

# Functional Correlates of the Aging Brain: Beta Frequency Band Responses to Age-related Cortical Changes

#### Mario Christov and Juliana Dushanova'

Institute of Neurobiology, Bulgarian Academy of Sciences, Acad. G. Bonchev St 23, 1113 Sofia, Bulgaria

\*Corresponding author: Juliana Dushanova, Institute of Neurobiology, Bulgarian Academy of Sciences, Acad. G. Bonchev St 23, 1113 Sofia, Bulgaria, Tel: 359 2 979 3778; E-mail: juliana@bio.bas.bg

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#### Abstract

**Background:** Cognitive decline and symptoms of attention deficits, executive dysfunction, and memory impairments describe dementia in the elderly. Particular frequency oscillations that occur within the affected brain regions could be used to classify some idiopathic dementias as specific diseases. The approach, applied in this study, can be useful for early discrimination between normal and pathological brain aging, and could contribute additional information to the clinical data in evaluating dementia that is of benefit for treatment of cognitive alterations and dementia.

**Methods:** In this study, the age effect on the brain electrical activity was examined auditory discrimination task (low–frequency and high–frequency tone) at particular cortical locations in beta–frequency bands ( $\beta$ 1: 12.5–20;  $\beta$ 2: 20.5–30 Hz) during sensory (post–stimulus interval, 0–250 ms) and cognitive processing (250–600 ms).

**Results:** The beta1 activity is less affected by age during sensory processing. The reduced beta1 was more widespread during cognitive processing. This difference increased in fronto-parietal direction more expressed after high-frequency tone stimulation. Beta2 activity was more pronounced with a progressive age during sensory processing and diminished with age on cognitive processes. Reducing regional-process specificity with progressing age characterized age-related and tone-dependent beta2 changes during sensory processing.

**Conclusions:** The age influence was higher on the cognitive processes than on the perceptual ones.

**Keywords:** Age effect; Eeg; Auditory discrimination; Sensory-motor task; Event–related high-frequency oscillations

#### Introduction

Age-related brain changes could lead to dedifferentiation and reduced regional-process specificity or hemispheric asymmetry diminution while a right hemi-aging hypothesis posits a larger decline with age in a right than in a left hemisphere. The increased activity in the frontal brain could be a result of a functional deficit, dedifferentiation and compensation co-occur. Such a constellation of effects could be caused by atrophy in the frontal brain regions or to a change in strategy, caused by this atrophy [1]. According to the scaffolding theory, a compensatory process supposes patterns of a frontal cortex over-activation with age, but may include parietal, medio-temporal and occipital regions in a response to declining neural structures and function [2,3]. Pervasive recruitment of frontal areas, altered lateralization and changing the specificity of the visual and auditory cortex, indicate the dynamic nature of functional brain organization that can be relevant to the recovery and compensatory processes across the lifespan.

Research on age-related brain alterations has been conducted with electroencephalographic (EEG) studies mainly in the time domain. By far the most popular and classical EEG time-domain method is this of event-related potentials (ERPs). Early modal-dependent and obligatory N1 and P2 components of the ERPs, permitting sensory analysis of the events, are more pronounced with increasing age, while later N2 and P3 components of the potentials, reflecting cognitive processes, diminished with increasing age and hemispheric asymmetry of N2 reduced with age [4]. Spectral domain development EEG studies have shown reduced low-frequency density and increased high-frequency density with age [5]. Frequency phase-locked brain oscillations in the alpha frequency band were more apparent with the progressive increase in age during sensory processing and age-related changes in alpha band activity were focused at frontal and sensorimotor areas [6,7]. Functional brain specificity diminished with increasing age and did not observe for amplitudes of low-frequency (delta, theta, and alpha) oscillations during cognitive processing [7]. The high frequency network was characterized by a shift towards more random topology, especially in the beta frequency band during resting state [6]. Attentional modulation with age, related to alertness deficits or vigilance deficits, was conducted with a beta-band EEG decreased activity during a simple visual attention task in elderly with low behavioral performance accuracy [8,9]. Alterations in beta-band activity have also been related to pathological processes [10]. So far, results from event-related high-frequency studies still remain inconclusive whether beta-band responses are related to plasticity in neural recruitment contributed to the stability of sensory/cognitive mechanisms accompanying aging or are underlined pathological cortical dysfunction in dementia, correlated to the degree of cognitive impairment seen in aging brain. Cognitive decline and symptoms of attentional deficits, executive dysfunction, and memory impairments describe dementia in the elderly. Dementia occurs in several major neurodegenerative disorders as fronto-temporal dementia and hippocampal sclerosis of aging Alzheimer's disease, Lewy body dementia, which vary between brain regions like the hippocampus entorhinal cortex, medial temporal lobe, frontal cortex and inferior parietal cortex and may explain a magnitude of deficits in different cognitive domains. Peculiar frequency oscillations that occur within affected brain regions have been used to classify some idiopathic dementias as specific diseases [10].

