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Age-related differences on event-related potentials and brain rhythm oscillations during working memory activation

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Abstract Previous functional imaging studies have pointed to the compensatory recruitment of cortical circuits in old age in order to counterbalance the loss of neural efficiency and preserve cognitive performance. Recent electroencephalographic (EEG) analyses reported age-related deficits in the amplitude of an early positive–negative working memory (PN_{wm}) component as well as changes in working memory (WM)-load related brain oscillations during the successful performance of the n-back task. To explore the age-related differences of EEG activation in the face of increasing WM demands, we assessed the PN_{wm} component area, parietal alpha event-related synchronization (ERS) as well as frontal theta ERS in 32 young and 32 elderly healthy individuals who successfully performed a highly WM demanding 3-back task. PN_{wm} area increased with higher memory loads (3- and 2-back > 0-back tasks) in younger subjects. Older subjects reached the maximal values for this EEG parameter during the less WM demanding 0-back task. They showed a rapid development of an alpha ERS that reached its maximal amplitude at around 800 ms after stimulus onset. In younger subjects, the late alpha ERS occurred between 1,200 and 2,000 ms and its amplitude was significantly higher compared with elders. Frontal theta ERS culmination peak decreased in a task-independent manner in older compared with younger cases. Only in younger individuals, there was a significant decrease in the phasic frontal theta ERS amplitude in the 2- and 3-back tasks compared with the detection and 0-back tasks. These observations suggest that older adults display a rapid mobilization of their neural generators within the parietal cortex to manage very low demanding WM tasks. Moreover, they are less able to activate frontal theta generators during attentional tasks compared with younger persons.

Keywords Aging · Event-related potentials (ERPs) · Event-related desynchronization and synchronization (ERD/ERS) · Rhythms · Working memory

Introduction

Working memory (WM) refers to the temporary on-line maintenance of new information in a form that can be manipulated to support on-going cognitive processing. It includes the active storage in a short-term memory buffer and retrieval processes under the control of an executive system that allocates cognitive resources. Old age is associated with progressive limitations of this function possibly reflecting the difficulty to activate the corresponding neural networks (Callicott et al. 1999; Goldberg et al. 1998; Reuter-Lorenz et al. 2000; Rypma and D'Esposito 2000). However, most elderly individuals show preserved performances in moderately demanding WM tasks of low complexity. In particular, simple maintenance tasks such as digit or letter span are relatively unaffected by aging, whereas performances in more complex WM tasks involving on-line manipulation decrease progressively in old age (Emery et al. 2008; Wager and Smith 2003). A long-standing assumption to

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explain this finding is that normal aging is associated with a decrease in neural efficiency implying the recruitment of more neural units to supply the required capacity for certain tasks compared with younger individuals (Reuter-Lorenz et al. 2000). As described in fMRI studies, this compensatory response could make it possible to preserve low-level cognitive performances despite the declining function of the canonical brain areas involved in WM activation (Cabeza et al. 2002; Cook et al. 2007; Rajah and McIntosh 2008; Stern 2009).

Despite their excellent spatial resolution, one main limitation of these fMRI studies is their relatively poor temporal resolution when addressing rapid cognitive processes such as WM activation that occur in the time range of several 100 ms. Event-modulated electroencephalographic (EEG) dynamic analysis can measure the functional activation of neocortical circuits with a high temporal resolution and may represent a more sensitive method in this context. Previous EEG studies have demonstrated that the successful performance of the *n*-back task is associated with significant changes in event-related potentials (ERP) and brain rhythm oscillations below 30 Hz. In particular, a significant positive–negative waveform (PN_{wm}) component occurs between 140 and 280 ms after stimulus onset during WM demanding conditions (1- and 2-back) as compared with memory-free control tasks (detection or 2-back passive) (McEvoy et al. 2001; Missonnier et al. 2003, 2004). This load-dependent component located in the parietal cortex is superimposed on the classical P200 and N200 components and is thought to reflect early encoding and retrieval phases of WM processing in healthy subjects that directly follow pure sensory driven processes (such as the P100 and the N145; Cowan 1984, 1988). In terms of brain rhythms, an increase in frontal theta power with WM load has been often described, although its temporal course and topographic distribution remains disputed (Onton et al. 2005; Jensen and Tesche 2002; Raghavachari et al. 2001; Krause et al. 2000; Kahana et al. 1999; Gevins et al. 1997). Directed attention and memory requirements also modulate oscillations at alpha frequency (8–12 Hz). Both decreased or increased alpha power has been described during WM activation (Jensen et al. 2002; Babiloni et al. 2004; Klimesch 1999) and a positive relationship was described between alpha peak frequency and WM performances (Richard et al. 2004; Klimesch et al. 2008; Palva and Palva 2007; Pesonen et al. 2007; Krause et al. 2010).

The effect of advanced age on WM-related brain EEG responses has been mainly investigated on late ERPs (Friedman 2000; McEvoy et al. 2001; Onofrj et al. 2001; Rugg et al. 1997). We reported earlier on age-related deficits of the early PN_{wm} component in healthy elderly

controls during the successful performance of the highly demanding 2-back task (Missonnier et al. 2004). Unlike ERPs, the impact of old age on brain oscillatory responses during memory processes has been poorly explored with the exception of a possible decrease of lower-to-higher frequency band oscillations during retrieval (Karrasch et al. 2004; McEvoy et al. 2001). In order to explore the age-related differences on ERP and brain rhythm patterns of activation in the presence of increasing WM load, we performed a complete analysis of endogeneous and exogeneous ERPs, as well as event-related desynchronization and synchronization in theta and alpha frequency-bands during the administration of an adapted 3-back WM task.

