

## Do the Changes of Event-Related Potentials and Frequency Band Responses to Sensory Stimuli Correlate to Age Cognitive Decline?

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### ABSTRACT

Cognitive decline and symptoms of attention deficits, executive dysfunction, and memory impairments describe dementia in the elderly. This review focuses on particular frequency oscillations that occur within the affected brain regions which could be used to classify some idiopathic dementias as specific diseases and could contribute additional information to the clinical data in evaluating age changes that are of benefit for a treatment of cognitive alterations. The main question, whether the changes of event-related potentials (ERPs) and frequency band responses (ERBRs) for sensory stimuli are related to plasticity in neural recruitment during stabilization of sensory/cognitive mechanisms accompanying aging or are

underlying pathological changes, remains unknown. We review the effect of aging on low ( $\delta$ ,  $\theta$ ,  $\alpha$ ) and high ( $\beta_1$ ,  $\beta_2$ ,  $\gamma_1$ ,  $\gamma_2$ ) ERBRs in auditory discrimination sensorimotor tasks (low-frequency – right hand movement, high-frequency tone – left movement) at frontal, central, parietal and occipital cortical locations at short latency (post-stimulus interval 0–250 ms; putative sensory processing period) and long latency (250–600 ms; putative cognitive period). High tone stimulation and movement requirements lead to a delay of ERP components in elderly subjects and their amplitudes diminish with increasing age. The amplitudes of  $\beta_2$ ,  $\gamma$ , and low-frequency activity are more pronounced with progressive age, but the  $\beta_1$  component is less affected by age during the sensory processing. The age difference with respect to scalp distribution is tone-independent for  $\delta/\theta$ , but not for  $\alpha$ -activity. Age- and tone-dependent  $\alpha$ -changes are focused on frontal and sensorimotor areas. The low- and high-frequency amplitudes during the cognitive processing diminish with increasing age, except for the frontal  $\beta_2$  and  $\gamma$  high tone responses, while the  $\beta_1$  activity is more widespread than in the shorter latency period. This age difference increases in fronto-parietal direction more expressed after high tone stimulation. The age influences more the cognitive processes than the sensory ones.

**Key words:** Age effect; Sensory discrimination; Sensory processing; Cognitive processes; Low ( $\delta$ : 2-4,  $\theta$ : 4.5-7,  $\alpha$ : 7.5-12 Hz); High ( $\beta_1$ : 12.5-20;  $\beta_2$ : 20.5-30 Hz;  $\gamma_1$ : 30.5-49;  $\gamma_2$ : 52-69 Hz) frequency oscillations

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### INTRODUCTION

Event-related potentials (ERPs) and particular frequency oscillations in the time course analysis of the EEG record are convenient indica-

tors of cortical dysfunction in dementia and correlate to the degree of cognitive impairment and could be used to classify some idiopathic dementias as specific diseases. Event-related studies still remain inconclusive whether specific frequency 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. The cognitive decline and symptoms of attention 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 varies 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 in affected brain regions have been used to classify some idiopathic dementias as specific diseases<sup>[1]</sup>.

Identifying the effects of aging on the specific stages of information processing in the cortical low- and high-frequency domain, we could relate the more pronounced frequency pattern correlated with sensory processing and progressive deficits in event-related frequency processing with advancing age specifically correlated with poorer cognitive abilities during auditory discrimination task.