In the study, we aimed to identify the effects of aging on the specific stages of information processing in the cortical high-frequency domain. The hypothesis was that more pronounced high-frequency pattern correlated with sensory processing and progressive deficits in event-related high-frequency processing with advancing age specifically correlated with poorer cognitive abilities during auditory discrimination task.

# Methods

#### **Subjects**

Forty-eight healthy volunteers participated in the study. Screening confirmed that subjects were free of past or current psychiatric and neurological disorders. All were right-handed and without deficits in hearing, based on a qualitative analysis of electrophysiological evaluation [11]. Handedness was assessed by a questionnaire adapted from the Edinburgh Handedness Inventory [12]. Subjects were assigned to two age groups: a young group (YG, 25–31 years of age, mean age of 27 years, 13 males and 11 females) and an older group (OG, 55–60 years of age, mean age of 57 years, 13 males and 11 females. A study has been approved by a research ethics committee. All subjects were thoroughly instructed about the nature of the experiment. Participants gave a written informed consent in accordance with the Declaration of Helsinki to take part in the study.

# Apparatus and stimuli

The subject was comfortably seated in an ergonomically designed chair within an electromagnetic shielding Faraday's cage during measurements. Subjects were acoustically stimulated binary using two pure tones: a low-frequency tone at 800 Hz (LT), and a high-frequency tone at 1000 Hz (HT). Acoustic intensity was 60 dB. Loudspeakers were situated in front of the subjects. All measurements were executed with closed eyes. Each experimental series consisted of 50 HT and 50 LT computer's generated acoustic stimuli with duration each of 50 ms and an inter-stimulus interval of 2.5-3.5 s presented to the subject in a randomized order. A task was a binary choice-reaction sensorimotor task. Generation of motor response was a behavior measure of agingrelated slowing. While listening to acoustic stimuli, subjects reacted to a high tone by pressing a key with the left index finger, and to a low tone with the right index finger. Participants were instructed to press the key as fast as possible with their correct index finger, so speed and accuracy had equal importance. Participants were instructed to press the key as fast as possible with their correct index finger, so speed and accuracy had equal importance. Electroencephalography (EEG) was recorded with a Nihon Kohden EEG-4314F (cut-off frequencies of 0.3-70 Hz) using 12 Ag/AgCl Nihon-Kohden electrodes attached to the subject's scalp, according to the international 10-20 systems: F3, C3, P3, T3; Fz, Cz, Pz, Oz; F4, C4, P4, T4. Simultaneously, hand movement performance was tracked by a force profile and a surface electromyographic activity pattern (EMG) of first dorsal interosseus muscles (bandpass filtered 0.03-500 Hz). EEG records were controlled

for EMG artifacts. EEG signals were referenced to both processi mastoidei and a ground electrode placed on a forehead. Records were synchronized to the stimulus onset. An oculogram (EOG) was recorded from electrodes placed above and below the lateral canthus of the left eye for a detection of eye movements and blink artifacts. Only artifact – free EEG records were processed. The skin impedance was controlled to be less than  $4 \text{ k}\Omega$ . A second-order notch filter was applied in order to discard the 50 Hz AC noise component, using the built-in MATLAB function. The EEG signals were digitized on-line with a sampling frequency of 500 Hz.