Subjects and methods

Participants

Sixty-four healthy right-handed volunteers participated in this study. There were 32 young adults (aged 22–32, 25.8 ± 4.6 years; mean ± SD; 19 women, 13 men) and 32 elderly individuals (aged 60–88, 70.2 ± 7.9 years; mean ± SD; 22 women, 10 men). All participants had normal or corrected-to-normal visual acuity, and none sustained a head injury, or neurological or psychiatric disorders. Moreover, none exhibited alcohol or drug abuse or the presence of a severe physical impairment. Participants with regular use of psychotropic medicines (antidepressants, neuroleptics, regular use of benzodiazepines), stimulants and β-blocker drugs were excluded. The young adult group included undergraduate or graduate students of the University of Geneva. Elderly participants, with a high school degree or equivalent, were recruited through the University of Geneva and the Department of Geriatrics. Both groups were tested with an extensive neuropsychological battery including the Mini Mental State (MMS, Folstein et al. 1975), Verbal Fluency Test (Butters et al. 1987) and the Trail Making Test (Reitan 1958) for executive functions, Boston Naming Test (Kaplan et al. 1983) for language abilities, a standardized praxis examination including ideomotor (Schnider et al. 1997), and reflexive praxis (Poeck 1985), Ghent's Overlapping Figures Test (Ghent 1956) for gnosis abilities, digit symbol test (Wechsler 1981) for attention, Digit Span Forward (Wechsler 1955), Corsi Block-Tapping test (Milner 1971), and French adaptation (Van der Linden et al. 1999) of the Buschke Double Memory Test (Buschke et al. 1997) for memory, as well as the Shapes Test (Baddeley et al. 1994). Both young and elderly individuals had normal performances compared with the age-adapted norms. All of the subjects had at least a high school diploma or equivalent with a lower socio-cultural level in elderly (mean

1.88 ± 0.75) as compared with young subjects (mean 3.00 ± 0.50, $P < 0.001$) over a scale ranging from 1 to 3. Informed written consent was obtained from all participants and the local Ethics Committee approved the study.

Experimental design

Subjects watched a continuous stream of letters (pseudo-random sequences of consonants and vowels) common to the French alphabet on a computer screen and pressed a computer-controlled pushbutton with the index finger of their right hand as soon as a target appeared (response trials). For non-target trials, no motor response was required (no-response trials). Targets were defined according to the n-back design.

Stimuli consisted of white letters, type "Arial" ($2° \times 2.5°$ visual angle), with 10% gray noise, embedded in a 50% random noise grey rectangular background patch ($6° \times 6.7°$ visual angle). They were presented for 0.5 s, separated by 3-s intervals (onset to onset) during which a dot helped subjects maintain fixation.

Four different tasks were used: in a simple detection task (control), sequential letters or background patches without letters were presented. Subjects responded as fast as possible when background patches without letters appeared. In the 0-back task, the target was any letter that was identical to the one presented for the first time in the sequence. In the 2- and 3-back tasks, the target was any letter that was identical to the one presented two trials back and three trials back, respectively. Thus, WM load increased from control (memory free-condition) to 0-back (mildly demanding), 2-back (moderately demanding) and 3-back tasks (highly demanding).

Each task was tested in three stimulus sequences of 40 images each (13 targets), adding up to 120 trials per task. Before each sequence block, subjects were informed about the nature of the task, and several warm-up trials were performed. The protocol started with a detection task sequence followed by a sequence of the 0- and 2-back tasks, three sequences of the 3-back task, two sequences of the 2- and 0-back tasks and two sequences of the detection task. Reaction time (RT) and performance were systematically recorded, but no feedback on performance was provided. Before and after the experimental paradigm, an open and close eye EEG session without task was realized during a period of 3 min. Electrophysiological and neuropsychological assessments were performed in the morning following a 1-week interval.

Electrophysiological recordings

Continuous EEG (Micromed, Brain Quick system 98, Treviso, Italy) was recorded using 20 surface electrodes placed over the scalp according to the 10–20 international electrode placement system (Homan et al. 1987), with linked earlobes as reference. Skin impedance was kept below 5 kΩ. Electrophysiological signals were sampled at 1,024 Hz, with a lower cut-off of 0.33 Hz and an upper cut-off of 120 Hz (DC amplifiers Micromed). The electrooculogram (EOG) was recorded using two pairs of bipolar electrodes in both vertical and horizontal directions. Single pulses (TTL) synchronized with stimulus onset (letter or background patches) were recorded and used off-line to segment the continuous EEG data into epochs time-locked to stimulus onset.

Data processing

EEG data were analyzed using NeuroScan software (NeuroScan Inc., Herndon, VA, USA). EEG signals were corrected for ocular artifacts using a threshold reduction algorithm (NeuroScan Inc.). The EEG data were automatically scanned for contamination by muscular or electrode artifacts and the remaining trials were inspected visually to control for minor artifacts. EEG data were detached into epochs of 7,000 ms, starting 2,000 ms before stimulus onset. Electrophysiological analyses were performed over a shorter window of 3,000 ms with a 1,000-ms pre-stimulus onset. EEG data corresponding to correct answers without motor response were analyzed with three different types of electrophysiological analysis: (1) spectral power analysis, (2) ERPs, (3) and ERD/ERS.

Spectral power analysis

Artifact-free open eye EEG recordings at rest were converted into the frequency domain using a FFT function computed on overlapping 2-s windows (10% Hanning filter). For resting EEG data, theta frequency band power was measured at frontal (F3, Fz, F4) electrode sites, as the average power between 4 and 7.5 Hz. The culmination peak power between 8 and 12 Hz (alpha) was measured over right (P4, T6) and left (T5, P3) parietal electrode sites.

Event-related potentials

Event-related potentials (ERPs) were averaged over a window of 700 ms with a 200 ms pre-stimulus onset and low-pass filtered at 30 Hz (−48 dB/octave). ERPs were averaged with a 200-ms baseline epoch prior to stimulus onset. Latencies of the ERP components were measured at the time of the maximum peak. The visual P100 and N145 component latencies were measured at the occipital (O1, Oz, O2) electrode sites.

To isolate the PN_{wm} component, we performed an ERP waveform subtraction analysis between the n-back and the

control tasks. The tangential orientation of the parietal PN_{wm} component dipole engendered gradient amplitude maximal over anterior (F3, Fz, F4, C3, Cz, C4) electrode sites selected for this analysis. The temporal limits for the measurement of positivity–negativity area (in μV^2) was the time-range window between the longer and shorter N145 and N200 peak latency from detection and either the 0- , 2- or the 3-back waveform. These temporal limits were not identical in both age groups and tasks. To correct for this difference, the area of the PN_{wm} component was divided by the ad hoc time range defined by the temporal limits for each task in all subjects. To examine load effects, the PN_{wm} component areas were compared with a baseline area, obtained over a period of 150 ms before stimulus onset.

