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Effect of beta and gamma neurofeedback on memory and intelligence in the elderly

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ABSTRACT

Recent research showed a correlation between cognitive decline and a decrease of EEG gamma activity. In the present double-blind randomized control study, we investigated whether gamma and beta neurofeedback protocols, that have been shown to modulate performance on cognitive control and memory in young adults, also leads to increased brain activity and cognitive performance in elderly. Twenty older adults either performed eight 30-min gamma neurofeedback session or beta neurofeedback session within a period of 21 days. Cognitive performance was determined before and after the training through an IQ and memory task and we added a subjective well-being questionnaire. Both neurofeedback training protocols resulted in a significant increase of the brain activity within each training session, suggesting that the aging brain is still trainable. However, we found no effects on cognitive performance or transfer of the feedback beyond the trainings. We discuss several possible reasons for the lack of training on rest measurements and cognition and ways to improve the feedback protocols for future studies.

1. Introduction

Normal aging has been frequently reported to decrease cognitive performance and to affect neural features and brain activity. Studies on cognitive functions in healthy aging (i.e. in individuals who are free of overt diseases) show that elderly people perform worse than young adults on tasks measuring fluid intelligence (Horn & Cattell, 1967), episodic memory (Craik, 2000), and working memory (McEvoy, Pellouchoud, Smith, & Gevins, 2001). Fluid intelligence is the ability to reason and deal with complex information, and to think logically and abstractly by perceiving relationships independent of previous specific practice or instructions (Cattell, 1963). Episodic memory involves memory for details from specific contexts and can be differentiated into two distinct processes, recollection and familiarity (Mandler, 1980; Migo, Mayes, & Montaldi, 2012). Recollection occurs when a stimulus cues the recall of details linked to it in a previous encounter. Familiarity is experienced as the feeling that one has been exposed to a stimulus before without the recall of any associated details from prior exposure(s). Both recollection and familiarity can lead to recognition.

Older adults perform as well as younger adults on memory tasks that require a judgment about whether a stimulus has been seen before or not (which can be based on familiarity and/or recollection – Craik & McDowd, 1987), but worse when retrieval of the context information is also required (for which recollection is needed – Spencer & Raz, 1995). Evans and Wilding (2012) showed by means of magnetoencephalography (MEG) that recollection and familiarity are not simply strong and weak versions of the same process but contribute independently to respectively remember and know judgments.

Not only cognitive performance changes with age, but also brain activity patterns, which are measured by means of electroencephalography (EEG). EEG is the recording of electrical activity at the scalp and can be decomposed in different EEG frequency bands that to some extent reflect different cognitive, sensory and motor processes.

EEG beta band activity (12–20 Hz) has been associated with memory (Hanslmayr, Staudigl, & Fellner, 2012), language processing (Weiss & Mueller, 2012), motor functions (Baker, 2007) and attention (Fan et al., 2007). Egner and Gruzelier (2001) showed that specific bands within the overall range of the beta band frequency are associated with different functions. Enhanced low beta band rhythm over the motor cortex (12–15 Hz; sensorimotor rhythm, SMR) was associated with fewer commission errors and improved perceptual sensitivity on a continuous performance task, while the opposite behavioral results were found with enhanced

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beta in a higher frequency band (beta1; 15–18 Hz). In a recent review, Hanslmayr et al. (2012) related successful memory encoding and retrieval to a decrease in beta power (not specified to a particular range within the beta band).

EEG gamma band activity (>30 Hz) has been linked with fluid intelligence (Jaušovec & Jaušovec, 2005, 2007; Stankov et al., 2006) and memory functions (Fell, Fernandez, Klaver, Elger, & Fries, 2003; Jensen, Kaiser, & Lachaux, 2007; Sederberg et al., 2003). While both gamma and beta have thus been found to be implicated in memory functions, Keizer, Verment, and Hommel (2010) found that more specifically familiarity and recollection are reflected by different EEG frequency ranges; beta band activity (12–20 Hz) was associated with familiarity and gamma band activity (36–44 Hz) was associated with recollection.

With age, fast rhythms such as gamma have been found to decrease (Werkle-Bergner, Shing, Müller, Li, & Lindenberger, 2009) while power in the beta band has been found to increase (Marciani et al., 1994). These changes might be related to some of the mentioned alterations in cognitive functions. Obrist (1976) proposed that, as fast activity is prevalent among intellectually well-preserved individuals at the beginning of old age, its presence in the EEG of an old adult could be considered a good sign for healthy aging. Loss of gamma band synchronization has been found in patients with dementia (Stam et al., 2002) and mild cognitive impairment (MCI, Missonnier et al., 2010). Park et al. (2012) also showed a link between gamma band activity and MCI, as well as between gamma band activity and clinical memory measures.

Beta and gamma activity have both been associated with cognitive and memory functioning in general and gamma with age related cognitive decline, therefore, increasing gamma or beta activity may help to improve or maintain cognitive functioning in elderly. This increase may be achieved by neurofeedback training. Within a neurofeedback protocol, individuals receive continuous, real time (visual or auditory) feedback over their brain activity patterns so they learn to modulate these signals in the desired direction (Heinrich, Gevensleben, & Strehl, 2007). The induced change in brain activity may subsequently lead to improvement of behavior and skills or to the recovery of a mental or physical disorder.

Neurofeedback as a training mechanism for altering brain activity has been used with both healthy persons and neurologically or mentally affected patients. Beta neurofeedback (aimed to increase beta band activity) has been shown to improve cognitive abilities in healthy individuals, for example in enhancing attentional performance with SMR (but not with beta1) Egner & Gruzelier, 2001, 2004). Alpha neurofeedback (aimed to enhance alpha activity) has been effective in enhancing relaxation (Dempster & Vernon, 2009; Gruzelier, 2002; van Boxtel et al., 2012). Moreover, different beneficial effects like improved creativity were found with increasing the theta (4–8 Hz)–alpha ratio (see Gruzelier, 2009 for a review). Neurofeedback has also been an effective tool for normalizing abnormal brain activity in cases of epilepsy, for example with SMR and slow cortical potentials (Tan et al., 2009), or in treating ADHD by increasing SMR relative to theta (Moriyama et al., 2012) and in reducing anxiety disorders by means of alpha neurofeedback (see Angelakis et al., 2007; Gruzelier, 2009, for overviews).

Recent studies with healthy young adults have differentiated effects of beta (12–20 Hz) and gamma neurofeedback (36–44 Hz) on intelligence and memory performance (Keizer, Verment, et al., 2010; Keizer, Verschoor, Verment, & Hommel, 2010). In the first study by Keizer, Verschoor, et al. (2010), a positive correlation was found between the change in gamma (as defined by the difference between before and after the training) and the change in performance on a fluid intelligence task. Comparable results were found in the concurrent study by Keizer, Verment, et al. (2010) on the effect of beta/gamma neurofeedback on episodic memory. The effect of neurofeedback training on performance on the episodic memory task was very specific; the gamma group improved significantly on recollection (as indicated by accuracy), whereas the beta group improved significantly on familiarity (as indicated by accuracy). It is currently unknown whether these results of gamma and beta neurofeedback on memory and intelligence found with young adults can also be generalized to, and replicated, in elderly people. Several attempts using neurofeedback to improve cognitive performance in the elderly have been applied with mixed success (Angelakis et al., 2007; Becerra et al., 2012; Lecomte & Juhel, 2011).

1.1. Present study

The current study will compare two types neurofeedback training (gamma and beta, double-blind, similar to the design by Keizer, Verment, et al., 2010; Keizer, Verschoor, et al., 2010) in elderly people in terms of enhanced brain activity subsequent to the training (within the frequency range that they were trained with), and performance on a fluid intelligence and episodic memory task, and subjective experience of daily living.