The reaction times were determined from the force-time curves. Pressing with the index finger produced a negative deflection in the force records. The criterion for detection of the reaction onset was a drop of the force curve more than 10% below a baseline, defined for the first 40 ms after the stimulus offset.

# Procedure

Repeatable signals with, at least, a biphasic waveform component with a similar shape within 1.5 s window, were termed as averaged event-related "waveforms" (ERWs). The parameters of the waves were computed relative to the corrected baseline based on 300 ms prestimulus period. The signals were later verified to have a signal-tonoise ratio (SNR) above mean 1.1. SNRs were calculated using the following formula SNR = A /  $(2*SD_{noise})$ , where the amplitude A was the peak-to-peak voltage of the mean ERW and SD<sub>noise</sub> was the standard deviation of the noise. The noise (ɛ) was obtained by subtracting the mean from each individual averaged event-related wave (AERW). In other words, for a given single electrode,  $\varepsilon$  was just the collection of residuals when the mean AERW was subtracted from each individual ERW, and SD<sub>noise</sub> was the standard deviation of this collection. Only those single trials satisfying the rejection criterion after noise removal were included in the time-frequency analysis. The time-frequency analysis represented the time-resolved amplitude spectra of the recorded EEG signals and performed within the MATLAB software. For this purpose, the signals were processed using the fast Fourier transformed algorithm with 200 ms-long sliding Hamming window and a step size of 10 ms. The average spectrograms were calculated from the single-trials spectrograms. For each tone condition, the average spectrogram was used to calculate the baseline for each frequency bin. The relative single-trials spectrograms were the absolute ones divided by each time-frequency bin comparative to the baseline corresponded to this frequency bin. The calculation was done for each tone condition separately. Relative single-trial band power amplitude modulation was investigated in beta-frequency sub-bands: beta1 ( $\beta$  1) – [12.5, 20] Hz; beta2 ( $\beta$  2) – [20.5, 30] Hz. The amplitude modulation in time for each of the frequency bands was averaged amplitude across all bins in a corresponding frequency range. Relatively, sensory processing takes place during the first post-stimulus interval (T1: 0-250 ms) and cognitive processing during the second post-stimulus interval (T2: 250-600 ms). Activity in each frequency band was examined during the sensory processing stage (T1), according to the interval when the sensory wave components (N1, P2) appearance and during cognitive processing (T2), according to the time interval of the cognitive wave components (N2, P3).

#### Statistics

Statistical analysis of the amplitudes of each frequency component ( $\beta$ 1,  $\beta$ 2) was performed during the post-stimulus interval and the difference between the groups was assessed for each tone type by a

bootstrap nonparametric procedure [13]. The characteristics were grouped by tone, young and elderly healthy controls and analyzed by a permutation test for multiple comparisons between time points for time course analysis. The computed random distribution was analyzed with a nonparametric test, i.e. Kruskal–Wallis's test (P < 0.05) for pair's comparison of the scalp electrodes between groups. This procedure should reduce the influence of any arbitrary variations in experimental conditions between trials. Reaction times were compared between groups and tone condition by Kruskal–Wallis nonparametric test ([KW test], P < 0.05).

# Results

#### **Reaction time analysis**

The right hand reaction time was no significantly shorter than the left hand reaction time in both groups (OG: left hand 477.12  $\pm$  8.56 ms, right hand 455.41  $\pm$  8.82 ms, F<sub>1, 828</sub> = 12.31, P = 0.06; YG: left hand 456.86  $\pm$  8.62 ms, right hand 445.10  $\pm$  8.75 ms, F<sub>1, 830</sub> = 0.17, P = 0.28). In between – group's comparison YG presented faster reactions, but significantly only for the left hand (YG 456.86  $\pm$  8.62 ms; OG 477.12  $\pm$  8.56 ms; F<sub>1, 830</sub> = 19.87, P < 0.046), not for the right hand (YG 445.10  $\pm$  8.75 ms; OG 455.41  $\pm$  8.82 ms; F<sub>1, 830</sub> = 0.51, P < 0.079).