Event-related desynchronization and synchronization

To obtain synchronization data, the epoch was digitally filtered in the 4–7.5 Hz (theta) and 8–12 Hz (alpha) frequency bands, using narrow band pass filter (−48 dB/octave). The filtered epochs were then squared to obtain a signal proportional to the power of EEG frequency. Within each task and for each electrode, the power from the stimulus onset to 2,000 ms was determined as the power during the experimental condition (A), whereas the mean power during −1000 to 0 ms relative to stimulus onset was determined as reference period power (R). Then, the averaged data over trials were computed as the percentage power increase (ERS, positive value) or percentage power decreased (ERD, negative value) for a particular time interval in the particular frequency band of interest, using the following traditional formula: %ERS: $[(A - R)/R] \times 100$.

For each subject, the culmination peak (ms) and magnitude (%) of the transient theta ERS were measured in the 0–500 ms time window after stimulus onset over frontal (F3, Fz, F4) electrode sites. Alpha (8–12 Hz) ERS magnitude was analyzed in the 1,100–1,700 ms window after stimulus onset. The corresponding analyses were performed over right (P4, T6) and left (T5, P3) parietal electrode sites for alpha rhythm.

Statistical analysis

Demographic characteristics at inclusion as well as differences in n-back performances among groups were assessed using the Mann–Whitney non-parametric U test. To normalize the variance of the EEG data (i.e. PN_{wm} area, magnitude of theta and alpha power at rest and %ERS), a logarithmic transformation was used. RT, performance and EEG measures were each analyzed using three-way repeated measures ANOVA, with group (young and elderly), task condition (detection, 0-, 2-, 3-back) and education level (1 vs. 2 + 3), with all their interaction terms. Task condition was the within-subject factors. The significance values were determined using the Greenhouse–Geisser method. Post hoc analysis was performed using the Scheffé test (Milliken and Johnson 1984). Significance threshold was set at $P < 0.05$. Spearman correlation coefficients were used to evaluate the relationship between the PN_{wm} amplitude and performances in n-back, memory (Buschke) and attention (Shape and Trail Making test A) tests. Statistical analyses were performed using the Stata software package, release 11.1.

Results

Behavioral data

Averaged reaction times increased significantly with age [$F(1, 183) = 10.75$, $P < 0.005$; Table 1]. Young subjects responded faster than did elderly subjects whether the performed task required WM (0-, 2- and 3-back) or not (detection). A significant task effect was also observed [$F(3, 186) = 12.66$, $P < 0.005$] as subjects responded the fastest in the detection and 0-back tasks and the slowest in the 2- and 3-back tasks, independently of their age. All subjects performed well in n-back and detection tasks, with a minimum of 88% correct responses (Table 1). In line with a widely accepted idea (Jaeggi et al. 2009; Mattay et al. 2006; Stern 2009), performances were modulated by task [$F(3, 183) = 65.13$, $P < 0.001$]. Although performances for the detection and 0-back tasks did not differ significantly, in both groups, all subjects performed significantly worse in the 2- and 3-back task compared with the other experimental conditions (Scheffé, $P < 0.001$). Subject performances were also affected by age [$F(1, 183) = 64.11$, $P < 0.001$]. Post hoc analyses revealed that this effect was restricted to the 2- and 3-back task (Scheffé, $P < 0.001$). There was a significant interaction between age and task [$F(3, 183) = 13.39$, $P < 0.01$]. It is, however, noteworthy that even in the 3-back task, elderly subjects responded correctly in more than 85% of the trials. Education level was not associated with either RT or performances. The only significant correlation concerned the Shape test performance and PN_{wm} amplitude in 0- and 2-back task in elderly individuals (rho values of 0.354 and 0.355 respectively, $P < 0.05$). However, these correlations did not persist after Bonferroni correction.

Table 1 Mean reaction times (in ms) and mean performances (in %) with standard deviations (±SD) for the detection task, 0-, 2- and 3-back working memory tasks in young ($n = 32$) and elderly subjects ($n = 32$)

Tasks	Reaction times		Performances	
	Young subjects	Elderly subjects	Young subjects	Elderly subjects
Detection	643.94 (±114.99)	750.96 (±138.59)***	99.87 (±0.37)	98.25 (±1.07)
0-back	681.31 (±123.24)	783.79 (±134.47)***	99.90 (±0.28)	98.54 (±3.24)
2-back	796.73 (±145.78)	995.20 (±246.99)***	97.84 (±2.08)	89.38 (±5.86)***
3-back	916.62 (±203.42)	1075.19 (±241.43)**	94.22 (±3.33)	88.13 (±3.77)***
Group effect	**0.002**		**0.001**	
Task effect	**0.002**		**0.001**	
Education effect	0.108		0.590	
Group × task interaction	0.735		**0.002**	
Education × task interaction	0.551		0.576	

Average reaction times increased as a function of task difficulty in young and older participants. Subjects responded slower in the 2- and 3-back conditions when compared with the easier conditions, and in the 3-back compared with the 2-back conditions in young cases

Performances were related to task difficulty in young and older participants. Post hoc statistical analysis revealed lower performances in 2- and 3-back compared with easier conditions in both groups

Bold values are statistically significant

*** $P < 0.0001$, ** $P < 0.001$, * $P < 0.01$; *ns* no significant; compared with young subjects. See text for details

Electrophysiological data

Spectral power analysis

The magnitude of frontal theta power open eyes at rest was free from group effect [young 0.60 ± 0.19 log(μV^2) and old 0.53 ± 0.23 log(μV^2); $P = 0.13$]. In contrast, the maximum of alpha (8–12 Hz) frequency power, measured over the left and right parietal electrode locations, slowed significantly in older participants (young 9.8 Hz and old 9.0 Hz; $P < 0.05$). No other main factors or interaction-related effect was observed.

