta (β) and theta (θ) threshold were 50 % higher than the preceding baseline value resulting in a difficulty of 1 for the first session for Group 1 (Fig. 1). To ensure that a distance of zero and negative distance values still show reasonable results, a logarithmic transformation was used:

$$\text{Difficulty} = 1 / 10^{\Delta_{\text{norm}}}$$

$$\Delta_{\text{norm}} = \left(\sum_{i=\mu\beta\theta} \Delta_{\text{obs}_i} - \sum_{i=\mu\beta\theta} \Delta_{\text{std}_i} \right) / \left(\sum_{i=\mu\beta\theta} \Delta_{\text{std}_i} \right)$$

The hitrate decreased significantly over sessions ($F_{3.3,36.6} = 11.1, p < .01, \eta^2 = .5$; linear contrasts $p < .01, \eta^2 = .7$; Fig. 3b). Group 1 achieved a higher hitrate than Group 2 ($F_{1,11} = 16.0, p < .01, \eta^2 = .59$). This was related to the fact that Group 2 had higher levels of difficulty than Group 1 ($F_{1,11} = 24.6, p < .01, \eta^2 = .69$), especially during the social interactions ($F_{1,11} = 28.3, p < .01, \eta^2 = .72$). This is in line with the study design: Due to the bidirectional training, Group 2 had to decrease below the mu threshold in the social interactions although this threshold was already 30 % lower than the baseline value in the beginning (Figs. 1, 3a). Difficulty increased over sessions ($F_{3.7,41.2} = 3.4, p < .05, \eta^2 = .24$; linear contrasts $p < .01, \eta^2 = .82$), being significantly higher for the social interactions than the non-social gaming episodes ($F_{1,11} = 28.3, p < .01, \eta^2 = .72$).

Due to the shaping of the thresholds for mu, beta and theta based on the preceding baseline measurement, substantial variations in the level of difficulty occurred between sessions as well as participants. For example, if a participant was very calm in one baseline session, the beta threshold was lowered. If the same participant was more agitated in the next session again, the low beta threshold from the last session made it hard for the participant to be below the beta threshold again. This variation in difficulty resulted in a substantial variability in hitrate. The hitrates in the interaction and game episodes varied between 6 and 116 hits per minute between participants and sessions. The average hitrate over participants and sessions was 40 hits per minute with a standard error of 1.