#### Brain oscillation components during T1

The patterns of grand average time amplitude–frequency changes overall YG and OG trials in response to HT and LT were spatially distributed for the two tones (Figure 1).

Beta1 amplitude was significantly lower for OG compared to YG over the right temporal area, either tone, during the early post-stimulus interval 50-250 ms (T4:  $F_{1, 828} > 15.3$ , P < 0.05, KW test; Figure 1A and 1B). Beta1 amplitude was appeared earlier with a shorter duration in OG than in YG over the right temporal area, earlier after HT than LT. Significantly lower  $\beta$ 1 amplitude was observed at the left parietal area after HT ( $F_{1, 828} = 10.4$ , P < 0.05; Figure 1B).

Beta2 amplitude, for either tone, was significantly higher at central and left frontal areas in OG than in YG (HT:  $F_{1, 830} > 25.3$ , P < 0.01, Figure 1C; LT: F1, 828 > 13.3, P < 0.05, Figure 1D). The duration of beta2 amplitude's difference between groups was longer after HT than LT. Beta2 activity was significantly lower in OG over a right temporal side for LT (LT,  $F_{1, 828} > 19.1$ , P < 0.01 for a time interval 50–250 ms) (Figure 1D) and over the occipital side for either tone ( $F_{1, 828} > 13.1$ , P < 0.05).

#### Brain oscillation components during T2

OG showed whole–head significantly lower  $\beta 1$  during cognitive processing for either tone (400–600 ms, Figure 1A and 1B; except Oz, either tone, F3 and T3 by LT stimulation). Between–group's difference increased in fronto–parietal direction, more expressed after HT (F<sub>1, 830</sub> > 28.7, P < 0.001 for more of the channels) (Figure 1A) and started earlier with a prolonged duration after HT than after LT (F<sub>1, 828</sub> > 19.1, P < 0.01 for more of the channels) (Figure 1B).



**Figure 1:** Scalp distributions and statistical comparisons of the amplitudes of beta frequency band modulations for the groups (YG – blue and OG – red) for the sensory-motor task: beta1 frequency band (A) HT and (B) LT; beta2 frequency band (C) HT and (D) LT. The vertical bars represent 95% confidence intervals. The colors correspond to different critical values of significance (magenta – p < 0.001, green – p < 0.01, yellow – p < 0.05) analyzed by a permutation test for multiple comparisons at each time point for pair's comparison of scalp leads between young and elder groups (K-W test).

Lower  $\beta 2$  amplitude was observed in OG than in YG during cognitive processing (250–600 ms), although significant changes occurred only at F3, C3, P4, T4, and Oz after HT (P < 0.05) (Figure 1C).

#### Comparison of the brain oscillations of LT to HT

YG did not show a significant difference in the high-frequency oscillation activity with regard to the tones.

Higher  $\beta$ 1 activity was found only for OG after LT during cognitive processing at the right sensorimotor (400–500 ms;  $F_{1, 830} > 14.7$ , P < 0.05), left temporal areas (400–425 ms;  $F_{1, 830} > 13.4$ , P < 0.05), and later – at fronto–central side (700–800 ms;  $F_{1, 830} > 16.4$ , P < 0.05) (Figure 2A).

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**Figure 2:** Scalp distributions and statistical comparisons of the amplitudes of beta-frequency modulations for OG (HT – blue and LT – red): (A) beta1 and (B) beta2 frequency band. The format is the same as Figure 1.

OG demonstrated a significant difference in  $\beta2$  frequency band with regard to the tone types (Figure 2B). Beta2 amplitude was higher after HT at left frontal (200–300 ms; 500–525 ms;  $F_{1,\ 830}>14.2,\ P<0.05)$  and centro-occipital lead (380–410 ms; 750–800 ms;  $F_{1,\ 830}>12.0,\ P<0.05).$  Opposite amplitude relation, higher  $\beta2$  amplitude after LT than after HT, was observed at the right sensorimotor (475–500 ms;  $F_{1,\ 830}>14.1,\ P<0.05)$ , centro–parietal (490–570 ms;  $F_{1,\ 830}>15.6,\ P<0.05)$  and right parietal lead (435–580 ms;  $F_{1,\ 830}>16.2,\ P<0.05)$  (Figure 2B).