ERP components

Sensorial ERP components

In Fig. 1a, averaged waveform ERPs were plotted for each of the four tasks (detection, 0-, 2- and 3-back). As expected, the visual stimuli elicited two topographically distinct positive and negative responses over occipital and anterior regions 100 ms and 145 ms after stimulus onset (P100 and N145 component, respectively). The P100 latency was free from group-, electrode- or task-related effects. In contrast, the latency of the N145 component was significantly increased for all experimental conditions in the older group [$F(1, 183) = 105.57$, $P < 0.001$; Table 2]. This difference persisted when adjusting for education level. No interaction was observed (Fig. 1a).

The positive–negative working memory component

Figure 1b shows the PN$_{wm}$ component, obtained by subtracting ERP waveforms for the detection task from the *n*-back tasks. In line with our previous results, the PN$_{wm}$ component was delayed in the older group for all tasks (Fig. 1b; Table 2). This delay was due to the N145 component latency increase for all tasks in the elderly group (Kolev et al. 2002; McEvoy et al. 2001; Missonnier et al. 2005). Table 2 shows normalized area values of the PN$_{wm}$ component for the two age groups. The PN$_{wm}$ density was significantly higher in younger compared with elderly subjects [$F(1, 122) = 9.85$, $P < 0.005$]. There was also a significant task effect [$F(2, 122) = 3.97$, $P < 0.05$] revealing a higher amplitude in the 2- and 3-back conditions when compared with the easier 0-back condition in younger but not in older subjects (Scheffé, $P < 0.001$). An education effect was also observed [$F(1, 122) = 4.34$, $P < 0.05$] indicating lower PN$_{wm}$ densities in less educated participants after adjusting for age group and task. No other main factors or interaction-related effect was observed. Moreover, PN$_{wm}$ densities were not significantly associated with *n*-back performances in both young and elderly groups.

ERD/ERS analysis

Theta band

After stimulus presentation, a phasic increase of theta ERS was observed during 0–500 ms for all tasks and groups (Fig. 2a). Theta ERS culmination peak (ms) and phasic amplitude [log(%)] data are presented in Table 3. The theta ERS mean power culmination peak latency was delayed [$F(1, 183) = 4.13$, $P < 0.05$] in young participants (Fig. 2), but theta ERS amplitude was lower in older individuals [$F(1, 183) = 12.84$, $P < 0.001$]. The theta ERS

Fig. 1 **a** Occipital (O1, Oz, O2) and Anterior (F3, Fz, F4, C3, Cz, C4) grand average ERPs for the 3-, 2- and 0-back tasks and detection task in young (*upper*) and elderly (*lower*) participants. Note the increased N145 latencies for all tasks in elderly compared with young participants. **b** Grand average waveforms of the PN_{wm} component, representing ERP differences between the *n*-back tasks (0- to 3-back tasks) and detection for young (*right*) and elderly (*left*) subjects. Note the presence of the waveform ERP differences between 0-back and detection in elderly. Comparable amplitudes of the PN_{wm} component were observed in 2- and 3-back tasks in young subjects
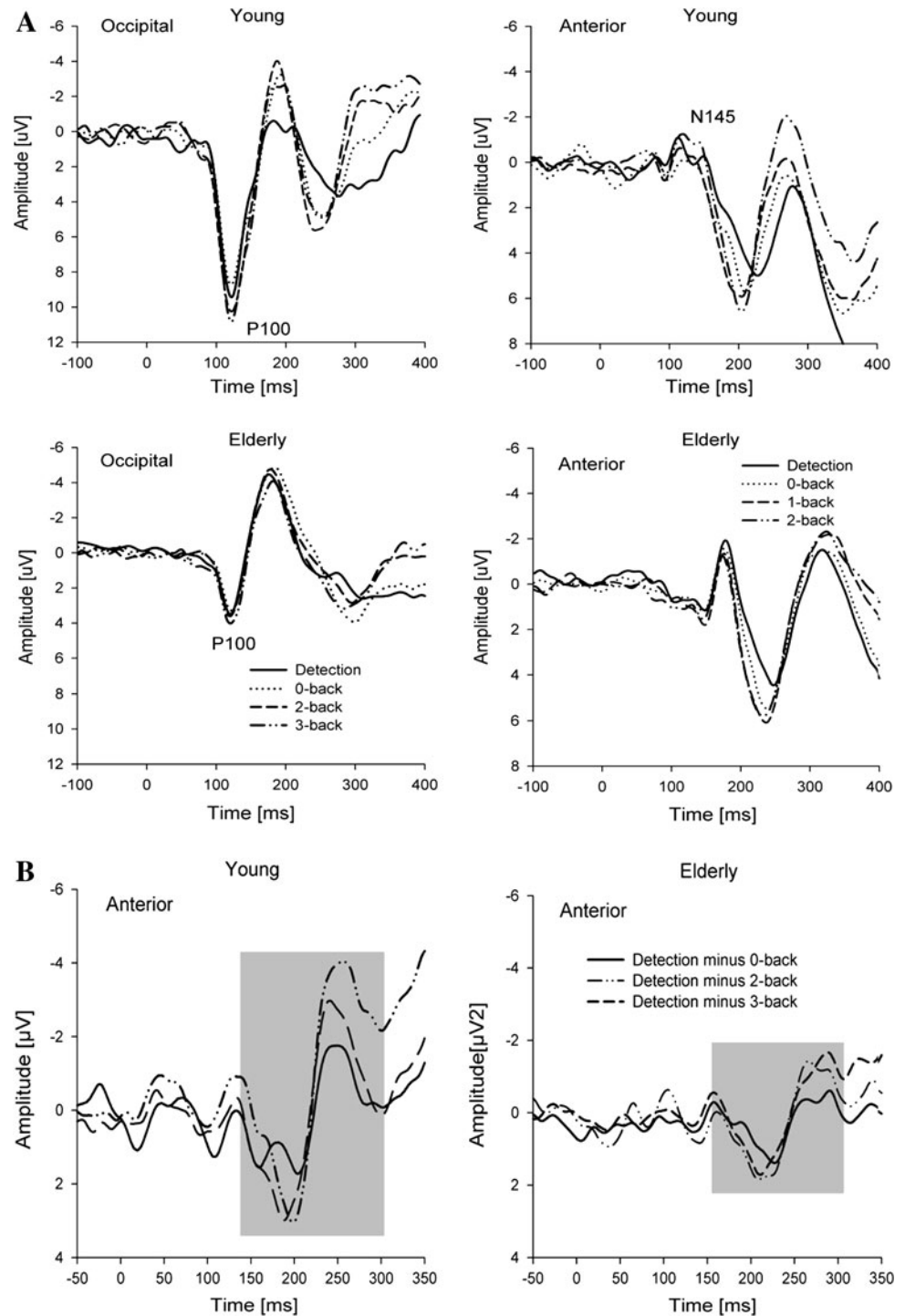
mean power culmination peak latency and amplitude was free from task and education level effects. No other significant interactions were observed.