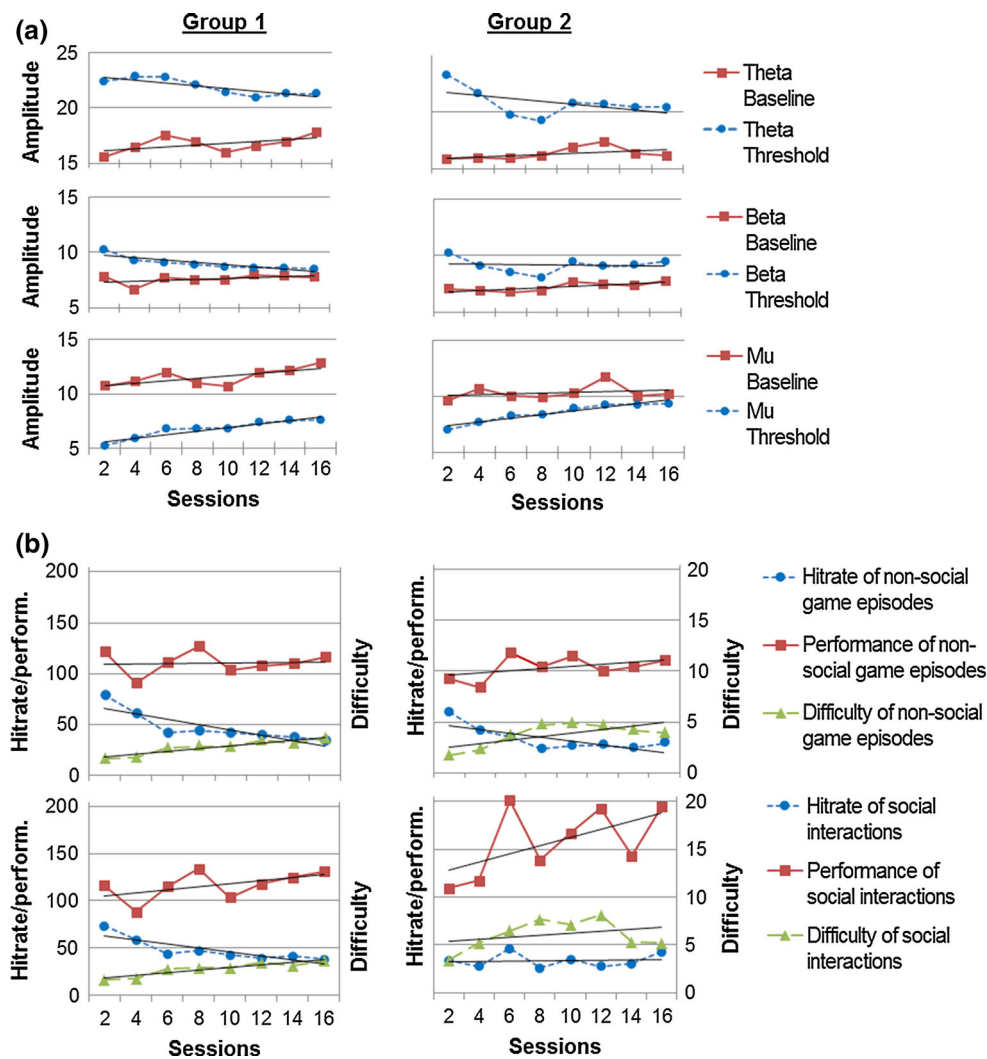


Fig. 3 Control of EEG frequency bands and game performance in the course of NFT sessions. **a** Peak-to-peak amplitude for the theta, beta and mu baseline and threshold values across NFT sessions. Two consecutive sessions are always averaged in order to reduce the 16 NFT sessions to 8 levels. For theta and beta, the distance between baseline and threshold in the first session was always +50 % and participants were trained to be below the threshold. For mu in Group 1, the distance between baseline and threshold was -50 % and mu power was trained to be increased. For mu in Group 2, the distance between baseline and threshold was -30 % and participants were rewarded for a mu value above the threshold in the non-social gaming

episodes but rewarded for a mu value below the threshold in the social interaction sequences. In the course of sessions, baseline and threshold values for theta and beta converged for both groups as did mu levels for Group 2. **b** Hitrate, difficulty and performance across NFT sessions. Hitrate decreased as difficulty increased for both groups in non-social gaming episodes as well as social interaction sequences. For Group 2, in the social interaction sequences, difficulty was especially high as the participants had to be below the threshold for mu power while the baseline was higher than the threshold (-30 %, **a**). Performance was the product of hitrate × difficulty and showed an increase

However, when controlling the hitrate for the level of difficulty, performance showed an increasing trend over sessions ($F_{7,77} = 1.8, p = .1, \eta^2 = .14$; linear contrasts $p < .05, \eta^2 = .38$) and was higher for the social interaction than the non-social gaming episodes ($F_{1,11} = 12.3, p < .01, \eta^2 = .53$). Group 2 performed better in the social interactions than both groups in the non-social gaming episodes ($F_{1,11} = 7.9, p < .05, \eta^2 = .42$).

Pre- and Post-Tests: Evaluation of Training Success

To address the second hypothesis, a series of outcome measures before and after the 16 NFT sessions were recorded to evaluate whether the NFT led to a reduction in autism symptoms. This would be indicated by more mu suppression to movement observation, social or emotional stimuli, more imitation behavior and behavioral improvements in the

post- compared to the pre-test. Additionally, the differences between groups in these tasks were examined (i.e. hypothesis 3).

Resting State EEG

In channel space as well as component space (i.e. ICA), there was significantly more mu power in the closed eyes than in the open eyes condition ($F_{1,11} = 52.3/8.9$, $p < .01/05$, $\eta^2 = .83/.45$; Fig. 4). In component space, an independent component over sensorimotor cortex between 8 and 12 Hz was shown for every participant. However, the increase in mu power in the post- compared to the pre-test during the closed eyes condition did not reach statistical significance.

MSI Task

As expected, the MSI at electrode positions C3 and C4 indicated significantly more mu suppression for the executed movement than for the movement observations conditions ($F_{1,8,20.3} = 12.3$, $p < .01$, $\eta^2 = .53$; Fig. 5). Moreover, there was a significant interaction between EEG electrode, group and pre- and post-test ($F_{1,11} = 6.4$, $p < .05$, $\eta^2 = .37$). In the condition “Biomotion” and “Social”, Group 2 had more mu suppression at C4 than Group 1 in the pre-test ($F_{1,11} = 12.4/4.3$, $p < .01/.1$, $\eta^2 = .53/.28$). In the “Biomotion” condition, there was marginally more mu suppression in the post-test compared to the pre-test at C3 ($F_{1,11} = 4.3$, $p < .1$, $\eta^2 = .28$) over both groups. In the “Social” condition, Group 2 showed more mu suppression than Group 1 at C4 ($F_{1,11} = 8.0$, $p < .05$, $\eta^2 = .42$).

RMET

The MSI was also computed for the RMET but no statistical significant differences between groups and pre- and post-test were found. However, significant correlations between the MSI during the RMET in the pre-test and the percentage of correct responses as well as the reaction time in the RMET in pre- and post-test were found (Table 2). All correlation coefficients showed in the expected direction: The more mu suppression (i.e. the lower the MSI), the higher the percentage of correct responses and shorter the reaction time. Behaviorally, children had significantly more correct responses in the post- than in the pre-test in the emotion task ($F_{1,11} = 7.3$, $p < .05$, $\eta^2 = .4$) suggesting improvement in emotion recognition as a function of training (Fig. 6). Additionally, Group 2 showed shorter reaction time in the post- than in the pre-test in the emotion task ($F_{1,11} = 9.0$, $p < .05$, $\eta^2 = .45$). In the gender task, which functions as control baseline, children with ASD

achieved significantly more correct responses than in the emotion task ($F_{1,11} = 69.4$, $p < .01$, $\eta^2 = .86$), however, no significant differences were found between groups or sessions within the gender task ($p > .1$).