## EFFECT OF THE AGE ON SENSORY ERP COMPONENTS

The effect of age on ERP components in active auditory oddball tasks are described in a well-balanced group of normal subjects<sup>[2]</sup>. The studies provide a reliable estimate of the effects of aging, allowing comparison between ERP waves from early sensory to late cognitive components. The amplitude and latency of the exogenous components relate to the stimulus and are indices of the early processing stages (automatically or obligatory). The amplitude of the early sensory component N1 is, in general, larger for elderly as compared to young subjects at the frontal, motor and parietal areas and are lagged over the left frontal cortex of elderly (high tone stimulation), at the right parietal and temporal area of young subjects (low tone stimulation). Six brain processes could contribute to N1 generation: components generated in auditory cortex on a supratemporal plane, in association cortex on a lateral side of the temporal and parietal cortex, in motor and premotor cortices, mismatch negativity, and also components generated in temporal and frontal cortices<sup>[3]</sup>. The first three components, generated in the supratemporal plane, on the lateral side of the temporal - parietal cortex, in motor and premotor cortices, were considered as 'true' N1 components and assumed to be affected by stimulus physical and temporal features and by the subject state. The latter three components (generated in the temporal and frontal cortices) are caused not by the stimulus itself, but by the conditions in which it occurs. The age difference in N1 amplitude could be due to a general greater alertness of elderly people with respect to the acoustic stimuli during early sensory processing. Frontal N1 amplitude, parietal N1 latency<sup>[4]</sup> as well as pre-frontal and temporal N1 amplitude<sup>[3]</sup> increase with advancing age for standard but not target tone. Habituation or the recovery cycle (refractory period) of the neural generators underlying N1<sup>[5]</sup> might be more expressed in young subjects. The temporal brain areas of elderly subjects have an opposite sensory processing with respect to tone stimulus and hand movement. The hemispheric lateralization at left and right motor areas as well as a higher N1

at left compared to right motor area for elderly subjects (high tone stimulation) suggest either a more widespread activation in the contralateral cortex with increasing age<sup>[6,7]</sup>, when a dominant hand movement is executed or a hemispheric tone lateralization in the processing of high- and low-frequency tones respectively in left and right hemisphere<sup>[8]</sup>. An increased frontal brain activity in comparison to the other brain areas is seen only for elderly subjects<sup>[9]</sup>. Paradigms for actively performed tasks such as discrimination<sup>[10]</sup> and working memory tasks<sup>[11]</sup> can affect the early sensory component, which is interpreted in terms of forward suppression<sup>[12]</sup>, repetitive suppression<sup>[13]</sup>, and feedback modulation from downstream neural populations<sup>[14]</sup>.

The topography of the late sensory component P2 appears to be similar across auditory, visual and somatosensory modalities and has been shown to have a maximum over the vertex<sup>[15,16]</sup>. The late sensory processing is steadily delayed in elderly subjects as the reported effects of aging on the P2 latency with advancing age<sup>[2,17-19]</sup>. The increases of P2 latency and amplitude are dependent on the electrode position by EEG studies and only apparent at anterior leads<sup>[2,4,20,21]</sup>. The P2 peak is detected earlier at the right frontal and right motor areas under low-frequency tone stimulation, at the left frontal area and vertex under high-frequency tone stimulation in elderly subjects. Under low- and high-frequency tone stimulation, the late sensory component shows a delay in the contralateral hemisphere of young subjects with respect to the non-dominant hand movement probably due to the higher cognitive or motor requirements as compared to dominant hand movement whereas this hand dominant distinction during the sensory stage is diminished or lost with advancing age. The functional role of the late sensory component observed at the fronto-central sites in an oddball paradigm is interpreted as reflecting an attention-modulated process required for the performance of an auditory discrimination task<sup>[22]</sup>. The P2 wave is linked to a process of sensory gating involved in protecting higher-order cognitive functions by affecting response bias, behavioural inhibition, working memory or attention, and stronger P2 gating as represented by prolonged peak latency lead to better stimulus discrimination ability<sup>[22]</sup>. Only the results obtained for elderly subjects could be explained by the inverse relation between attention and P2 amplitude. The P2 increase with age shows an age-related decline in the ability to withdraw attentional resources from the sensory stimuli, and also this effect is more pronounced in the frontal brain regions as they are most affected by aging<sup>[23]</sup>. The prevalent P2 differences at frontal brain areas are linked to the involvement of these brain areas in protecting against interference by irrelevant stimuli<sup>[16]</sup>. An increase in the level of attentiveness produces a decrease in P2 amplitude and serves as an index of the ease with which relevant information can be distinguished from the irrelevant<sup>[3,16,24]</sup>.

## AGE EFFECT ON COGNITIVE ERP COMPONENTS

The endogenous cognitive components develop mostly during later (after 250th ms) post-stimulus time intervals and are thought to represent internal higher brain processes related to stimulus evaluation. The early cognitive component delays all over the scalp and frontally attenuated in elderly subjects<sup>[2,4,25]</sup>. Larger early cognitive component after low tone compared to high tone stimulation are observed in young and old subjects. The significant differences are however only in the right frontal area of elderly, whereas for young subjects these differences are more widespread: at the centro-frontal, occipital and right frontal areas as well as the left hemisphere (except frontal).