The present study deliberately adjusted the protocol of Keizer, Verment, et al. (2010) by providing feedback at F_z to specifically enhance frontal activity. The protocol used by Keizer, Verment, et al. (2010) showed that increased beta activity was found at electrode location F_z using both the F_z and O_z electrode for auditory feedback, and that increased gamma activity was found at electrode locations F_z and O_z after gamma neurofeedback using the O_z electrode for auditory feedback. McEvoy et al. (2001) proposed that in memorizing, older adults apply a more controlled, effortful strategy, relying on the processing ability of the frontal cortex, whereas younger people show activation in posterior areas that work more automatically. Grady (2008) found that older adults show increased activity in frontal lobes to compensate for decreased activity in occipital areas. While these studies indicate that elderly (have to) rely more on the frontal cortex to compensate for losses elsewhere, significant reductions in white and gray matter have been found in the brains of healthy elderly with the largest changes in, amongst other areas, the frontal cortex (Buckner, 2004; Fjell & Walhovd, 2010). Reduced frontal lobe functions have also been associated to age related impairments in episodic memory (Butler, McDaniel, Dornburg, Price, & Roediger, 2004). Moreover, Keizer, Verment, et al. (2010) showed a significant positive correlation between the percentage of change in frontal rather than occipital gamma band activity on the one hand and the percentage of change in recollection on the other hand, suggesting a more direct link between F_z and recollection, than between O_z and recollection. Therefore, we anticipated that by providing feedback at F_z rather than at O_z we would more specifically support the compensatory mechanism at the frontal cortex rather than trying to restore occipital activity.

We hypothesize that compared to the beta group, neurofeedback training in the gamma group will increase power in the gamma band, which will be associated with higher test scores on fluid intelligence and recollection. We hypothesize that compared to the gamma group, neurofeedback training in the beta group will increase power in the beta band which will be associated with improvement in familiarity scores.

2. Methods

2.1. Participants

Twenty right-handed participants, 14 males and 6 females, took part in this experiment. The mean age was for the group trained with gamma feedback was 69.2(SE +1.87) years (6 males, 4 females) and the mean age for the beta group was 66.4 (SE +1.90) years (8 males, 2 females). There was no significant age difference between the groups, $t(18) = -1.05$, $p = 0.31$. Participants were volunteers and enrolled via the participant's pool of TNO or via personal contacts. They received a monetary reward for their participation. Inclusion criteria for the participants were normal or corrected-to-normal hearing functions

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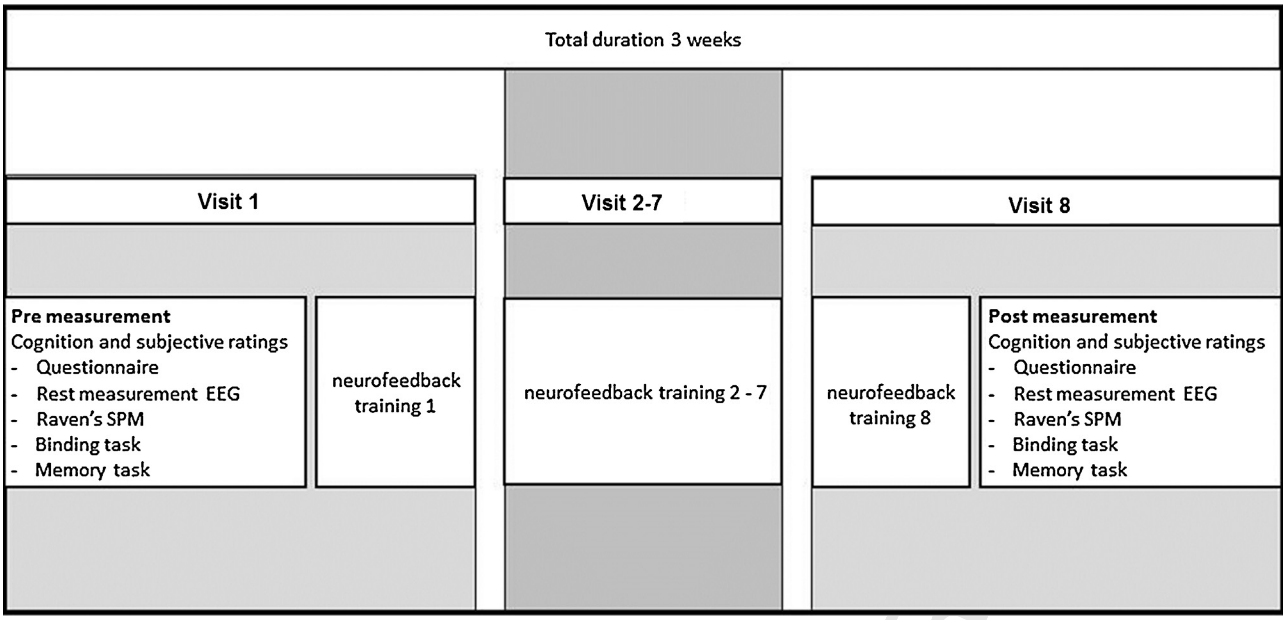

Fig. 1. A schematic overview of the neurofeedback training procedure and the pre and post measurements.

and normal or corrected-to-normal vision; exclusion criteria were color blindness or one of the following conditions; neurological (stroke, seizure disorder, head injury resulting in unconsciousness, brain disease or tumor), cardiac (heart disease, heart attack, pacemaker, defibrillation, high blood pressure), pulmonary disease, diabetes, thyroid, alcoholism (current or past), drug use (current or past) and psychiatric (anxiety or depression) as well as any medication use that could influence cognitive performance and/or brain activity. The anamnesis and screening procedure were conducted by an independent physician. The study was approved of by the local ethics committee. All participants gave their informed consent.

2.2. Procedure

Ten participants were placed in the gamma group and ten participants were placed in the beta group according to a double-blind randomized design: neither the participants nor the experimenters were aware of group assignments until the experiment was completed. Prior to the experiment, ten participant IDs were randomly assigned to the beta training and ten to the gamma training. The randomized key of participants' ID and group assignment was unknown to both experimenter and participant until the complete experiment finished.

Based on entrance of the particpants' ID a TNO developed program implemented the associated neurofeedback settings (i.e. beta or gamma feedback).

Fig. 1 provides a schematic overview of the procedure. Participants visited the laboratory for eight neurofeedback sessions on different days within three weeks (a maximum of 2 days was allowed between trainings). The experiments were conducted in a closed room with artificial light. The participants were seated in front of a table and were instructed to sit still and increase the occurrence rate of a tone (participants were instructed keep their eyes open). They were explained that particular brainwaves would generate the tones and that they had to find out themselves how to generate these brainwaves. Each neurofeedback session lasted 30 min.

The participants filled out a questionnaire prior to every training. Before the first and after the last neurofeedback session, participants' cognitive abilities were assessed by means of an intelligence test, a memory task, and a cognitive control task.[1] Furthermore, resting EEG activity was recorded over a 5-min interval before the first and after the last training session (eyes open).

2.3. Tasks and stimuli

Neurofeedback. In the gamma group, a tone was generated whenever the gamma power of F_z exceeded an upper threshold, whereas in the beta group this tone was generated whenever the beta power of F_z exceeded an upper threshold (for details on the determination of the thresholds, see below). The maximum rate of the tones was set to one tone per second. The used tone was a standard windows sound ('windows vista battery low.wav'). The volume was adjusted to each participant's preference. The sound was presented via loudspeakers to the right side of the participant. The participants had to sit still and produce the tone as often as possible by applying self-developed strategies.