Alpha frequency band

In the alpha frequency band, stimulus presentation elicited an ERD at right and left parietal electrode sites for all tasks and

groups (Fig. 3). The time course of alpha activity differed substantially between the two age groups. In the older subjects, there was a rapid development of an alpha ERS that reached its maximal amplitude at around 800 ms after stimulus onset and then remained sustained at lower amplitude. In younger subjects, the alpha ERD lasted longer and converted slowly into late alpha ERS (>1,200–2,000 ms). During the 1,100–1,700 ms time interval, the sustained alpha ERS

Table 2 Early (P100) and late (N145) sensorial ERP latencies (ms ± SD), and normalized area values [in log (μV^2) ± SD] of the PN$_{wm}$ component for detection, 0-, 2- and 3-back tasks in young ($n = 32$) and elderly ($n = 32$) participants

Tasks	Sensorial ERPs				Cognitive ERP	
	P100 (occipital)		N145 (anterior)		PN$_{wm}$ (anterior)	
	Young	Elderly	Young	Elderly	Young	Elderly
Detection	126.07 (±7.48)	122.49 (±11.92) ns	145.71 (±16.51)	171.17 (±11.98)***		
0-back	124.04 (±9.96)	123.04 (±13.56) ns	144.50 (±16.39)	169.28 (±9.89)***		
2-back	124.03 (±7.61)	121.76 (±11.60) ns	142.76 (±15.84)	168.45 (±10.12)***		
3-back	124.48 (±8.21)	123.44 (±14.53) ns	146.19 (±14.21)	168.67 (±10.20)**		
0-back minus detection					0.62 (±0.91)	0.44 (±0.84) ns
2-back minus detection					1.48 (±0.53)	0.76 (±0.72)***
3-back minus detection					1.37 (±0.52)	0.72 (±0.99)**
Group effect	0.081		**0.001**		**0.003**	
Task effect	0.966		0.980		**0.024**	
Education effect	0.713		0.806		**0.041**	
Group × task interaction	0.994		0.923		0.311	
Education × task interaction	0.963		0.883		0.973	

The PN$_{wm}$ density was significantly modified by tasks in young but not in older cases. Post hoc statistical analysis revealed higher PN$_{wm}$ densities in the 2- and 3-back conditions when compared with the easier 0-back condition

Bold values are statistically significant

*** $P < 0.0001$; ** $P < 0.001$; *ns* no significant; compared with young subjects. See text for details
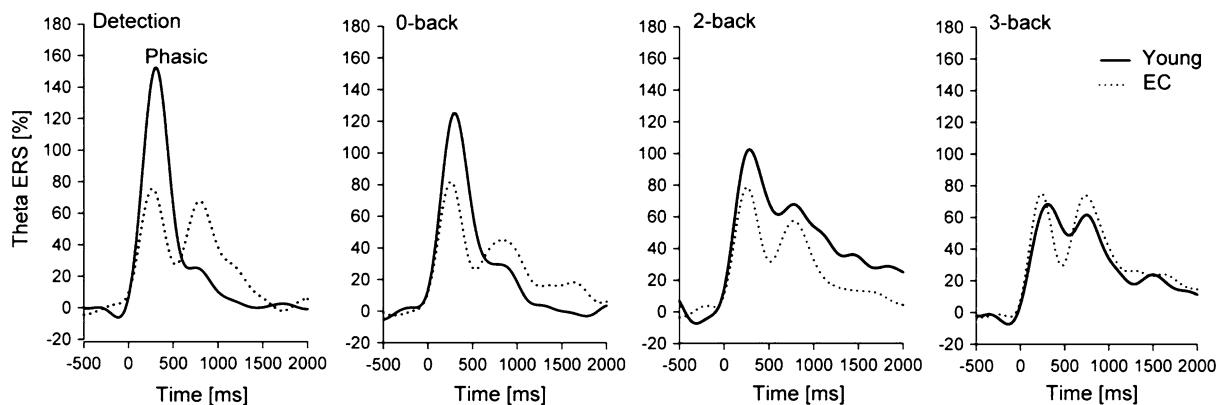

Fig. 2 Event-related synchronization of theta (4–7.5 Hz) frequency band as a function of time (ms), for the 3-, 2- and 0-back tasks and detection task in young (*black line*) and elderly (*dotted line*) subjects measured at frontal (F3, Fz, F4) electrode location. The y axis depicts relative (%) power values; positive values stand for synchronization. Phasic theta oscillatory activity combines both evoked and induced activity. Note the increase of phasic theta synchronization during detection and 0-back tasks in young compared with elderly subjects

amplitude was significantly higher in younger compared with older subjects on both the left [$F(1, 183) = 6.17$, $P < 0.05$] and right [$F(1, 183) = 5.05$, $P < 0.05$] sides (Table 4). This group difference persisted when adjusting for education level differences. An education level effect was present only for the left electrode location [$F(1, 183) = 5.19$, $P < 0.05$]. No other main factor or interactions were observed.