# Discussion

The obtained results confirmed that event-related oscillatory responses in beta frequency bands modulate with age during sensory and cognitive processes. Functional differences were found between event-related beta-frequency oscillatory activity in sensory-motor information processing of elderly and young groups in both stimulusencoding and cognitive processing.

# Age relation of high-frequency bands' modulations with the sensory processes

The beta activity was supposed to be correlated with attention and perception [8,9,14,15], and also with the long-range synchronous activity of neocortical regions [16]. Thus, the lower beta1-activity in the elderly group than in the young group during the sensory processing of high tone stimulation might reflect an attentional shift towards the high-frequency acoustic stimuli. Greater beta2 oscillations in the elderly were observed on the anterior sides and at the posterior sides in the young group during sensory processing. This early appearance of beta2 group's difference could be explained by disparate levels of the processes as attention or stimulus perception because of more variable neural synchronization responses to auditory input in the young group than in the elderly.

### The age reduces the cognitive processes

The beta1 activity in the elderly was significantly lower than for the young group at all leads during cognitive processing. The beta1 difference between groups increased in fronto-parietal direction and was more expressed after a high-frequency tone than after lowfrequency tone stimulation. The beta rebound effect was the greatest between-group difference, present at the contralateral sensorimotor areas. The early lower beta1 oscillations in the elderly were a result of an attentional shift towards the movement task at the expense of the high tone perception. The latter detected significant between-group's difference demonstrated that brain processes, leading to cognitive beta1 changes in the elderly group, lagged as compared to the young group. This observation could account for by different temporal eventrelated desynchronization effects due to cognitive processes or by motor imagery in response to the non-adequate tone stimulus [17]. The observed differences in beta1 oscillations between the groups in the central brain areas might reflect a stronger beta1 event-related desynchronization (ERD) effect on the adult subjects when the movement was involved, because over the sensorimotor areas, eventrelated ERD and a latter rebound synchronization in the beta range have found to refer to the execution of the movement [18]. Therefore, the auditory perception involved processing loops between auditory and motor regions. Correlated modulation of activity in the beta band was seen across a wide range of motor-related areas. Because of that the beta cortical rhythms serve cognitive processes such as linking perception to action [19,20] or being involved in movement planning [21]. Hence, the beta1-frequency responses (mainly ERD) have been associated with an auditory memory [22,23], cognitive control of behaviour or "executive functions" [24,25]. The young and elderly groups performed equally well behaviourally, but the aging effects have been seen in the oscillatory beta responses, particularly during working memory retrieval in the 400-700 ms period, at central and right temporal areas [22]. Those memory-related brain processes are the first affected in older age. The lower beta1 activity observed for elderly might be explained by enhanced ERD due to changes in the cognitive processes. Close to the task end, greater beta1 decrease in the elderly than in the young group most probably causes by stronger movement-related effect, whereby increasing age may lead to a more widespread expression of this effect. Late post-stimulus frontal beta1 increase was evident only in the young group following high-frequency tone stimulation (i.e. non-dominant left-hand movement), which may represent an inhibited frontal cortical network, at least as noted under certain circumstances [24,25].

The groups manifested opposite beta2 amplitude relations during the sensory and cognitive stage. Significantly more pronounced beta2 decrease in the elderly was elicited over the anterior left hemisphere, posterior right hemisphere, after high-frequency tone stimulation, may explain with higher attention or arousal levels with respect to this stimulation. Late beta2 and beta1 age-related decrease could be a result of higher levels of movement-related desynchronization or different motor-related cognitive behaviour as high attentional level after hightone stimulation. High-frequency beta sub-bands in voluntary motor control relate to initiation of movement, i.e. ERD in the 20-30 Hz band while ERS in a low-frequency beta sub-bands (12-16 Hz) relates to the stopping of planned action [24,25]. Therefore, the low-frequency beta sub-bands represent inhibitory components of cognitive control and were more generalized, while higher-frequency beta sub-bands take part in response choice and were more specialized in terms of both function and cortical distribution. The beta2 decrease during the early cognitive period may reflect cognitive ERD related to tone type