Emotion Imitation Task

The EEG analyses of the Emotion Imitation Task showed significant mu suppression 400–1000 ms after onset of the emotional stimuli as shown in Fig. 7a. Group 2 had more mu suppression in the post- than in the pre-test and more than Group 1 in the post-test ($F_{1,11} = 7.6$, $p < .05$, $\eta^2 = .41$). In contrast, Group 1 exhibited greater mu suppression in the pre- than in the post-test and more than Group 2 in the pre-test.

The EMG analyses revealed significant facial muscle activity in response to the emotional stimuli as can be seen in Fig. 7b. In the pre-test, no significant differences in muscle activity were found ($p > .1$). In the post-test, in the positive condition, activation was higher at the zygomaticus major between 700 and 1000 ms than at the corrugator supercilii ($F_{1,8,19.6} = 4.3$, $p < .05$, $\eta^2 = .28$), indicating smiling. Additionally, Group 2 had significantly more EMG activity than Group 1 in this condition in the post-test ($F_{1,11} = 5.7$, $p < .05$, $\eta^2 = .34$). In the negative condition, activation was higher at the corrugator supercilii than at the zygomaticus major between 400 and 600 ms ($F_{2,1,22.8} = 3.5$, $p < .05$, $\eta^2 = .24$), indicating frowning.

Parental Assessments

Using the VABS, parents rated their children significantly more adaptive in the daily living, socialization and communication domains in the post- than in the pre-test ($F_{1,11} = 5.7$, $p < .05$, $\eta^2 = .34$; Fig. 8a). In the SRS total score, parents rated their children significantly more socially responsive in the post-test than in the pre-test ($F_{1,11} = 8.2$, $p < .05$, $\eta^2 = .43$; Fig. 8b). In the sub-scales, especially the “social motivation” improved significantly from pre- to post-test ($F_{4,44} = 4.3$, $p < .01$, $\eta^2 = .28$). In the ATEC total score, parents indicated significant reduction of ASD symptoms in the post-test compared to the pre-test ($F_{1,11} = 6.1$, $p < .05$, $\eta^2 = .36$; Fig. 8c). In the sub-scales, especially the “sociability” and the “health/physical/behavior” improved significantly from pre- to post-test ($F_{3,33} = 3.0$, $p < .05$, $\eta^2 = .21$).

The significant results from all three measures indicate that children with ASD from both groups improved (1) in coping with their daily lives, (2) in their social skills and relationships and (3) in their communication. On a more specific sub-scale level, they firstly showed less behavioral problems (e.g., ATEC, in terms of hits or injures self;