Discussion

In line with our previous work, the successful performance of WM tasks was associated with a significant deflection of early ERPs components giving rise to the PN$_{wm}$ component (Missonnier et al. 2004; Missonnier et al. 2003). Importantly, PN$_{wm}$ densities increased with higher memory loads (3- and 2-back > 0-back tasks) in the younger but not in the older group indicating that the two age groups adopt distinct neural strategies during the successful performance of the *n*-back task (Missonnier et al. 2004). Although both young and elderly subjects recruit the same number of PN$_{wm}$-related parietal neural generators in detection and mildly demanding WM tasks, older adults may not be able to activate additional neuronal populations in this area when dealing with the

Table 3 Theta ERS mean power culmination peak (ms) and normalized phasic (%) theta ERS amplitude (%) ± SD for detection, 0-, 2- and 3-back tasks over frontal (F3, Fz, F4) electrode location in young (*n* = 32) and elderly (*n* = 32) participants

Tasks	Theta ERS culmination peak (ms)		Theta ERS phasic amplitude [log(%)]	
	Young	Elderly	Young	Elderly
Detection	282.20 (±72.48)	288.02 (±57.51)	2.07 (±0.28)	1.76 (±0.53)**
0-back	270.02 (±48.17)	252.94 (±72.07)	1.97 (±0.30)	1.74 (±0.51)*
2-back	278.10 (±57.03)	254.05 (±75.54)	1.84 (±0.55)	1.74 (±0.59)
3-back	290.14 (±70.70)	255.03 (±79.15)**	1.85 (±0.46)	1.58 (±0.95)
Group effect	**0.046**		**0.001**	
Task effect	0.360		0.628	
Education effect	0.450		0.935	
Group × task interaction	0.520		0.620	
Education × task interaction	0.600		0.564	

In both groups, theta ERS culmination peak were not affected by the task difficulty, and amplitude was significantly modified by tasks in young but not in older cases. Post hoc statistical analysis revealed higher theta ERS amplitude in the detection compared with the 2- and 3-back conditions

Bold values are statistically significant

** $P < 0.01$, * $P = 0.05$; *ns* no significant; compared to young subjects. See text for details

Fig. 3 Time course of ERD/ERS for alpha rhythm (8–12 Hz) over right (P4, T6) and left (T5, P3) parietal electrode sites for the 3-, 2- and 0-back tasks and detection task in young (*upper*) and elderly (*lower*) participants. The y axis depicts the relative (%) of frequency band power, with positive values standing for ERS and negative values for ERD. Note the increase alpha ERS in 3- and 2-back compared with 0-back and detection tasks in elderly but not in young subjects cases in the 1,100–1,700 ms time window (*grey square*)
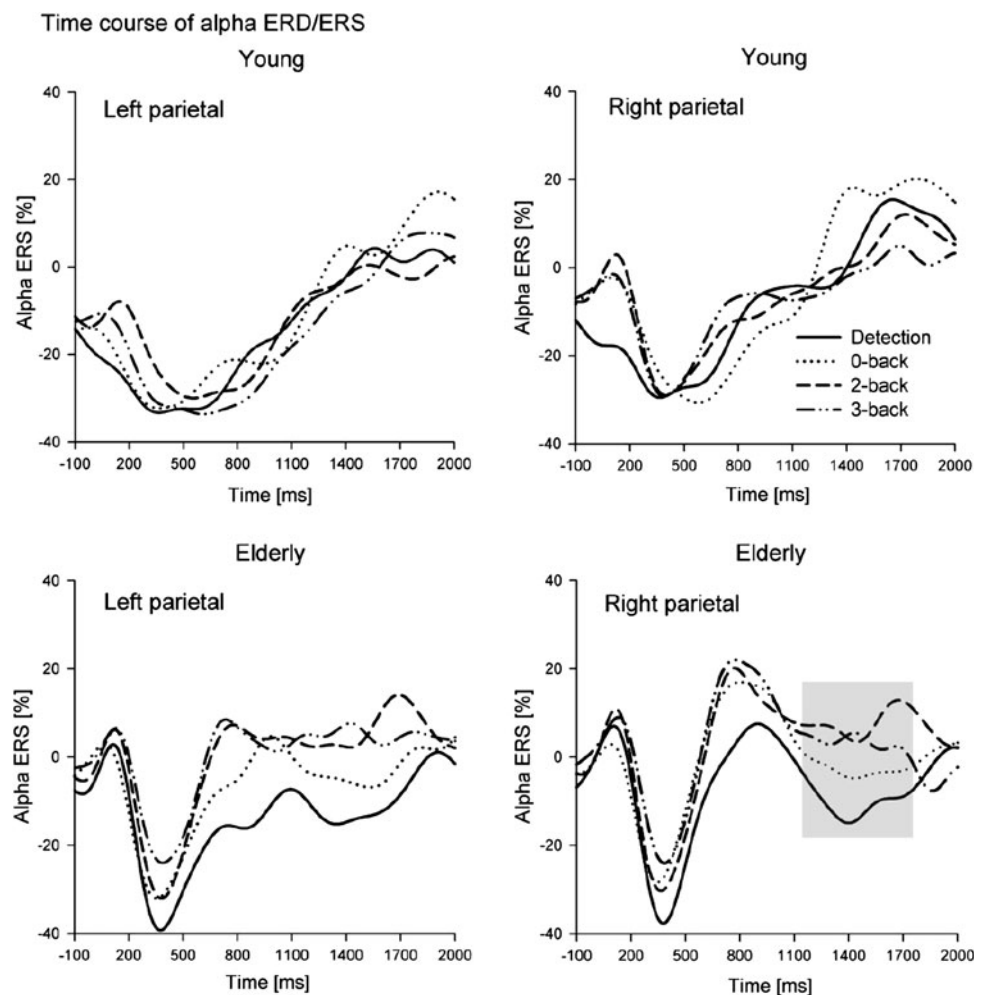
Table 4 Alpha normalized ERS amplitude [log (%) ± SD] for detection, 0-, 2- and 3-back tasks in young ($n = 32$) and elderly ($n = 32$) participants