Thus, the larger early cognitive component is obtained when movement with the dominant hand is executed. During the early cognitive processing only in young, but not in elderly subjects the high tone stimulus is faster processed in the left hemisphere, low tone stimulation – in the right hemisphere, related to hemispheric lateralization with regard to auditory attention and differences in the processing of high- and low-frequency tones<sup>[8]</sup>. This suggests that discrimination processes are related to the motor tasks and the underlying N2 generation may be lateralized, as reported for P3 component<sup>[26]</sup>. No hemispheric lateralization differences are observed for elderly after low tone stimulation. With increasing age, a systematic increase in the N2 latency only<sup>[14,24]</sup> or together with a decrease in N2 amplitude have been reported<sup>[18]</sup>. The increase in N2 amplitude reflects the existence of an age-related slowing in memory comparison processes<sup>[25]</sup> or the ability of the auditory system to detect stimulus changes attenuates with aging<sup>[26]</sup>.

The late cognitive component P3 diminishes and delays with the age<sup>[3,18,20,27]</sup> in both auditory and visual paradigms<sup>[14,28]</sup>, and its scalp distribution alters potential field shifts to frontal regions<sup>[3,20]</sup>. This P3 delay of the elderly subjects is a slowing of the decision process whether to respond or to inhibit the response when required<sup>[28]</sup>. When comparing low tone stimulation and high tone stimulation processing, significant P3 amplitude hemisphere lateralization in the cognitive processing of high and low frequencies is manifested only in elderly subjects, primarily at anterior-medial locations<sup>[2,6]</sup>. The P3 behavior depends on stimulus expectation (the less expected stimulus elicits larger P3 amplitude<sup>[29]</sup>), on selective attention and motivation. The task complexity processing (as represented by P3) is different between age groups and influences the involvement of different brain areas<sup>[2]</sup>.

## EVENT-RELATED DELTA OSCILLATORY RESPONSES MODULATED BY SENSORY AND COGNITIVE PROCESSES WITH THE AGE

Event-related oscillatory responses in different frequency bands are modulated by sensory and cognitive processes and with the age<sup>[30,31]</sup>. Widespread enhanced delta and theta activity for elderly subjects are present during the sensory processing independent of a tone type<sup>[30]</sup>. Higher elderly delta is observed during the cognitive processing at the frontal areas and vertex after low tone stimulation and more widespread after high tone stimulation. While the tendency of higher delta for elderly (as compared to young) subjects is preserved at the end of the motor task, the age theta amplitude relation reverses during the cognitive processing for the different brain areas. The greater elderly delta activity during the early sensory processing coincides in time with the generally greater N1 and P2 amplitudes for elderly<sup>[2]</sup>. Hence, as long as event-related potentials are assumed to arise by superposition of event-related oscillations in different frequency ranges<sup>[32]</sup>, evoked brain waves in the delta frequency range could be one of the constituting components of the N1-P2 waveform reflecting sensory stimulus processing. The early sensory processing for elderly subjects is significantly diminished over the whole-head brain areas in a discrimination motor task. The latter beginning of this delta decrease for elderly subjects is in agreement with the significantly later appearance of the P3 peak in elderly subjects seen for the bimanual hand reaction task<sup>[2]</sup>. The decreased delta power corresponds with increased task-evoked arousal<sup>[33]</sup> and the ability to express may be diminished or lost with progressing age. Increased load correlates with increased spectral power in the delta frequency range for adult subjects<sup>[34]</sup>. Increased task-evoked arousal with increasing task com-

plexity could explain the age differences in delta behavior during cognitive processing<sup>[33]</sup>. The higher delta activity in elderly subjects could be accounted for by different attentional focus. The attention to the external environment during mental concentration or due to an evaluation of a memory trace in the sense of ‘target detection/evaluation’<sup>[35,36]</sup> may change the amount of delta activity and its lack in the elderly may point at age differences in this process. However, the significantly age differences appear later in response to high tone stimulation, which may signify that cognitive processes related to movements with the non-dominant hand might set later. The delay could be also caused by the later onset of the reaction time (RT) for the non-dominant (left) hand, although this is seen in elderly subjects only.