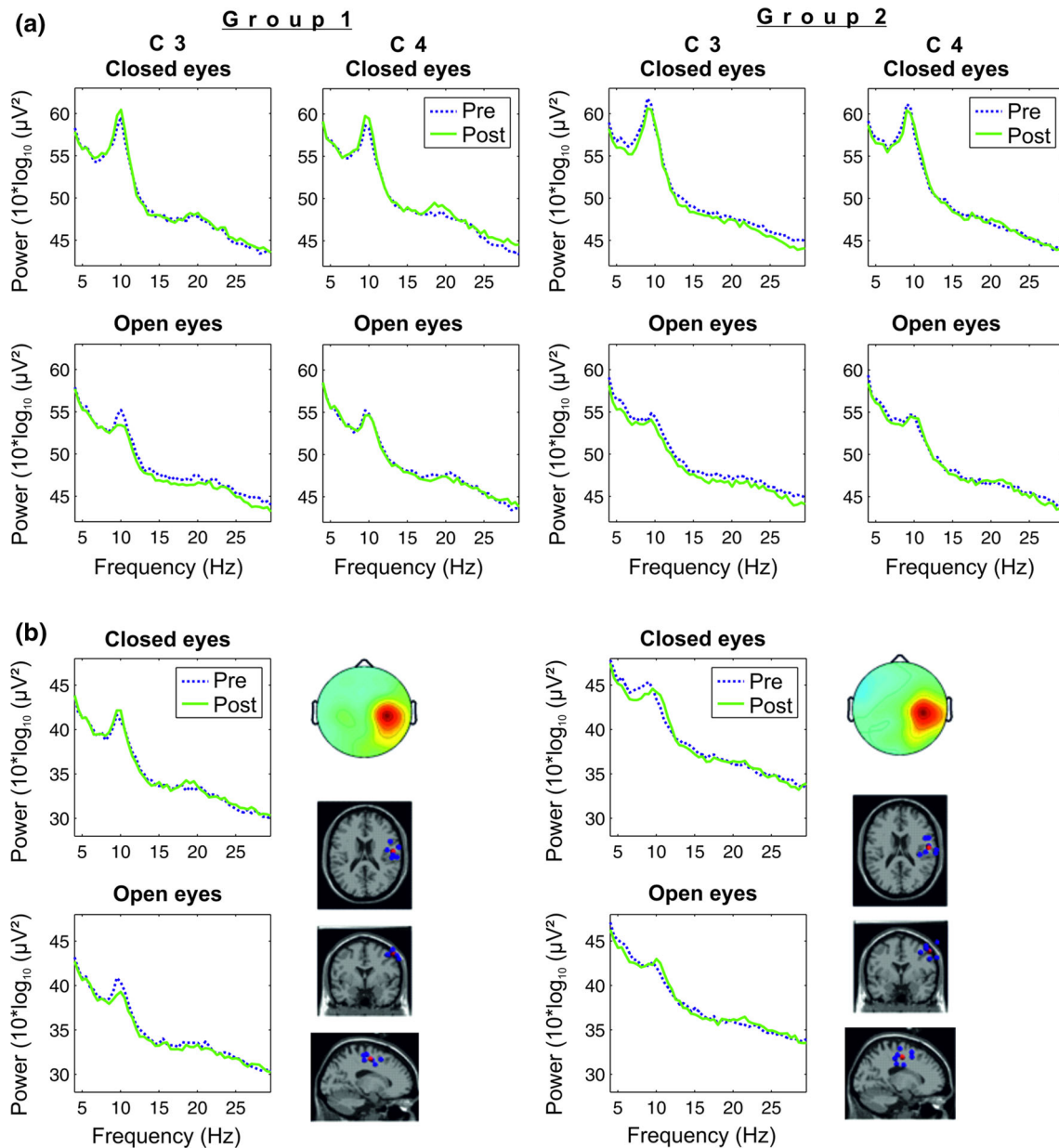


Fig. 4 Resting state EEG. **a** Channel space. Power spectra for the closed eyes (*top*) and open eyes (*bottom*) conditions for electrode positions C3 and C4 in both groups are shown. As can be seen, the general power level is not identical between groups and pre- and post-test. Therefore, mu power values between 8 and 12 Hz were considered relative to the general power level for statistical analyses (see Methods). When considering the relative mu power, mu was higher in the post- compared to the pre-test during the closed eyes condition at both electrode sites and for both groups. **b** Component space. Independent Component Analysis (ICA) was computed and a mu component closest to the sensorimotor cortex including all participants was selected. First, power spectra for the closed eyes

(*top*) and open eyes (*bottom*) conditions of the Mu Cluster are presented. When considering the mu power values between 8 and 12 Hz relative to the general power level, mu power for both groups was higher in the post- compared to the pre-test during the closed eyes condition. Second, scalp maps of the Mu Cluster are presented. Third, dipole analyses for the top, coronal and sagittal view are shown. The mu cluster for all participants (*red dot*) had the mean coordinates of 54, -7, 47, which corresponds to right cerebrum, frontal lobe, gray matter, precentral gyrus, BA 4 (primary motor cortex) according to the Coordinates Talairach Client. These areas are also indicated for both groups individually (Color figure online)

shows rigid routines) as well as improved personal hygiene (VABS, e.g. asks to use toilet; washes and dries face using soap and water), domestic (VABS, e.g. is careful around hot objects; uses tools) and community daily living skills

(VABS, e.g. follows household rules; obeys traffic lights). Secondly, children with ASD showed significant improvements in interpersonal relationships (VABS and ATEC, e.g. imitates simple movements; recognizes the

likes and dislikes of others), in play and leisure time (VABS, e.g. chooses to play with other children; takes turns without being asked), in coping skills (VABS, e.g., accepts helpful suggestions or solutions from others; controls anger or hurt feelings due to constructive criticism) and in social motivation (SRS, e.g., would rather be alone than with others; avoids starting social interactions with others). Thirdly, children with ASD improved in their receptive (VABS, e.g. listens to instructions; listens to a story for at least 30 min), expressive (VABS, e.g., says first and last name when asked; has conversations that last 10 min) and written communication (VABS, e.g., reads at least 10 words aloud; writes simple correspondence at least three sentences long). Although the other sub-scales did not reach significance in the post hoc analyses, Fig. 8 supports

the clear trend of improvements from pre- to post-test for children with ASD in the majority of sub-scales.