Questionnaire. The questionnaire contained five items reflecting subjective experience of some aspects of daily living and was administered before every neurofeedback training session. The participants had to indicate their level of appetite, need of sleep, concentration, memory and mood (how do you estimate your current 'appetite', 'need for sleep', 'ability to concentrate', 'ability to retain information', 'mood') on a 9-point Likert scale ranging from low, to average, to high.

Intelligence task. Fluid intelligence was tested by using Raven's Standard Progressive Matrices (SPM). The test consists of maximal 60 trials of increasing difficulty. On each trial, the participant was asked to identify the missing element that completes a pattern by pressing the appropriate key on a keyboard (see e.g. Fig. 1). Participants either received the even 30 trials on the pretest and the odd 30 trials on the posttest or vice versa (counterbalanced across participants). Participants were instructed to solve as many trials as possible within 10 min.

Memory task. We used the same memory task as Keizer, Verment, et al. (2010). This task distinguishes between familiarity (old-new) and recollection (color encoding). We used 160 line drawings that were divided in 4 lists of 40 items. A separate set of drawings was used for the practice block and fillers. Each subject performed the memory task four times; two times before the start of the first neurofeedback training and two times after the last neurofeedback training. Each time the task was performed it consisted of two phases; an encoding and a retrieval phase, for which different lists of drawings were used. The encoding phase consisted of randomly presented 20 red and 20 green pictures and two fillers at the beginning and two fillers at the end on which participants were not tested, to avoid primacy and recency effects. Twenty-six black/white pictures were used in the retrieval phase, of which 12 were old (6 that were previously in red and 6 in green) and 14 were new. Performance on the two tasks administered before the first training was combined as was performance on the two tasks after the end of the last training.

Subjects were instructed to determine whether the picture was 'old-remembered', 'old-know' or 'new', by pressing one of three buttons as indicated on the screen. The distinction between 'remember' and 'know' responses is believed to capture two distinct states of recognition memory, namely familiarity and recollection.

If the subjects judged the picture to be new, the next picture was presented after a blank interval of 1000 ms. If the subject judged the picture to be old (remembered or know), the picture remained on the screen and subjects were asked to judge whether the picture was presented in red of green during the encoding phase with a button-press as indicated on the screen. Prior to the first encoding phase on the pre and post training measurement, participants completed a practice phase to get accustomed to the experimental setting and show that they completely understood the task. In the practice phase different pictures were used than in the test phase.

[1] The cognitive control task (a modified version of the task designed by Hommel, 1998 to study the behavioral effects of implicit feature binding) proved to be too difficult for most participants (i.e. too many missing values and slow response times) preventing proper analysis of the data. It will not be further discussed in this manuscript.

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2.4. Apparatus

EEG Recording. EEG was recorded through Au electrodes mounted in an EEG cap (g.tec medical engineering GmbH). Following the 10–20-system, the electrode positions used in the first and the last training sessions (including the 5-min rest measurements before the first training and after the last training) were F_{pz} (ground), F_z, F_3, F_4, C_z, C_3, C_4, P_z, P_3 and P_4. With training session 2 through 7, electrodes P_z, P_3 and P_4 were not included. The F_z electrode was used for feedback purposes – the other electrodes were only used to examine EEG off-line. Four electrodes were positioned above and below the left eye and just outside the left and right eyes, to monitor vertical and horizontal eye movement. The EEG electrodes were online referenced to the left mastoid (and offline re-referenced to the average of left and right mastoid electrode). The impedance of each electrode was below 10 kΩ. Data was sampled with a frequency of 256 Hz and filtered before storage using a 0.1 Hz high pass-, a 60 Hz low pass- and a 50 Hz notch filter (USB Biosignal Amplifier, g.tec medical engineering GmbH). The experiment (stimulus presentation and data recording) was controlled by a combination of custom-built software and MatlabR/Simulink tools.

Neurofeedback. EEG power spectrum analysis (fast Fourier transform, FFT) was performed online with negligible delay (1 s), using custom-built software. A filter was applied to the signal, extracting frequencies from the F_z electrode in the gamma range (36–44 Hz) for the gamma group and in the beta range (12–20 Hz) for the beta group, referenced to the left mastoid. An upper threshold was implemented for both groups that adapted to the power of the frequency band it was applied to, i.e. the power level was based on a moving average of 30 s that was updated continuously with the average power that was calculated over epochs for every second. The thresholds were set to the power level that would be surpassed at 75% of the power in the preceding 30 s window.

Cognitive tasks. Stimulus presentation, timing, and cognitive data collection of the memory and cognitive control task (see footnote 1) were achieved by using the E-prime© 1.1 experimental software package on a Dell Latitude D530 laptop, running Windows XP Professional, Version 5.1. Stimuli were presented on a 15 Inch display running at 1024 by 768 pixel resolution in 32 bit color at a refresh rate of 60 Hz. The viewing distance was approximately 60 cm.

2.5. Data analysis

EEG analysis. The EEG data was processed using Brain Vision Analyzer 2.0 (Brain-Products). All EEG channels were re-referenced to the average between left and right mastoids. Subsequently, the data was subjected to ocular correction (Gratton, Coles, & Donchin, 1983). Epochs with amplitudes exceeding +75 mV or voltage steps of more than 150 mV within a window of 200 ms were rejected from further analysis. Next to that, the data was filtered to select the frequencies of interest, i.e. 12–20 Hz and 36–44 Hz. For each of the channels F_z, F_3, F_4, C_z, C_3, C_4, P_z, P_3, and P_4, the average power for the gamma band and the beta band was computed for the 5-min rest measurements (excluding the first 30 s), and for the first and last 5 min of the first and last trainings sessions (again excluding the first 30 s). Activation patterns within and across experimental conditions and sessions were analyzed by means of Repeated Measures (RM) ANOVAs (see next section for details).

Statistical analyses. First, we investigated whether neurofeedback training (gamma or beta) effectively changed gamma power and beta power after the last training (rest measurement). Repeated measures ANOVAs were conducted with, *TestInstance* (pre versus post training rest measurement) and *ElectrodePosition* (F_z, F_3, F_4, C_z, C_3, C_4, P_z, P_3, P_4) as within-subjects variables and *Group* (gamma feedback versus beta feedback) as between-subjects variable separate for gamma and beta power resting measurements.

Second, we analyzed the EEG data from the training sessions to investigate whether changes in gamma and beta power due to training with gamma neurofeedback relative to training with beta neurofeedback would be visible throughout (and within) the first and last training session. Separate RM ANOVAs were performed on gamma and beta power within and between the first and last training sessions, with *WithinSession* (first versus last 5 min of the training), *TestInstance* (training 1 versus training 8), *FCP* (frontal, central and parietal electrodes) and *Laterality* (left, midline and right electrodes) as within subjects factors and *Group* as between subjects factor.

Third, to examine whether the neurofeedback training would affect subjective well-being, the SPM scores or the memory task, separate ANOVAs were applied. To test the effect of neurofeedback training on responses to the questionnaire (rating on a scale 1–9), we performed the RM ANOVAs with *TestInstance* (pre versus post training scores) as a within subjects factor and *Group* (gamma feedback versus beta feedback) as a between subjects factor on ratings prior to the first and the last training for each of the five items separately. Finally, the same type of RM ANOVAs were performed on the Ravens IQ scores (number of correct trials), and on encoding (percentage correctly color-discriminated pictures during the encoding phase), familiarity (percentage correct of old-new responses combined over remember/know responses during the retrieval phase) and recollection scores (percentage correct on color retrieval) of the memory task. Whenever the assumption of sphericity was violated, degrees of freedom were adjusted according to the Greenhouse–Geisser correction method. An alpha level of 0.05 was taken to indicate significance. Effects with *p*-values below 0.10 are reported as well.