When comparing the low tone stimulation and high tone stimulation effects within a bimanual motor task during the sensorimotor processing, high tone stimulation produces higher delta activity over lateral sensorimotor, left parietal, right temporal and occipital areas for elderly subjects and overall brain areas of elderly except the frontal area at the end of the motor task. There is no age difference in delta band responses with respect to tone frequency difference. However, the topographical activity distribution is different, concentrated mainly in the posterior brain areas at the expense of the frontal regions of elderly subjects.

## EVENT-RELATED THETA OSCILLATORY RESPONSES MODULATED BY SENSORY AND COGNITIVE PROCESSES WITH THE AGE

During the early sensory processing, the higher theta activity for elderly subjects like delta overlaps in time with the N1-P2 complex appearances<sup>[30,37]</sup>. Both N1 and P2 are higher for elderly subjects<sup>[2]</sup> and are responsible for the elderly higher theta modulation. Additionally, theta frequency rhythms are dominant oscillations within the hippocampal formation, which is of crucial importance for the encoding of new information<sup>[38]</sup>. Increased age produces a reduced theta activity, which underlies in P3 amplitude age-related decrease<sup>[20,39]</sup>. Theta activity is further suggested to be most engaged in memory operations, like memory encoding<sup>[33,40,41]</sup>. Late post-stimulus theta activity decrease has also been linked to memory processes for elderly subjects during cognitive processing<sup>[42,43]</sup>.

The higher theta amplitude is present in elderly for high tone stimulation than for low tone stimulation at the right sensorimotor area during early sensory processing. Higher theta is observed after low tone stimulation as compared to high tone stimulation at the left hemispheric frontal and sensorimotor areas during the early cognitive processing for elderly subjects only and overlaps in time with appearances of smaller N2-P3 complex and may constitute its main frequency component<sup>[44]</sup>. The delay of theta amplitude reversal between the tone tasks, performed by elderly subjects, could be accounted for by the delay in P3 peak appearance after high tone stimulation<sup>[30]</sup>. The latter observed tone difference in theta modulation may be linked to different memory performance processes between the tones as the theta activity has been hypothesized to mediate the memory-related interaction between the prefrontal cortex and medial temporal lobe<sup>[45]</sup>. The increased theta activity for elderly at the right sensorimotor area during the sensory stage for high tone stimulation could hint at the attention shift from the stimulus to the motor left-hand reaction. Its presence for elderly, but not for young subjects may be an indication of the age different strategies for motor task accomplishment.

## ALPHA RHYTHMS MAY HAVE BEEN FUNCTIONAL CORRELATES IN PRIMARY SENSORY PROCESSING AND PREPARATORY PROCESSES

The higher alpha activity at the centro-occipital area of elderly during sensory processing coincides in time with the N1-P2 complex, but widespread lower alpha modulation during cognitive processing might partially contribute to the observed age differences in the N1-P2 and N2-P3 complexes<sup>[2,30]</sup>. Alpha oscillations are mainly generated by cortico-cortical and thalamocortical neuronal networks<sup>[46]</sup>. An increase of alpha band amplitude most probably demonstrates active working memory or attentional processes<sup>[41]</sup>, more pronounced in elderly subjects during sensory processing and could be accounted for by different attentional levels. The N2-P3 peaks are lower for elderly as the late alpha decrease after either tone<sup>[2]</sup>. EEG alpha band power decreases with the increase in age<sup>[20,47]</sup>. Alpha activity, named also ‘idling rhythm’, decreases upon the movement onset<sup>[48]</sup>. Auditory oddball stimulation elicits long-lasting alpha responses during the cognitive processing<sup>[38,44]</sup>. The decrease of alpha activity for elderly subjects during the cognitive processing might reflect memory search processes<sup>[38,49]</sup>. The suppression of alpha activity is correlated with actual task demands<sup>[50]</sup>.

The event-related, evoked and induced alpha rhythms may have been functional correlates in primary sensory processing and preparatory processes<sup>[32,51]</sup>. The early higher alpha in bimanual motor task, when compares low to high tone stimulation, could mean a higher attention towards the relevant tone stimulus and could be caused by an attention shift from ‘reacting to the adequate tone’ to ‘hearing the adequate tone’<sup>[32,51]</sup> for elderly subjects after low tone and for young subjects after high tone stimulation. The proposed attention shift strategy might be more relevant for elderly subjects as their RTs are comparatively slower. The recognition of auditory stimuli elicits a widespread decrease in alpha activity. The differences in alpha activity related to increasing tone difference might be reduced or lost with increasing age as no tone differences are obtained for the elderly during the cognitive processing. Thus, possible dedifferentiation of brain functions for the tones is observed in elderly subjects during the cognitive, but not the sensory processing<sup>[30]</sup>.