Discussion

The results from the current study are consistent with and extend previous work (Pineda et al. 2008, 2014). Overall, the Social Mirroring Game was successful at engaging children with ASD during NFT (Friedrich et al. 2014b) and produced positive effects on all measures. Electrophysiologically, there was more mu suppression in the post- than in the pre-test indicating activation of the MNS. In terms of emotional responsiveness, children displayed significantly more correct responses in the emotion recognition task and exhibited more appropriate spontaneous imitation behavior to emotional stimuli in the post- than in the pre-test. Behaviorally, parents indicated in every-day life situations a significant reduction of ASD symptoms, significantly

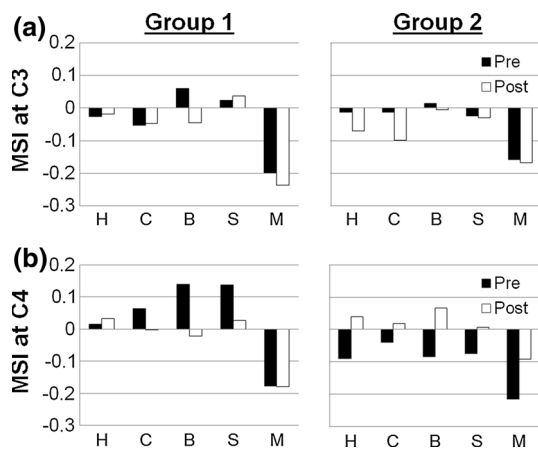


Fig. 5 Mu Suppression Index (MSI) for movement observation and movement. Negative Values for the MSI indicate mu suppression, a value of zero indicates no suppression and positive values indicate mu enhancement. The MSI for movement (M) shows higher mu suppression (i.e. high negative MSI values) than movement observations (H = Hand: hand opening and closing, C = Crayon: hand pulling crayons, B = Biomotion: dots representing a moving human, S = Social: people playing with a ball) at the electrode positions C3 (a) and C4 (b). Group 2 shows more mu suppression in the post-test than in the pre-test at C3 while the opposite occurs at C4

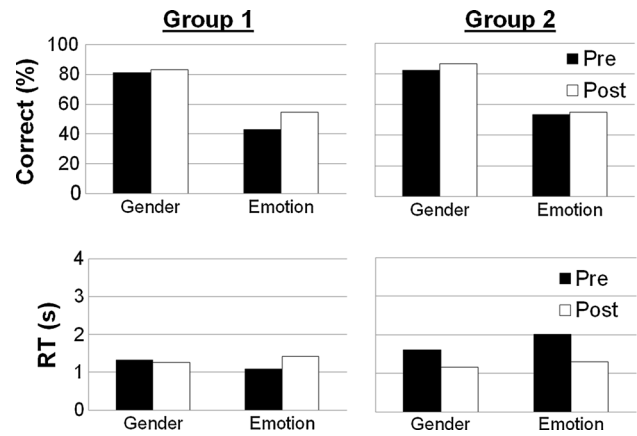


Fig. 6 Correct responses and reaction time in the Reading the Mind in the Eyes Test (RMET). **a** The percentage of correct responses (%) is higher in the post- than in the pre-test for both groups. **b** The long reaction time (s) for correct responses in Group 2 in the pre-test decreases to the same level as Group 1 in the post-test

Table 2 Correlations between the performance and the MSI in the RMET

RMET	Performance							
	Pretest				Posttest			
	Gender		Emotion		Gender		Emotion	
	Corr%	RT	Corr%	RT	Corr%	RT	Corr%	RT
MSI								
C3	-.49 (*)	.14	-.50 (*)	.25	-.70*	.71*	-.51 (*)	.56*
C4	-.35	.37	-.53*	.49 (*)	-.52 (*)	.70*	-.56*	.57*

Bivariate partial correlation coefficients controlled for age and gender between the performance and the MSI in the RMET were calculated. The MSI of the RMET at electrode positions C3 and C4 in the pre-test showed correlations in the expected direction with the correct responses (Corr%) and the reaction time (RT) of the RMET in pre- and post-test. The significance level is indicated one-tailed with asterisks * $p < .05$, (*) $p < .1$