Finally, to explore a potential relation between change in EEG power from the first to the last training (averaged over the first and last 5 min of each training) and scores on the different cognitive tasks and the questionnaire, we used linear correlations. The difference in power between the first and the last training (for both frequency bands) was used to correlate with changes in scores from the first to the last measurement on SPM, subject well-being and memory. The correlations were applied on all subjects from both neurofeedback training groups together. One subject turned out to be an outlier and was removed from the correlational analyses.[2]

Table 1
Mean (+SE) gamma power difference between the pre and the post rest measurements, separated by group and electrode.

Electrode site	Mean		Mean	
	Gamma group Pre	Gamma group Post	Beta group Pre	Beta group Post
F_z	5.29(0.98)	4.51(0.90)	4.07 (0.98)	5.24(0.90)
F_3	5.56(1.09)	4.54(0.59)	5.63 (1.09)	4.99(0.59)
F_4	7.55(1.52)	4.69(0.68)	5.78(1.52)	5.38(0.68)
C_z	6.97(1.99)	6.06(1.02)	5.70(1.99)	5.25(1.02)
C_3	5.75(1.40)	4.92(0.65)	4.88(1.40)	4.31(0.65)
C_4	6.40(1.52)	5.08 (0.62)	5.97(1.52)	4.73(0.62)
P_z	7.07(1.81)	4.76(0.74)	4.79(1.81)	5.15(0.74)
P_3	5.44(1.07)	4.03(0.48)	5.05(1.07)	4.74(0.48)
P_4	5.09(1.05)	3.92(0.46)	5.85(1.05)	4.38(0.46)

Table 2
Mean (+SE) beta power difference between the pre and the post rest measurements, separated by group and electrode.

Electrode site	Mean		Mean	
	Gamma group Pre	Gamma group Post	Beta group Pre	Beta group Post
F_z	8.91(1.35)	6.95(1.52)	6.42(1.35)	9.33 (1.52)
F_3	9.32(1.51)	6.49(0.71)	7.18(1.51)	7.83(0.71)
F_4	10.4(1.62)	7.14(0.90)	7.47(1.62)	8.31(0.90)
C_z	10.52(2.15)	8.77(1.39)	7.59(2.15)	9.06(1.39)
C_3	10.12(1.75)	8.18(0.94)	7.57(1.75)	7.92(0.94)
C_4	10.59(1.67)	8.61(0.99)	7.49(1.67)	8.01(0.99)
P_z	11.34(1.95)	7.99(1.24)	7.19(1.95)	9.22(1.24)
P_3	9.70(1.43)	6.94(0.83)	7.37(1.43)	8.10(0.83)
P_4	9.25(1.42)	7.04(0.92)	8.00(1.42)	7.77(0.92)

3. Results

3.1. EEG

Tables 1 and 2 present, respectively, the mean gamma power for rest measurements separated by group and the mean beta power for rest measurements. Figs. 2 and 3 show, respectively, gamma and beta power within and between training sessions for each electrode, separate for each neurofeedback group.

The analyses performed on the training sessions showed significant within session changes in gamma power for the group trained with gamma and beta neurofeedback, whereas the analyses applied on the resting measurements did not reveal changes in gamma or beta power. The results of these analyses are described below in more detail.

[2] This subject showed a relative large increase on gamma and beta power on F_z from the first to the last training and large increase in mood which distorted the correlation. However, we included this subject in the RM ANOVA's performed on gamma power changes in rest measurements and trainings, because removing this subject from the RM ANOVA's did not change the *F*-values or significance of the results.

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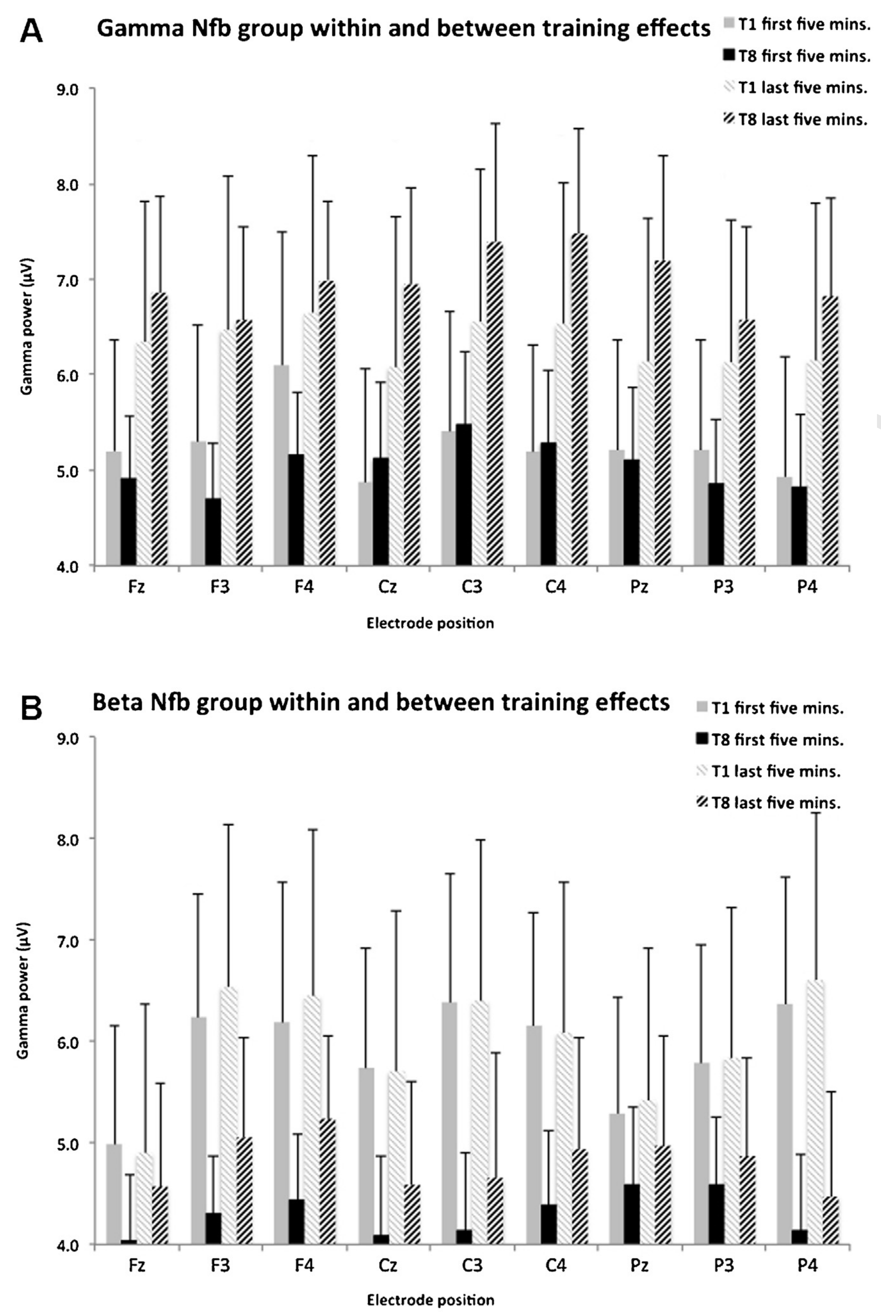

Fig. 2. Gamma power between and with the first and last training sessions, separate for each electrode position and gamma (a) and beta (b) neurofeedback group. Error bars represent standard errors.

3.2. EEG gamma power

3.2.1. Pre and post rest measurements

We did not find any main or interaction effects of *TestInstance*, *ElectrodePosition* or *Group* on rest measurement of gamma EEG power ($ps > 0.1$). This indicates that, relative to the rest measurements before the neurofeedback training, there was no effect of neurofeedback present on EEG gamma power in the rest measurements after the last training.