Tasks	Alpha ERS sustained amplitude			
	Left (T5–P3) electrode location		Right (P4–T6) electrode location	
	Young	Elderly	Young	Elderly
Detection	0.34 (±1.25)	−0.46 (±1.17)	0.43 (±1.21)	−0.69 (±1.10)
0-back	0.61 (±1.17)	−0.19 (±1.26)	0.43 (±1.25)	−0.32 (±1.18)
2-back	0.43 (±1.22)	0.36 (±1.24)	0.21 (±1.25)	0.26 (±1.23)
3-back	0.20 (±1.23)	0.03 (±1.22)	0.11 (±1.23)	−0.05 (±1.15)
Group effect	**0.015**		**0.028**	
Task effect	0.356		0.268	
Education effect	**0.026**		0.074	
Group × task interaction	0.515		0.393	
Education × task interaction	0.837		0.686	

The sustained alpha ERS amplitude was significantly modified by tasks on both left and right sides in elderly but not in younger cases

Bold values are statistically significant

See text for details

2- and 3-back tasks. In contrast, younger individuals reached the maximal activation of PN_{wm} in the 2-back task. Altogether, these data suggest that elderly persons are able to mobilize rapidly these brain resources to preserve cognitive performances once the first WM demand appears. It is thus plausible that the successful 2-back task performance in the older group is highly dependent on the activation of additional neuronal sub-populations outside the parietal cortex.

The fast increase in alpha ERS in elderly individuals remained sustained during the time-interval between 1,000 and 2,000 ms. Younger adults displayed a later development of alpha ERS during the 1,100–1,700 ms time interval but of higher amplitude compared with elders. The exact neurophysiological significance of this observation remains unclear. Alpha power increase was observed during the encoding phase of WM tasks that involves top–down attentional control (Freunberger et al. 2003; Palva and Palva 2007). A posterior alpha amplitude increase (Jensen et al. 2002; Busch and Herrmann 2003; Jokisch and Jensen 2007) as well higher phase synchronization (Sauseng et al. 2005; Klimesch et al. 2008; Kawasaki et al. 2010) was also described during the retention of visual material in WM. Using the *n*-back task in young adults, Krause et al. (2000) also described a parietal alpha ERD that converted slowly to a late alpha ERS in all memory load conditions. Recent 3-back memory task investigations using time–frequency analysis (Pesonen et al. 2007; Krause et al. 2010) confirmed these findings. Consistent with the idea that apha rhythm modulation surrounds both the attentional and pure WM components of the *n*-back task, they reported that the duration of the alpha ERD increases

with RT and higher memory load. In the present series, the alpha ERD and ERS amplitudes were task-independent. However, there was a significant education effect on both the PNwm component and alpha ERS amplitudes. Although we cannot exclude that this weak association represents an alpha statistical error, a decreased alpha ERD was observed during various WM tasks in individuals with higher education levels suggesting an association between this demographic parameter and WM-related EEG parameters (Grabner et al. 2004). The duration of alpha ERD was shorter in elders reflecting the rapid mobilization of their attentional ressources. Conversely, the late alpha ERS that is temporally close to the activation of pure WM showed a lower amplitude in older compared with younger cases in all experimental conditions. In conjunction with the previously reported PN_{wm} data, our data on alpha rhythm suggest that old age is associated with a rapid recruitment of neural generators within the parietal areas occurring even in very low demanding WM conditions.

Theta synchronization and attentional networks

Within 500 ms after stimulus, a frontal phasic theta increase was observed following the appearance of the stimulus in all age groups. Theta ERS was of higher amplitude in the detection task as compared with the highly WM demanding 2- and 3-back tasks in young subjects. These results are consistent with previous investigation results reporting that early frontal theta activity primarily reflects neural networks involved in the allocation of attention related to target stimuli rather than pure WM processes (Missonnier et al. 2004; Deiber et al. 2007). In

contrast, older adults did not reveal any task-related effect on phasic theta ERS and its amplitude was reduced compared with younger adults in the detection and 0-back tasks that primarily engages attentional processes. This age-related change in neural reactivity during attentional demands was further confirmed by our theta ERS culmination peak findings. Although no task effect was observed in both groups as already described in younger cohorts (Missonnier et al. 2005), there was a significant decrease of the theta ERS culmination peak in older compared with young participants. Altogether, these observations support the idea that older adults recruit fewer resource units even at low levels of computational complexity to maintain their performances (Reuter-Lorenz et al. 2000; Reuter-Lorenz 2002). Furthermore, the concomitant decrease in the frontal theta ERS and increase of parietal alpha ERS independently of WM load in elderly subjects may be also compatible with the enhanced parietal activity modeled as the anterior–posterior shift in aging (Davis et al. 2008).

Conclusions

Strengths of the present study include the careful selection of cases without cognitive decline on the basis of detailed neuropsychological assessment, exclusion of cases receiving a regular treatment with antidepressants, neuroleptics or benzodiazepines and combined analysis of ERP and brain oscillations in the same individuals. Several limitations should, however, be considered when interpreting the present data. First, our EEG findings concerned the *n*-back task and should be confirmed in other WM experimental paradigms. In order to be close to routine clinical settings, we opted for the use of 20-electrode EEG recordings. Subsequently, our spatial sampling is not optimal to detect the activation of additional neural generators outside the parietal cortex that may be involved in the successful performance of the 3-back task in both age groups. Finally, given the high performances in our older group, it was not possible to identify individual EEG strategies of low-versus high performers. Future activation studies in larger series including the combination of multichannel EEG recordings with other functional imaging modalities are warranted to explore the age-related patterns of brain activation in various WM paradigms.