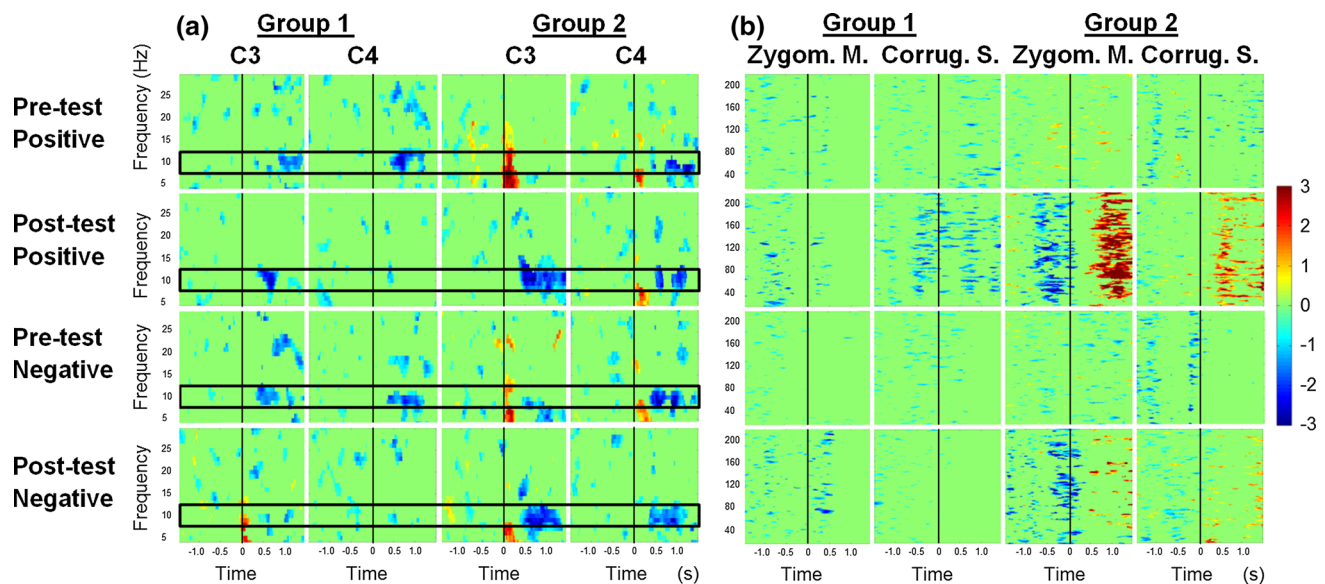


Fig. 7 Time–Frequency plots for the Emotion Imitation Task. The significant changes in log power (dB) ($p < .01$) in relation to the baseline (i.e. $t = -1.5$ to -0.5 s; cue $t = 0$ s is indicated by a vertical line) are displayed. *Red color* indicates an increase in power and *blue color* a decrease. The *x-axis* indicates the time in s and the *y-axis* indicates the frequency in Hz. **a** Time–Frequency plots for the EEG electrodes C3 and C4 between 4 and 30 Hz. The *black frame* indicates

the mu frequency band and the blue color indicates mu suppression. Group 2 shows more mu suppression in the post- than in the pre-test and more than Group 1 in the post-test. **b** Time–Frequency plots for the EMG activity at the facial muscle zygomaticus major (Zygom. M.) and corrugator supercilii (Corrug. S.) between 12 and 216 Hz. The *red color* indicates muscle activation. Group 2 showed more EMG activity than Group 1 (Color figure online)

better social responsiveness, and better behavioral adaptation, respectively, in the post- than in the pre-test. These results suggest that the Social Mirroring Game provided functionally significant feedback based on imitation and emotional responsiveness and was successful in linking and improving brainwave responses, behavior and emotional reactions during social interactions in children with ASD. The results provide the most substantial argument to date that mu-based NFT can be an effective tool for improving aspects of behavior necessary for successful social interactions in children with ASD.

As positive feedback during NFT was inhibited by exceeding theta and beta frequency bands as well as EMG of the hand, it gave greater assurance that children with ASD did gain control of the mu rhythm itself rather than via blinks or muscle movements. In the pre- and post-tests, participants showed significantly enhanced mu suppression in executed movement compared to movement observation, greater correct responses in the gender than in the emotion imitation task and more muscle activation at the zygomaticus major while watching positive and more at the corrugator supercilii while watching negative faces. These results indicate that the children understood the tasks, followed the instructions and that the data are indeed valid and can be considered reliable indicators of improvement.

Training in the Social Mirroring Game

Several studies have reported that children with ASD are able to learn to increase power in the mu frequency band in order to control an action in a video game, similar to what those in a TD group can do (Pineda et al. 2008; Coben et al. 2010; Thompson et al. 2010; Pineda et al. 2014). To our knowledge the current study is the first time that a group of children with ASD were trained to both increase as well as decrease mu rhythm depending on the specific context within the game. Both of the groups (unidirectional and bidirectional control) were able to learn control over the mu rhythm and improve performance in the game across sessions. Thus, children with ASD are able to learn to switch between increase and decrease control of the mu rhythm and in both cases it leads to improvement. An ICA showed that in every participant there was a component centered over sensorimotor cortex between 8 and 12 Hz, which is indicative of mu rhythm phenomenology. Furthermore, mu power over central electrodes was consistently higher in the closed than in the open eyes condition, which is a general phenomenon characteristic of most frequency bands and cortical regions, as well as common in TD and individuals with ASD (Geller et al. 2014; Barry et al. 2009; Mathewson et al. 2012). Moreover, mu increased across NFT sessions, although during the resting