## FUNCTIONAL DIFFERENCES IN THE BETA-OSCILLATORY ACTIVITY IN STIMULUS ENCODING AND COGNITIVE PROCESSING OF ELDERLY

Functional differences are found between high-frequency event-related oscillatory activity in sensory–motor information processing of elderly and young subjects in both stimulus encoding and cognitive processing<sup>[31]</sup>.

The beta activity is implicated in attention, perception, initiation and motor planning<sup>[31,52]</sup>, and also correlates with the long–range synchronous activity of neocortical regions<sup>[53]</sup>. The lower  $\beta_1$ -activity in the elderly than in the young subjects during the sensory processing of high tone stimulation might reflect an attentional shift towards the high-frequency acoustic stimuli. This early age-related  $\beta_2$  difference could be explained by different levels of processes such as attention or stimulus perception.

The elderly  $\beta_1$  activity is significantly lower than for the young subjects at all brain areas during cognitive processing. The age-

related  $\beta_1$  difference increases in fronto–parietal direction more expressed after a high-frequency tone than after low-frequency tone stimulation. The beta rebound effect is the greatest age difference, present at the contralateral sensorimotor areas. The early elderly lower  $\beta_1$  activity is a result from an attentional shift towards the movement task at the expense of the high tone perception. Cognitive  $\beta_1$  changes in the elderly lag as compared to the young subjects. Thus, the age-related  $\beta_1$  oscillation differences in the central brain areas might reflect stronger  $\beta_1$  event–related desynchronization (ERD) effect on the adult subjects when the movement is involved<sup>[31,52]</sup>. Beta frequency responses (mainly ERD) have also been associated with an auditory memory<sup>[49,54]</sup>, cognitive control of behavior or ‘executive functions’<sup>[55]</sup>. Some investigations propose beta and gamma cortical rhythms may serve cognitive processes such as linking perception to action or being involved in movement planning<sup>[42]</sup>. By investigating the effects of normal aging, even young and older subjects perform equally well behaviorally, but there are aging effects in beta oscillatory responses, especially during working memory retrieval at central and right temporal regions<sup>[54]</sup>. Memory-related brain processes are the first affected in older age. The lower  $\beta_1$  activity observed for the elderly subjects might be explained by enhanced ERD due to changes in the cognitive processes. Close to the task end, a greater  $\beta_1$  decrease in the elderly subjects is most likely caused by a stronger movement-related effect, thus increasing age may lead to a more widespread expression of this effect. Late post-stimulus frontal  $\beta_1$  increase is evident only in the young group following high tone stimulation (non-dominant left-hand movement), which may represent an inhibited frontal cortical network, at least as noted under certain circumstances<sup>[55]</sup>.

Significantly more pronounced elderly  $\beta_2$  decrease is elicited over the anterior left hemisphere and posterior right hemisphere after high-frequency tone stimulation by higher attention or arousal levels to the high-tone stimulation. Late  $\beta_2$  and  $\beta_1$  age-related decrease are a result of higher levels of movement-related desynchronization or different motor–related cognitive behavior as high attentional level after high-tone stimulation. During the early cognitive period, the  $\beta_2$  decrease may reflect cognitive ERD related to tone type discrimination and a suppression of movement in response to low tone type. The cognitive  $\beta_2$ -ERD, more prominent by movements, made with the left hand, becomes more evident with progressing age. Close to the end of the motor task, elderly  $\beta_2$  oscillations increase significantly (more than in the young subjects) at the central and left frontal areas after the high tone, but not after low-frequency tone stimulation. Thus, cognitive strategies change with age for high tone discrimination (non-dominant reaction) and relate to late inhibited frontal cortical networks after movement execution. Information processing of movement-related behavior predominantly engages an earlier high beta range for young subjects and later, low beta frequency range also includes, however the beta desynchronization is more pronounced with progressing age. The appearance of age-related  $\beta_2$  differences at the task end corresponds 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 and this decreased motor inhibition may facilitate neuronal plasticity and promote motor learning<sup>[31,52]</sup>.