3.2.2. Within and between training measurements

Significant main effects were found for *WithinSession*, $F(1,18) = 10.46$, $p < 0.01$, and *Laterality*, $F(1,18) = 3.85$, $p < 0.05$. Gamma power was higher at the end of each training (last 5 min) compared to the start of a training (first 5 min), ($M_{first5} = 5.13$, $M_{last5} = 6.13$). With respect to the *Laterality* effect; a simple contrast ($F(1,18) = 6.87$, $p < 0.05$) indicated that gamma power was reduced at midline electrodes ($M = 5.37$) compared to right side electrodes ($M = 5.73$).

Additionally, the analyses revealed a significant interaction between *TestInstance* and *Laterality*, $F(1,18) = 4.24$, $p < 0.05$. Simple contrasts for *TestInstance* and *Laterality* revealed a significant effect of right side compared to left side electrodes, $F(1,18) = 4.72$, $p < 0.05$, pointing at a larger decrease of gamma power between the first and the last training for the right side electrodes ($M_{FirstTraining} = 6.12$, $M_{LastTraining} = 5.34$) compared to the midline electrodes ($M_{FirstTraining} = 5.49$, $M_{LastTraining} = 5.25$).

Most importantly, a significant interaction between *WithinSession* and *Group* was found, $F(1,18) = 4.58$, $p < 0.05$). Participants trained to increase their gamma EEG, seemed to be more

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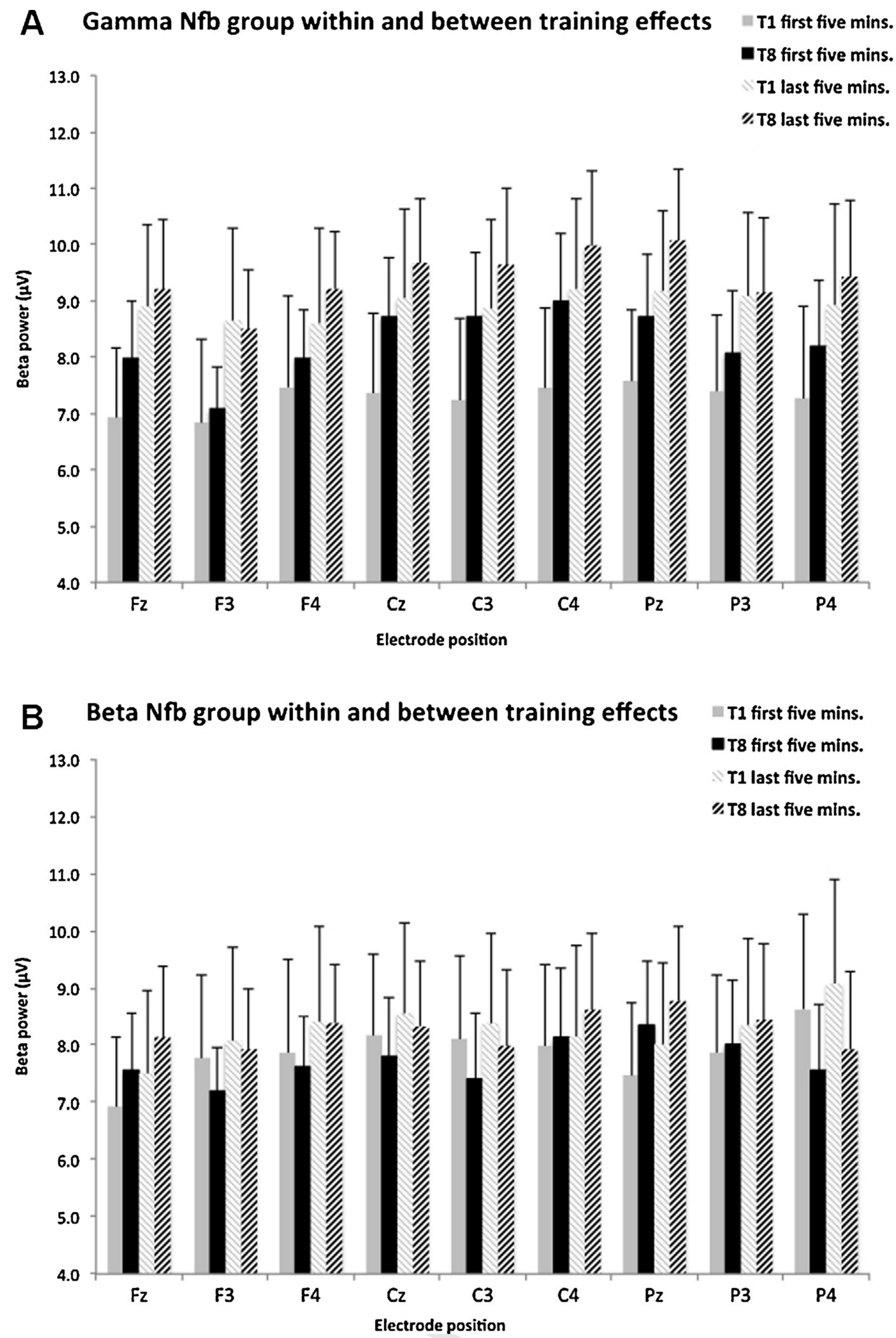

Fig. 3. Beta power between and with the first and last training sessions, separate for each electrode position and gamma (a) and beta (b) neurofeedback group. Error bars represent standard errors.

effective at enhancing gamma power *within* a training (M_{first5} = 5.16, M_{last5} = 6.67) compared to the group that was trained to increase beta (M_{first5} = 5.10, M_{last5} = 5.41) (this interaction of *WithinSession* and *Group* will be more elaborately tested below).

No main effect of *FCP*, *TestInstance* or *Group* on any of the electrode positions was found, all $ps > 0.6$, thus gamma power did not differ *between* the first and last training, FCP electrode position or neurofeedbacktraining. Additionally, no interactions between *FCP* and *Group*, *TestInstance* and *Group* or *TestInstance*, *WithinSession* and *Group* were found, all $ps > 0.14$.

To further investigate the source of the *WithinSession* by *Group* interaction, we performed similar analyses separately for participants trained with gamma and beta feedback. These analyses indicated that gamma power significantly increased within training sessions in the gamma group, *WithinSession*, $F(1,9) = 11.03$, $p < 0.01$, whereas the difference between gamma power from the first to the last part of each training in the beta group was not significant, *WithinSession*, $p = 0.4$ (see Fig. 2a and b). No other main or interaction effects of *TestInstance*, *Laterality* and *FCP* were found for the gamma group, $ps > 0.18$. The group trained on beta neurofeedback showed results similar to the overall analysis; a main effect of *Laterality* and an interaction between *TestInstance* and *Laterality*. Simple contrasts indicated that gamma power was smaller at midline electrodes ($M = 4.91$) compared to right side electrodes ($M = 5.45$), ($F(1,9) = 4.34$, $p = 0.06$). Also, gamma power seemed to be more reduced between the first and the last training on right

Table 3
Mean (+SE) scores for the SPM, memory task (mean percentages for each memory component) and questionnaire pre and post training separate for both neurofeedback groups.