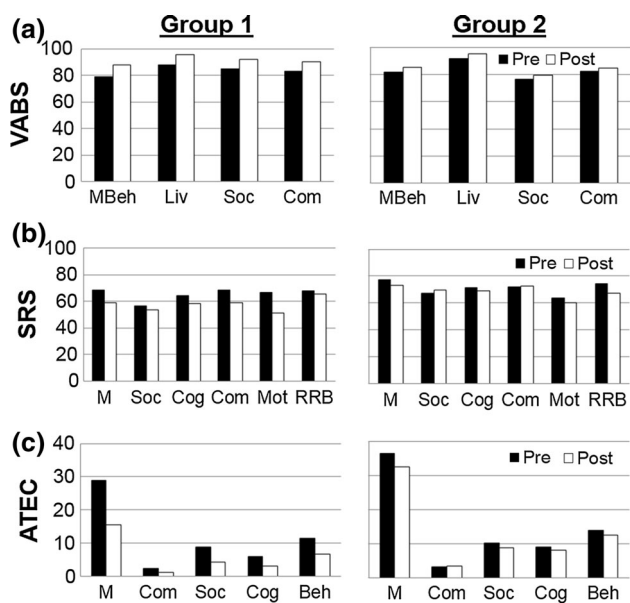


Fig. 8 Parental assessment before and after the NFT. **a** VABS scores. The standard scores for daily living (Liv), socialization (Soc) and communication (Com) domains and the resulting Adaptive Behavior Composite (MBeh) are displayed for the pre-and post-test for Groups 1 and 2. The higher scores in the VABS in the post- compared to the pre-test indicate better adaptive behavior. **b** SRS scores. The *T* scores for the total score for autistic social impairment (M) and the subscales social awareness (Soc), social cognition (Cog), social communication (Com), social motivation (Mot) and autistic mannerisms (RRB) are displayed for the pre-and post-test for Groups 1 and 2. Scores ≤ 59 indicate normal social responsiveness and scores of 60–65 mild, 66–75 moderate and ≥ 76 severe dysfunction in social responsiveness. The lower scores in the post- compared to the pre-test indicate improvements in social responsiveness. **c** ATEC scores. The scores for the total scale (M) and the subscales speech/language/communication (Com), sociability (Soc), sensory and cognitive awareness (Cog) and health/physical/behavior (Beh) are displayed for the pre- and posttest for Groups 1 and 2. The lower scores in the post- compared to the pre-test indicate treatment success

state it did not change significantly between groups or pre- and post-tests, suggesting a distinction between resting state and task-relevant mu levels.

Electrophysiological Changes in Mu Suppression

In line with the extant literature (Oberman et al. 2005), the participants of the current study exhibited significantly more mu suppression to movement than to movement observation in the MSI task. This pattern of mu suppression was shown only over central electrodes but not over occipital electrodes suggesting a differentiation of mu compared to occipital alpha (Oberman et al. 2008). This differentiation is important as the alpha rhythm in occipital regions and the mu rhythm over sensorimotor areas are in the same frequency range (8–12 Hz) and thus recordings over the central electrodes might be affected by this posterior activity. However, the results of the current study

show that the mu rhythm and not general alpha activity was recorded and targeted specifically. Using the MSI task, Pineda et al. (2008) have shown that mu suppression in children with ASD became more like those of a TD group, along with improvements in behavior, following several weeks of a mu-based NFT in contrast to a control group receiving placebo feedback. Consistent with this finding, both groups in the current study showed at least marginally more mu suppression for the “Biomotion” condition at C3 in the post-test compared to the pre-test. One potential reason for why other comparisons failed to reach significance is that the MSI was very different between groups at the electrode positions C3 and C4 in the pre-test. In contrast to our prediction, Group 2 did not show more mu suppression in the post-test than Group 1. That is, the specific strategy (unidirectional vs bidirectional mu training) did not make a difference perhaps as a function of these population differences.

In terms of brain response to the observation of facial expressions, Moore et al. (2012) previously reported event-related desynchronization of the mu component in healthy adults. The present results confirmed mu suppression in response to facial expressions, with a better outcome provided by the bidirectional training strategy of Group 2, which showed more mu suppression in the post-test compared to Group 1.

Emotional Responsiveness

Facial emotion processing accuracy has been associated with social adaptation in individuals with ASD (García-Villamizar et al. 2010). Several studies have reported that individuals with ASD have a deficit in recognizing emotional faces in comparison to a control group (Da Fonseca et al. 2009; Baron-Cohen et al. 2001). Using the RMET, Demurie et al. (2011) found that adolescents with ASD achieved significantly less correct responses than TD controls (Demurie et al. 2011). In the current study, both groups exhibited higher performance in the RMET in the post- compared to the pre-test, indicating that NFT helped children with ASD to reduce the reported deficits in emotion recognition (Demurie et al. 2011).

The correlations obtained between mu suppression and performance in the RMET in the current study indicate that mu suppression to emotional face stimuli facilitates correct and fast emotion processing, as well as gender recognition. This result is in line with recent studies demonstrating correlations between the performance in the RMET and heart rate variability in TD controls (Quintana et al. 2012) as well as autistic population (Friedrich et al. 2014a). The higher the heart rate variability in the resting state, the higher the percentage of correct responses and the shorter the reaction time in the RMET. These results suggest that

the autonomic nervous system and social cognition is closely linked in the autistic population (Quintana et al. 2012; Porges 2007) and that the brain, body and behavior components have to be addressed in order to achieve improvements in social cognition for children with ASD.