discrimination and a suppression of hand movement in response to the low-frequency tone type. The cognitive beta2-ERD, more prominent by movements, made with the non-dominant left hand becomes more evident with progressing age. Close to task end, elderly beta2 increased significantly (than in the young group) at the central and left frontal areas after the high-frequency tone, but not after low-frequency tone stimulation. Thus, the groups may apply different cognitive strategies for high tone discrimination (non-dominant reaction) and could be related to late inhibiting frontal cortical networks after movement execution. Information processing of movement-related behaviour predominantly engages earlier high beta frequency modulations for young subjects and later low beta frequency oscillations also include as beta desynchronization was more pronounced with progressing age. The appearance of between group ß2 distinctions close to task end may correspond to different extents of beta rebound response with increasing age. The beta rebound effect may reflect an age-dependent inhibitory process of the primary motor cortex [26] and this decreased motor inhibition may facilitate neuronal plasticity and promote motor learning. Post-movement beta synchronization also interpreted as a correlate of 'idling' motor cortex neurons with progressive age [27].

#### Age effect with regard to tone types

Only the elderly presented significantly different high-frequency beta activity with regard to tone types. With progressing age, motor task difficulty (higher for low-tone stimulation and dominant hand reaction) affected the attentional level and lead to less prominent movement-related beta desynchronization on the right sensorimotor area, more widespread effect on the parietal areas in beta2 sub-band and at the left temporal side in beta1 sub-band, after the low tone. In spite of, more expressed movement-related beta2 desynchronization (after low-tone stimulation and dominant hand reaction) over a left frontal side, and an increased fronto-central beta1 activity after right hand movement showed that frontal executive networks are effective to maintain the vigilance and attentional processes or may have a compensatory role on account of the functioning of the alerting network relevant to task difficulty.

# Limitations

The limitation of the present study is that the examination of the beta band activity is by using EEG, where EEG recordings are constrained comparing to magnetoencephalography (MEG) with regard to the spatial resolution. Although this disadvantage of the EEG, it is much easier to use EEG with old subjects in research. The advantages are that EEG is more tolerant of movement artifacts, and the attention spans are limited and elderly participants tire quickly, so experiments must be short. EEG can be useful in a clinic because functional magnetic resonance imaging, positron emission tomography, and single photon emission computed tomography required special settings that are not widely available.

# Conclusions

Fluctuations in beta power appeared stronger in the elderly compared to the young group, especially after the high-frequency tone stimulation. Moreover, the high-beta modulation was weaker in the young group than in the older group. Furthermore, this modulation of beta activity was found not only in the auditory cortex but also in a number of cortical and subcortical areas of the motor network. Increased age caused reduced beta1 activity irrespective of task requirements (left or right-hand movement) during cognitive processing. This difference shifted in fronto-parietal direction more expressed after a high-frequency tone. Periods of significant betweengroup beta1 differences and their topographical distribution were specifically dependent on the task requirements. Beta2 modulation depended on tone and age, and characterized by reducing regionalprocess specificity with progressing age during sensory, but not during cognitive processing. Beta2 activity was more pronounced with a progressive age during sensory processing, but reduced by age on cognitive processes. The influence of aging was higher on cognitive processes than on perceptual ones.

Future studies can focus on further disentangling the contributions of auditory perception and to investigate auditory encoding in the young and elderly group, even though after the auditory stimulus, there is no movement or requirement to move. This suggests that even the auditory perception may involve processing loops between auditory and motor regions and correlated modulation of activity in the beta band could be seen across a wide range of motor-related areas. Time course analysis of the EEG record is a convenient indicator of cortical dysfunction in dementia and correlates to the degree of cognitive impairment. Apparently, the temporospatial analysis may be useful in distinguishing patients with dementia from that experiencing normal aging. These data could contribute additional information to the clinical data in evaluating dementia.

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