Dependent measure	Mean		Mean	
	Gamma group Pre training	Gamma group Post training	Beta group Pre training	Beta group Post training
SPM	20.8(1.36)	19.6(1.14)	18.6(1.36)	22.2(1.14)
Encoding	87.5(7.3)	74.8(10.6)	71.3(7.3)	73.0(10.6)
Familiarity	69.0(3.4)	78.4(3.4)	70.0(3.4)	81.1(3.4)
Recollection	60.6(3.7)	64.4(3.7)	61.0(3.7)	63.5(3.7)
$Q_{Appetite}$	5.3(0.42)	4.1(0.72)	5.1(0.42)	4.5(0.72)
Q_{Sleep}	3.5(0.58)	3.6(0.71)	4.8(0.58)	5.1(0.71)
$Q_{Concentration}$	6.0(0.37)	6.3(0.37)	5.9(0.37)	6.1(0.37)
Q_{Memory}	5.9(0.38)	6.6(0.36)	5.6(0.38)	5.9(0.36)
Q_{Mood}	8.0(0.45)	8.1(0.33)	8.0(0.45)	7.9(0.33)

side electrodes ($M_{FirstTraining} = 6.31$, $M_{LastTraining} = 4.60$) compared to the midline electrodes ($M_{FirstTraining} = 5.34$, $M_{LastTraining} = 4.47$), ($F(1,9) = 6.61$, $p < 0.05$).

3.3. EEG Beta power

3.3.1. Pre and post rest measurements

We did not find any main or interaction effects of *TestInstance*, *ElectrodePosition* or *Group* on rest beta power ($ps > 0.08$). Numerically, beta power increased for the group trained on beta feedback ($m_{pre\ rest} = 7.36$, $m_{post\ rest} = 8.39$) and decreased for the group trained on gamma ($m_{pre\ rest} = 10.02$, $m_{post\ rest} = 7.57$), although this trend was not significant, *TestInstance * Group*, ($F(1,18) = 3.25$, $p = 0.09$). Post hoc tests comparing these averages separate for each group did not reveal a significant effect of *TestInstance* for the group trained on beta nor for the group trained on gamma, $ps > 0.2$. This points out that there was no transfer of the neurofeedback training to the rest measurements on beta power, similar to the absence of an effect of training on the gamma power rest measurements.

3.3.2. Within and between training effects

A main effect of *WithinSession* was found; beta power significantly increased *within* each training ($F(1,18) = 11.25$, $p < 0.01$, $M_{first5} = 7.79$, $M_{last5} = 8.73$). We also found a significant main effect of *FCP* ($F(1,18) = 5.26$, $p < 0.05$). Simple contrasts showed that beta power at central electrodes ($M_{central} = 8.44$) was significantly higher than at frontal electrodes ($M_{frontal} = 7.94$, $F(1,18) = 5.12$, $p < 0.05$). The interaction between *TestInstance* and *Laterality* trended near significance, ($F(1,18) = 3.09$, $p = 0.06$). Subsequent simple contrasts, however, did not show any significant differences. No other main effects of *Laterality*, *TestInstance* or *Group*, or interactions between *Laterality*, *FCP*, *TestInstance*, *WithinSession* and *Group* were found, all $ps > 0.12$. Beta power was not significantly enhanced *between* the first to the last training, nor did electrode position (FCP or laterality) or neurofeedback training affect changes in beta power.

Again, we applied the same analyses separately for participants trained with gamma and beta feedback to test whether beta power would be significantly increased within sessions due to specific neurofeedback training. For participants trained on beta neurofeedback training, beta power significantly increased from the first to the last 5 min within each training *WithinSession* ($F(1,9) = 20.52$, $p < 0.001$, see Fig. 3a and b). Furthermore, there was a significant interaction between *WithinSession*, *TestInstance* and *FCP* ($F(2,18) = 7.96$, $p < 0.01$). Separate analyses for the first and last training suggested that changes in beta power in the last training were larger on frontal electrodes ($M_{first5} = 7.46$, $M_{last5} = 8.15$) compared to parietal electrodes ($M_{first5} = 7.97$, $M_{last5} = 8.38$), although this was not significant ($F(1,9) = 3.94$, $p = 0.08$). No other main or interaction effects of *TestInstance*, *Laterality* and *FCP* were found for the beta group, $ps > 0.17$.

Participants trained with gamma neurofeedback also enhanced their beta power within each training, *WithinSession* ($F(1,9) = 6.49$, $p < 0.05$). Moreover, nearly significant main effects of *FCP* ($F(2,18) = 3.53$, $p = 0.05$) and *Laterality* ($F(2,18) = 3.26$, $p = 0.06$) were found in the gamma group. Follow up simple contrasts revealed no effect for *Laterality* and slightly larger beta power on central ($M = 8.74$) compared to frontal electrodes ($M = 8.11$), ($F(1,9) = 4.60$, $p = 0.06$).

No other main effect of *TestInstance* or other interaction effects of *TestInstance*, *Laterality* and *FCP* were found for the gamma group, $ps > 0.30$.

Questionnaire. Table 3 shows the mean scores for the intelligence test, the memory task and subjective well-being pre and post training separate for both neurofeedback groups. Fig. 4 shows the mean percentage of change pre and post training for each of the questionnaire items. No main or interaction effects of *Group* and *TestInstance* were found on memory, concentration, appetite or mood ($ps > 0.1$). Although the need for sleep did not significantly change due to neurofeedback training for either of the groups (a 48% increase in the gamma group and a 57% increase in the beta group, *TestInstance * Group*, $F(1,18) = 0.03$, $p = 0.9$), the average need for sleep was nearly significantly larger for participants trained with beta ($m = 5.0$) than the gamma ($m = 3.6$), *Group*, $F(1,18) = 4.31$, $p = 0.05$). Self-assessed memory increased over time (*TestInstance*, $F(1,18) = 6.34$, $p < 0.05$). Appetite tended to decrease over time (*TestInstance*, $F(1,18) = 3.84$, $p = 0.07$).

Intelligence. Fig. 5 shows the mean percentage of change pre and post training for the IQ test. There were no main effects of *TestInstance* or *Group* on intelligence scores ($ps > 0.1$). The interaction *TestInstance * Group* showed a trend toward significance, $F(1,18) = 3.81$, $p = 0.07$. Post hoc tests comparing the intelligence scores for each group pointed out that this trend was mainly due to an increase (although not significant) in the intelligence score in the beta group, *TestInstance*, $F(1,9) = 2.96$, $p = 0.1$, whereas the gamma group performed similar pre and post training, *TestInstance*, $F(1,9) = 0.87$, $p = 0.4$.

Memory. Fig. 6 shows the mean percentage of change pre and post training for the memory test. We did not find significant effects of *TestInstance* and *Group* on encoding or recollection scores ($ps > 0.1$). Both recollection and familiarity scores increased over time, but this effect was only significant for familiarity, *TestInstance*, $F(1,18) = 10.05$, $p < 0.01$. Post hoc analyses on familiarity scores separate for each group indicate that performance increased over time for both groups, although this was more significant for the gamma group, *TestInstance*, $F(1,9) = 6.30$, $p < 0.05$ than the beta group, *TestInstance*, $F(1,9) = 4.44$, $p = 0.06$.