Besides deficits in emotion recognition, Beall et al. (2008) found that children with ASD did not produce reliable rapid facial reactions to angry and happy face stimuli as measured by EMG in contrast to TD children. The results in the Emotion Imitation Task of the current study are comparable. Furthermore, in contrast to the pre-test, children with ASD showed appropriate emotion imitation in the post-test (Mcintosh 2006; Van Boxtel 2010; Dimberg and Lundquist 1990) supporting the argument that NFT helped to improve rapid facial reactions to normal emotional expressions. In this case, the strategy adopted by Group 2 (of bidirectional mu training) showed more EMG in the post-test compared to Group 1.

Changes in Behavior Assessed by the Parents

The tests used (ATEC, SRS, and VABS) are standardized parental assessments that are appropriate for measuring all aspects of every-day behavior of children with ASD (Magiati et al. 2011; Rimland and Edelson 1999; Constantino et al. 2003; Sparrow and Cicchetti 1985). The advantage of using these comprehensive parental assessments is that behavioral changes in the real-world rather than in laboratory settings can be determined, whereas the disadvantage is that they could be biased by parental expectations. Pineda et al. (2008) have previously reported improvements in the ATEC due to mu-based NFT in comparison to a control group receiving placebo feedback. In the current study, significant improvements in autistic symptoms, social responsiveness and adaptive behavior were shown in the post- compared to pre-test equally for both groups. These statistical improvements were also reflected in clinical improvements.

Limitations of the Study

The main limitation of the current study is the small sample size. Recruiting a large enough population sample is a common problem when working with special populations but even more so when parents are asked to bring their child to the lab 18 times, 2–3 times a week for about 2 months, to receive the neurofeedback training. Most families already face a very busy schedule with work and school responsibilities for all family members. In a large metropolitan area, driving distances are long, parking at a large university is fraught with problems, with monetary compensation that may not provide enough incentive for

some individuals. Furthermore, research studies such as this cannot promise any therapeutic outcomes, which is what most parents are seeking. These difficulties in recruitment were also the reason why it was difficult to match the two groups on age, gender, cognitive skills and diagnosis of autism evaluated with the same diagnostic tools. Most of the children have regularly undergone extensive testing and many are unwilling to complete another testing session consisting of several hours. Despite these limitations, we were able to record over 250 carefully supervised sessions with high quality data with children with ASD who had never done NFT before.

Other factors that were not possible to control for the sample of the current study included the participants' other treatments at the time of the current study. Nine out of 13 children were engaged in applied behavior analysis (ABA), occupational therapy (OT), speech therapy, music therapy, cognitive behavioral therapy (CBT), real opportunities for independence therapy (ROI), Son-Rise therapy, adaptive physical education (PE) or social skill practice at school. Most of these treatments were ongoing for several years, while only 2 participants in each of our groups started a therapy within the same year of the NFT. However, no changes were made right before during or right after the NFT. Moreover, the fact that the children were interacting with the staff on a regular basis might have influenced the results for all children. The families of the children with ASD were all very supporting and motivated as they had to invest a lot of time and effort for their participation. However, the differences observed between groups in the current study demonstrate that the two training protocols had a specific impact on the children.

Despite all the limiting factors, the presented results demonstrate large effect sizes (Richardson 2011) and show benefits given the heterogeneity in age and severity of symptoms as well as the considerable variability in physiological data, behavior and performance. We believe these are strong results showing the benefits of this type of training.

Future Directions

It is imperative to investigate the long term effects of the NFT in a longitudinal study. Moreover, the Social Mirroring Game is designed to be not only controlled by EEG but also by peripheral physiological measures such as respiration, heart rate or skin conductance. Therefore, combining NFT and biofeedback might be another promising approach to link appropriate behavior, neurophysiological and peripheral physiological reactions in social situations.

Conclusion

The current study has shown that games such as the Social Mirroring Game can be an appropriate tool to achieve improvements in children with ASD in various aspects of social interactions by targeting mu rhythm modulation using neurofeedback based on imitation and emotional responsiveness. Appropriate brain responses, behavior and emotions were linked during social interactions and thus resulted in significant symptom reduction for children with ASD in both groups. Group 2 was trained to show mu suppression while watching emotion imitation and thus trained to activate the MNS, which in turn is responsible for imitation behavior. Hence, Group 2 showed more appropriate imitation behavior in the post-test than Group 1 indicating that the two approaches could elicit specific improvements related to the training and specific feedback. As social interactions build the fundamentals of our lives, an improvement in social interactions could strengthen the relationships with the family, facilitate social relationships as well as academic interactions and profoundly improve the health and well-being of individuals with ASD across the lifespan.

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Author Contributions EF conceived of the study, designed and coordinated the study, performed the measurement, the analyses of the EEG and EMG data and the statistical analyses, interpreted the data and drafted the manuscript; AS and TL implemented the framework to connect the Social Mirroring Game to the NFT in a closed feedback loop in real-time. NS and SL developed the Social Mirroring Game. SP participated in the analyses of the EEG and EMG data. JP participated in the design, coordination, analyses and interpretation of the data and in drafting the manuscript. All authors read and approved the final manuscript.

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