Only the elderly subjects present significantly different high-frequency activity with regard to tone types. With progressing age, motor task difficulty (higher for low-tone stimulation and dominant hand reaction) affects the attentional level and leads to less prominent movement-related beta band desynchronization on the right sensorimotor area, more widespread effect on right parietal and

centro-parietal areas in  $\beta 2$  sub-band and at the left temporal side in  $\beta 1$  sub-band (400-460 ms after stimulus onset)<sup>[31]</sup>. In spite of this, more expressed movement-related  $\beta 2$  desynchronization (after low-tone stimulation and dominant hand reaction) over the left frontal side and an increased fronto-central  $\beta 1$  activity after right hand movement show that frontal executive networks are effective in maintaining the vigilance and attentional processes or may have a compensatory role on account of the functioning of the alerting network relevant to task difficulty.

## FUNCTIONAL DIFFERENCES IN THE EVENT-RELATED GAMMA ACTIVITY IN ELDERLY DURING STIMULUS ENCODING AND COGNITIVE PROCESSING

During the stimulus duration, significantly more prominent  $\gamma 1$  activity appears at right/left frontal area respectively for elderly / young subjects after either tone, but only the elderly subjects show short-term higher  $\gamma 1$  burst at stimulus offset over the frontal areas after either tone and the young  $\gamma 1$  activity are more pronounced in the other brain areas depending on the tone type. The primary neural source of the early gamma oscillations (around 40 Hz) has found in the auditory cortex and the early  $\gamma 1$  modulations reflect an essential component in perceptual processing<sup>[56]</sup> or phase-locked sensory phenomenon<sup>[57]</sup>, prone to different attenuation levels, important for preparing the brain for subsequent processing<sup>[31,58]</sup>. The task complexity may enhance most substantially the sensory processing in the frontal areas because of increased attention level. Hence, the ability of attention level in  $\gamma 1$ -band modulation, seen for the young subjects during early sensory processing in other cortical areas, may diminish or disappear with increasing age<sup>[31]</sup>. Age differences in  $\gamma 2$  activity are widespread and lasting during the binary motor task. With increasing age, the parietal areas become sensitive earlier to immediate auditory stimulation irrespective of tone frequency, perhaps due to higher arousal state<sup>[59]</sup>. During the high tone stimulus duration, the  $\gamma 2$  activity exaggerates more in the elderly over anterior brain areas and at posterior brain areas in the young subjects, while during the low-tone stimulus duration  $\gamma 2$  activity increases at right fronto-parietal sides for the elderly, and at left fronto-parietal areas for the young subjects. The centers of very early sensory processing, when a motor reaction is involved, are switched from posterior to anterior brain regions with advancing age<sup>[31]</sup>.

During the cognitive processing, the  $\gamma 1$  activity diminishes with the age, except for the increased left frontal  $\gamma 1$  activity for high-frequency tone stimulation (non-dominant hand reaction) and the right parietal  $\gamma 1$  activity for low-frequency tone stimulation (dominant hand reaction). Task-induced  $\gamma 1$  oscillations appear in different post-stimulus intervals<sup>[31]</sup>. Through the comparison of auditory choice reactions, the induced  $\gamma 1$  is enhanced by selective attention<sup>[58]</sup>. This effect is most prominent over the frontal and central scalp areas<sup>[31]</sup>. During cognitive processing, the  $\gamma 1$  oscillations are further linked to mechanisms of sensory information matching memory contents<sup>[31,60,61]</sup>, acquisition and retention of relevant stimulus features in memory<sup>[31,57]</sup>, and to post-discrimination processes, related to the late cognitive P3 wave<sup>[31]</sup>. Greater  $\gamma 1$  decrease in the elderly subjects reflect less efficiency in a spatially localized gamma-band network, specifically involved in auditory short-term memory to attain a mental representation of the specific tone stimulation in order to correct tone discrimination and avoid a wrong hand reaction, which could be affected by the age<sup>[31,60,61]</sup>. The enhancement of