3.3.3. Correlations EEG and behavior

There were no significant correlations between the mean percentage of change in gamma power (from first to last training) and

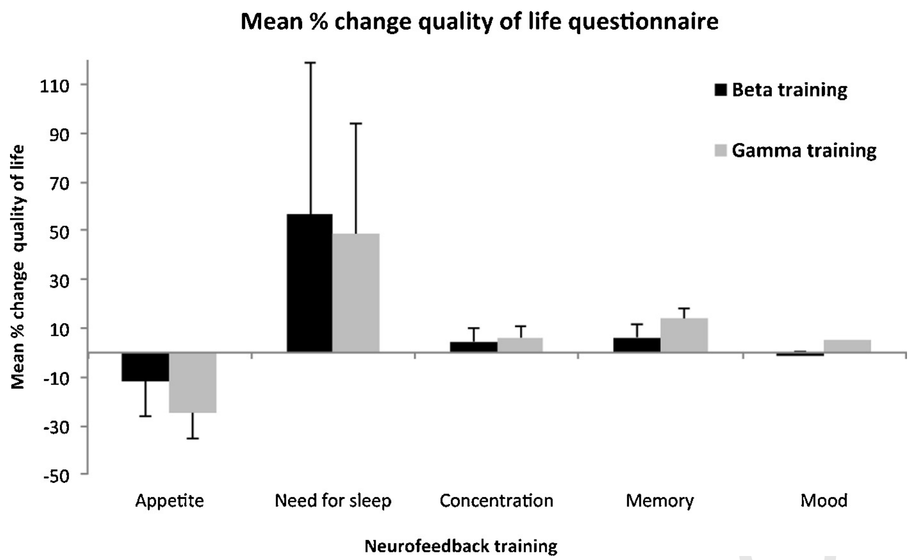

Fig. 4. Percentage of change on the quality of daily life questionnaire pre to post training for both neurofeedback conditions. Error bars represent standard errors.

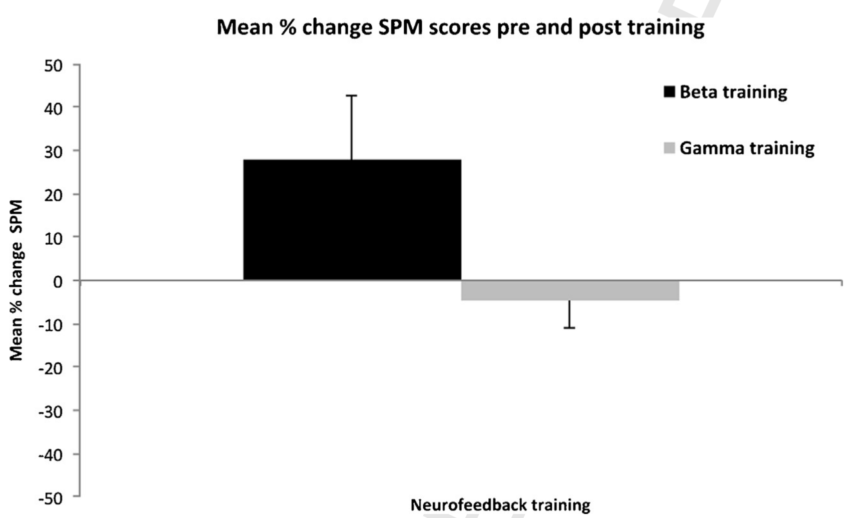

Fig. 5. Percentage of change in SPM scores pre to post training for both neurofeedback conditions. Error bars represent standard errors.

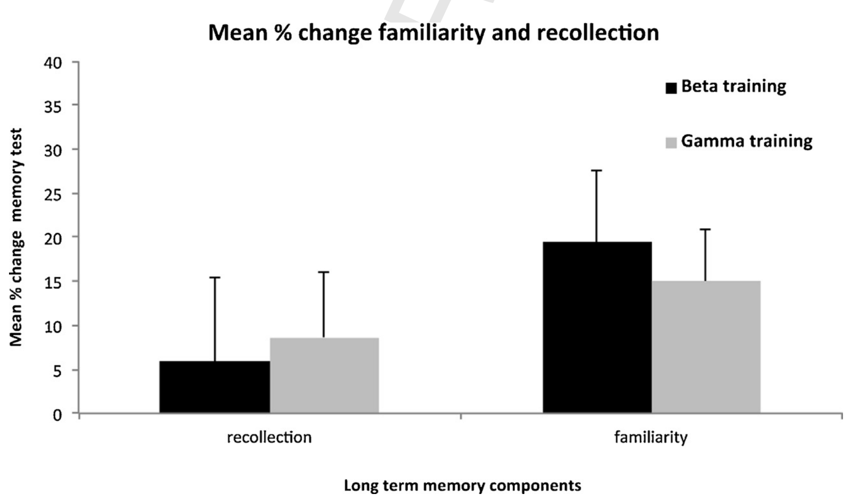

Fig. 6. Percentage of change on the memory task pre to post training for both neurofeedback conditions. Error bars represent standard errors.

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the behavioral changes on SPM, the memory task and the questionnaire items, r-values < 0.3, p-values > 0.2. The mean percentage of change in beta power (from first to last training) on F_4 showed a negative correlation with appetite: an increase in beta power resulted in a reduction in appetite, $r = -0.45$, $p = 0.05$. When separating the neurofeedback groups, this correlation turned out to be present in the beta group, $r = -0.65$, $p < 0.05$ but not in the gamma group, $p = 0.89$.

Also, an increase in beta power on F_4 ($r = -0.42$, $p = 0.07$) and C_4 ($r = -0.43$, $p = 0.07$) correlated with a smaller recollection score. When looking at both neurofeedback groups separately, this correlation was no longer present, $ps > 0.15$. No other correlations were found between the mean percentage of change in beta power (from first to last training) and the behavioral changes on SPM, the memory task and the remaining questionnaire items, r-values < 0.3, p-values > 0.1.

4. Discussion

Previous research suggests that beta and gamma brain activity play a role in intelligence and memory. We investigated whether in elderly participants, beta and gamma neurofeedback would enhance brain activity subsequent to the training (within the frequency range that they were trained with) and whether this increase would be associated with improvements in intelligence and memory. We used a randomized double-blind neurofeedback protocol similar to those previously implemented by Keizer, Verment, et al. (2010) and Keizer, Verschoor, et al. (2010). Participants were able to increase brain activity according to the protocol they were trained on within a training session, however, this did not transfer beyond the training or to a behavioral improvement.

4.1. Neurofeedback effect on gamma activity and behavior

Although there was no effect of neurofeedback on gamma power in rest EEG measurements (pre and post training), participants in the gamma feedback group showed an increase in gamma power within training sessions (but not between sessions). This increase was not visible in participants trained on beta power. Contrary to our expectations, gamma neurofeedback training did not affect the intelligence and recollection, nor did it affect subjective well-being.

Participants trained with gamma neurofeedback, as opposed to the beta group, showed the expected increase of their gamma activity within a session. The average size of the effect was comparable to the between-session effect found by Keizer, Verment, et al. (2010), who reported increases in gamma power of about 1.5 μV on F_z and 2.0 μV on O_z in their study on neurofeedback effects on memory. The effects found in the current study were somewhat smaller than those found by Keizer, Verschoor, et al. (2010) who reported an increase of 2.9 μV at O_z in their study on neurofeedback effects on binding and intelligence. The lack of expected gamma effects on behavioral and cognitive scores could be caused by a less robust and partly smaller effect of neurofeedback training in our study compared to Keizer, Verment, et al. (2010) and Keizer, Verschoor, et al. (2010). Possible reasons for this will be discussed in Section 4.3.

As in Keizer, Verment, et al. (2010) we found the increase in gamma power for the gamma group on F_z but also on central and parietal electrode sites (not used by Keizer, Verment, et al., 2010; Keizer, Verschoor, et al., 2010). Significant effects on electrode positions besides the feedback electrode (in our case, F_z), have been found before (see Hanslmayr, Sauseng, Doppelmayr, Schabus, & Klimesch, 2005). Frequency-specific neurofeedback training can be fairly location-unspecific in its effect on the underlying EEG (Fernandez et al., 2007); this could be explained by the fact that EEG frequencies are produced by different populations of neurons within the same system, and that relevant parts of this system may interact with other parts (Angelakis et al., 2007). Indeed, the low spatial resolution of EEG in general, and the limited coverage of brain areas in the current study, is a limitation. For future studies, we would recommend covering more electrode sites.