left frontal  $\gamma 1$  responses to high-frequency tone stimulation and right parietal  $\gamma 1$  responses to low-frequency tone stimulation (100-800 ms after stimulus onset) in the elderly subjects is associated with a compensatory function of these brain areas for an increased attentional level to memorize stimuli<sup>[31]</sup>. Correlations between  $\gamma 1$  activity and performance have been seen only after high tone stimulation<sup>[60,61]</sup>. Fast- and slow left-hand reacting subjects exhibit different patterns of  $\gamma 1$  band activity when responding as quickly as possible to high-frequency auditory stimuli. A more sustained  $\gamma 1$  representation of the memorized information are observed at the parietal sites in the young and at a left frontal side in the elderly subjects, but the increased  $\gamma 1$  activity in elderly subjects shifts from posterior to anterior sides at the task end (650-800 ms after high-tone stimulus onset)<sup>[31]</sup>.

During early cognitive processing, high-frequency tone perception evokes larger whole-head  $\gamma 2$  response in the elderly subjects. The parietal areas are more strongly involved in the late cognitive processing with increasing age, which may be related to different levels of effort in “high-level cognitive processes”<sup>[31,58,59]</sup>. The slow  $\gamma 2$  wave responses are observed in the elderly, accomplished by activation or reactivation of the brain regions, maintained by the sensory representation regions and the activation of executive networks. The  $\gamma 2$  responses reflect variations in memory load and are topographically distinct from more posterior activations for low tone stimulation to more anterior for high tone stimulation<sup>[31]</sup>.

The task difficulty (low tone stimulation/dominant hand reaction) reduces parieto-central  $\gamma 1$  activity during cognitive processing due to attentional shift from a high tone stimulus to left hand reaction, which links either to retention of the adequate stimulus in the memory or to the post-stimulus discrimination processing, related to the working memory. With increasing age, the higher frontal  $\gamma 2$  wave responses to high tone-stimulations (than to low tone) show that frontal brain areas become more sensitive to a high-frequency tone (or tone frequency differences) and influence sensory and cognitive processes, related to tone discrimination and hand reaction choice, reflect short-term memory variations and late engage more posterior sides.

## SUMMARY

The effect of aging on the profile of auditory ERPs could be usable for clinical evaluation of perceptual, attention-related and cognitive processes by auditory binary motor tasks. With aging, a neural circuit reorganization of the brain activity affects the cognitive processes. This reorganization could be compensatory or a deficit. The amplitudes of the phase-locked delta, theta and alpha activity are more pronounced with the progressive increase in age, independent of the tone. The age differences with respect to scalp distribution are tone-independent for both delta/theta oscillations, but not for the alpha activity. Age-related and tone-dependent changes in alpha band activity are focused at frontal and sensorimotor areas. Tone brain specificity is not observed for the low-frequency (delta, theta and alpha) amplitudes. The functional brain specificity diminishes with increasing age. The low-frequency event-related oscillations (delta, theta and alpha) overlap and possibly underlie the age-related decreases in P3 amplitude and memory operation. Increased age causes reduced beta1 activity irrespective of task requirements (left or right-hand movement) during cognitive processing. This difference shifts in fronto-parietal direction more expressed after a high-frequency tone. Beta2 modulation depends on tone and age, and is characterized by a reduced regional-process specificity with progressing age during sensory, but not during cognitive processing.

Beta2 and gamma activity are more pronounced with progressive age during sensory processing, but reduced by age on cognitive processes. Only elderly subjects show higher sensory frontal  $\gamma 1$  activity. Late cognitive  $\gamma 2$  changes are shifted from posterior to anterior brain regions with advancing age. With increasing age, the larger  $\gamma 2$  differences are more expressed over the frontal brain areas to tone discrimination and hand reaction choice, reflected short-term memory variations. The influence of aging is higher on cognitive processes than on perceptual ones. This can be useful for an early discrimination between normal and pathological brain aging for early treatment of cognitive alterations and dementia.

## CONCLUSION

Cognitive decline and symptoms of attention deficits, executive dysfunction, and memory impairments describe dementia in the elderly. Event-related potentials and particular frequency oscillations that occur within the affected brain regions could be used to classify some idiopathic dementias as specific diseases. Future studies can focus on further disentangling the contributions of auditory perception and to investigate auditory encoding in the elderly subjects, even though 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 a correlated modulation of activity in the specific frequency 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.

### Authors' contributions

All authors participated in the writing, review, and editing of this manuscript.

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