4.2. Neurofeedback effect on beta activity and behavior

For both neurofeedback groups we found an increase of power in the beta band within training sessions; beta power was enhanced at the end of a training session compared to beta power recorded at the start of the a training session. Not only the beta neurofeedback, but also the gamma neurofeedback showed increased power in the beta band. Beta and gamma frequencies may not be independently trainable, as suggested by earlier research that found that the gamma and beta power band seem to share some amount of common variance (Bird, Newton, Sheer, & Ford, 1978). The coexistence of lower frequency rhythms (like beta or theta) with higher frequency rhythms such as gamma has been observed in in vitro studies, for example in the hippocampus and neocortex (Roopun et al., 2008). Haenschel, Baldeweg, Croft, Whittington, and Gruzelier (2000) suggested that periods of synchronous gamma activity, induced by for example auditory stimuli in humans, might lead to subsequent beta frequency oscillations; gamma rhythms may switch to beta frequencies induced by increased after hyperpolarization. Another possible explanation for the beta power increase in both groups is that in general, participants may have increased attention or arousal within training sessions which may be reflected by enhanced beta power during training (Egner & Gruzelier, 2001, 2003). With an increase in beta power increased (visible in both groups) we expected improved performance on the familiarity measure of the memory task which is indeed what we found. However, the amount of beta power did not correlate with an increase in familiarity as in Keizer, Verment, et al. (2010). The increase in beta power showed a modest negative correlation with another aspect of memory: recollection memory. This seems to be in line with the review of Hanslmayr et al. (2012) who related successful retrieval to a decrease in beta power. Since the present study tested a relatively small number of participants, our EEG results were limited to within session effects, and the fact that the correlational analysis included both participants that exclusively enhanced beta as well as the participants that increased both beta and gamma, we need to be careful in interpreting these findings.

Future studies with larger samples and stronger neurophysiological results may shed light on whether beta band activity is more beneficial for some aspects of memory (familiarity) than for others (recollection).

Besides a general enhancement in beta power and an improvement in familiarity scores, we found that self-assessed memory increased for both neurofeedback groups. This increase of self-assessed memory may reflect participants' training expectations, or an actual improvement due to non-specific training effects.

4.3. Limitations and recommendations for future studies

The enhanced gamma and beta power found within the training sessions did not transfer to the rest EEG measurements nor did they show a clear relation with improvements on intelligence and memory. The increase in beta and gamma power found in the current study were limited to the training and the participants exclusively demonstrated feedback effects when actively engaging in enhancing their brain activity. This tentatively suggests that elderly people are still preserved with the flexibility to influence their own brain activity and trainability of gamma and beta rhythms in elderly people. However, since these effects did not implicate behavior we provide some explanations for the limited finding of the current study and suggest several improvements for future studies.

First, with increasing age, people show more intra- and inter individual variability in cognitive performance and associated neuronal noise increases (Li, Brehmer, Shing, Werkle-Bergner, & Lindenberger, 2006; Li, Lindenberger, & Frensch, 2000; Li, von Oertzen, & Lindenberger, 2006; MacDonald, Hultsch, & Bunce, 2006; MacDonald, Nyberg, & Backman, 2006). More neuronal and behavioral variability makes it more difficult to show effects in an experiment like the current one. In general, the lack of clear-cut norm groups and the accompanying difficulty in comparing participants is a clear limitation for research involving elderly (Klass & Brenner, 1995).

Second, although both gamma and beta band activity have been shown to be related to memory performance in young adults, other frequency bands, or a change in the balance between gamma/beta and other frequency bands, may play a role during memory performance in older adults. For example Axmacher et al. (2010), Canolty et al. (2006) and Park et al. (2012) recently suggested that the interaction between theta-phase and gamma power may be important during working memory. Similarly, beta neurofeedback training within a particular range may have stronger effects on memory (i.e. specific effects of SMR found on attention as in Egner & Gruzelier, 2001, 2004) than feedback in a broad range as applied in the current study. Q3

Third, a difference between the current study and those performed by Keizer, Verment, et al. (2010) and Keizer, Verschoor, et al. (2010) is the electrode used for feedback, that is F_z instead of O_z (although the increased gamma was found on F_z in Keizer, Verment, et al., 2010). We used F_z for feedback in elderly with the aim of increasing frontal activity to facilitate compensation rather than trying to restore the activation to the level of a young adult. However, this difference in protocol may have resulted in smaller and/or more variable increases or different effects on behavior. Additionally, results of an fMRI study conducted by Erickson et al. (2007) suggest that aiming for restoration (using O_z) rather than for compensation (using F_z) in elderly might be more effective. Erickson et al. (2007) trained a group of young and elderly people on dual task performance. After training, the behavioral improvement in the elderly group was more similar to performance in the young group while this was not associated with compensatory increases of frontal activity. Grady (2008) proposed that before cognitive training, older adults need more cognitive control to perform the dual tasks, which is indicated by more frontal activity, whereas the training allowed them to reduce their dependence on these control processes.

A final limitation concerns the questionnaire used; to compare our findings with the results of Keizer, Verment, et al. (2010) and Keizer, Verschoor, et al. (2010), the current study used the same questionnaire to investigate subjective changes with neurofeedback training. However, the questionnaire was not formally validated. A questionnaire measuring for example positive and negative mood, like the positive and negative affective scale (PANAS), may have been more sensitive to changes in well-being.

Although not every neurofeedback study finds transfer of the training to rest measurements, there might be several aspects that could enhance training effects in older adults in future studies.

The protocol as used in Keizer, Verment, et al. (2010) and Keizer, Verschoor, et al. (2010) was replicated as accurately as possible. However, in the current study an extended time schedule (3 weeks instead of 10 days) was used for the neurofeedback training to increase planning flexibility for the subjects. This less intensive neurofeedback training program could have contributed to more variable and smaller effects. Training effects and brain plasticity in elderly are generally smaller (Buitenweg, Murre, & Ridderinkhof, 2012, Nyberg, 2005). An increase in power may benefit young adults but the same increase may not be equally beneficial for older adults due to less efficient brain processes. Thus for older adults more neurofeedback sessions may be required.

Likewise, operant condition in older adults may require different parameter settings of the neurofeedback protocol (i.e. the filter settings and timing of the feedback related to changes in brain activity, Sherlin et al., 2011) which could be optimized in future studies. Q4

Furthermore, measuring EEG power during cognitive performance (subsequent to neurofeedback training) may also reveal benefits of feedback in relation to behavior. For example, Missonnier et al. (2010) and Van der Hiele et al. (2007) found specific EEG patterns that differentiated levels of mild cognitive impairment exclusively during memory tasks but not during rest measurements.

Moreover, the type of neurofeedback applied in the current study (learning by means of beeps) may not be optimal with respect to motivating this particular group of participants, which could have contributed to weaker, more variable effects of neurofeedback training. Finally, a more gradual feedback may have enabled participants to differentiate between successful and unsuccessful tendencies and fine-tune their cognitive approach to elicit feedback. An example of feedback that has been shown to be effective in a randomized double-blind alpha training protocol (van Boxtel et al., 2012) and that is both gradual and entertaining, is presenting the participants' favorite music where the quality of the music increases with the power in the trained frequency band. For future studies, we thus recommend more engaging and gradual feedback. This may be of particular importance for elderly who have more trouble staying alert and motivated compared to younger participants (Chao & Knight, 1997; Filley & Cullum, 1994).

5. Conclusions

In sum, although neurofeedback training on the gamma or the beta band does not improve cognitive performance in older adults, the current study suggests that the brain remains trainable with aging since the participants were able to change their brain activity based on neurofeedback within training sessions.

Uncited references Q5

Egner et al. (2004) and Gevensleben et al. (2009).

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