References

Babiloni C, Babiloni F, Carducci F, Cappa SF, Cincotti F, Del Percio C, Miniussi C, Moretti DV, Rossi S, Sosta K, Rossini PM (2004) Human cortical responses during one-bit short-term memory. A high-resolution EEG study on delayed choice reaction time tasks. Clin Neurophysiol 115:161–170

Baddeley A, Emslie H, Nimmo-Smith L (1994) The Doors and People Test: a test of visual and verbal recall and recognition. Thames Valley Test, Bury St Edmonds

Busch NA, Herrmann CS (2003) Object-load and feature-load modulate EEG in a short-term memory task. NeuroReport 14:1721–1724

Buschke H, Sliwinski MJ, Kuslansky G (1997) Lipton RB. Diagnosis of early dementia by the Double Memory Test: encoding specificity improves diagnostic sensitivity and specificity. Neurology 48:989–997

Butters N, Granholm E, Salmon DP, Grant I, Wolfe J (1987) Episodic and semantic memory: a comparison of amnesic and demented patients. J Clin Exp Neuropsychol 9:479–497

Cabeza R, Anderson ND, Locantore JK, McIntosh AR (2002) Aging gracefully: compensatory brain activity in high-performing older adults. Neuroimage 17:1394–1402

Callicott JH, Mattay VS, Bertolino A, Finn K, Coppola R, Frank JA, Goldberg TE, Weinberger DR (1999) Physiological characteristics of capacity constraints in working memory as revealed by functional MRI. Cereb Cortex 9:20–26

Cook IA, Bookheimer SY, Mickes L, Leuchter AF, Kumar A (2007) Aging and brain activation with working memory tasks: an fMRI study of connectivity. Int J Geriatr Psychiatry 22:332–342

Cowan N (1984) On short and long auditory stores. Psychol Bull 96:341–370

Cowan N (1988) Evolving conceptions of memory storage, selective attention, and their mutual constraints within the human information-processing system. Psychol Bull 104:163–191

Davis SW, Dennis NA, Daselaar SM, Fleck MS, Cabeza R (2008) Que PASA? The posterior-anterior shift in aging. Cereb Cortex 18:1201–1209

Deiber M-P, Missonnier P, Bertrand O, Gold G, Costa-Fazio L, Ibañez V, Giannakopoulos P (2007) Distinction of perceptual and attentional processing in working memory tasks: a study of phase-locked and induced oscillatory brain dynamics. J Cogn Neurosci 19:158–172

Emery L, Heaven TJ, Paxton JL, Braver TS (2008) Age-related changes in neural activity during performance matched working memory manipulation. Neuroimage 42:1577–1586

Folstein MF, Folstein SE, McHugh PR (1975) "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 12:189–198

Freunberger R, Fellinger R, Sauseng P, Gruber W, Klimesch W (2003) Dissociation between phase-locked and nonphase-locked alpha oscillations in a working memory task. Hum Brain Mapp 30:3417–3425

Friedman D (2000) Event-related brain potential investigations of memory and aging. Biol Psychol 54:175–206

Gevins A, Smith ME, McEvoy L, Yu D (1997) High-resolution EEG mapping of cortical activation related to working memory: effects of task difficulty, type of processing, and practice. Cereb Cortex 7:374–385

Ghent L (1956) Perception of overlapping and embedded figures by children of different ages. Am J Psychol 69:575–581

Goldberg TE, Berman KF, Fleming K, Ostrem J, Van Horn JD, Esposito G, Mattay VS, Gold JM, Weinberger DR (1998) Uncoupling cognitive workload and prefrontal cortical physiology: a PET rCBF study. Neuroimage 7:296–303

Grabner RH, Fink A, Stipacek A, Neuper C, Neubauer AC (2004) Intelligence and working memory systems: evidence of neural efficiency in alpha band ERD. Brain Res Cogn Brain Res 20:212–225

Homan R, Herman J, Purdy P (1987) Cerebral location of international 10–20 system electrode placement. Electroencephalogr Clin Neurophysiol 66:376–382

Jaeggi SM, Schmid C, Buschkuehl M, Perrig WJ (2009) Differential age effects in load-dependent memory processing. Neuropsychol Dev Cogn B Aging Neuropsychol Cogn 16:80–102

Jensen O, Tesche CD (2002) Frontal theta activity in humans increases with memory load in a working memory task. Eur J Neurosci 15:1395–1399

Jensen O, Gelfand J, Kounios J, Lisman JE (2002) Oscillations in the alpha band (9–12 Hz) increase with memory load during retention in a short-term memory task. Cereb Cortex 12:877–882

Jokisch D, Jensen O (2007) Modulation of gamma and alpha activity during a working memory task engaging the dorsal or ventral stream. J Neurosci 27:3244–3251

Kahana MJ, Sekuler R, Caplan JB, Kirschen M, Madsen JR (1999) Human theta oscillations exhibit task dependence during virtual maze navigation. Nature 399:781–784

Kaplan EF, Goodglass H, Weintraub S (1983) The Boston naming test. Lea and Febiger, Philadelphia

Karrasch M, Laine M, Rapinoja P, Krause CM (2004) Effects of normal aging on event-related desynchronization/synchronization during a memory task in humans. Neurosci Lett 366:18–23

Kawasaki M, Kitajo K, Yamaguchi Y (2010) Dynamic links between theta executive functions and alpha storage buffers in auditory and visual working memory. Eur J Neurosci 31:1683–1689

Klimesch W (1999) EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis. Brain Res Brain Res Rev 29:169–195

Klimesch W, Freunberger R, Sauseng P, Gruber W (2008) A short review of slow phase synchronization and memory: evidence for control processes in different memory systems? Brain Res 1235:31–44

Kolev V, Yordanova J, Basar-Eroglu C, Basar E (2002) Age effects on visual EEG responses reveal distinct frontal alpha networks. Clin Neurophysiol 113:901–910

Krause CM, Sillanmäki L, Koivisto M, Saarela C, Häggqvist A, Laine M, Hämäläinen H (2000) The effects of memory load on event-related EEG desynchronization and synchronization. Clin Neurophysiol 111:2071–2078

Krause CM, Pesonen M, Hämäläinen H (2010) Brain oscillatory 4–30 Hz electroencephalogram responses in adolescents during a visual memory task. Neuroreport 21:767–771

Mattay VS, Fera F, Tessitore A, Hariri AR, Berman KF, Das S, Meyer-Lindenberg A, Goldberg TE, Callicott JH, Weinberger DR (2006) Neurophysiological correlates of age-related changes in working memory capacity. Neurosci Lett 392:32–37

McEvoy LK, Pellouchoud E, Smith ME, Gevins A (2001) Neurophysiological signals of working memory in normal aging. Brain Res Cogn Brain Res 11:363–376

Milliken GA, Johnson DE (1984) Designed experiments, vol 1. Van Nostrand Reinhold, New York

Milner B (1971) Interhemispheric differences in the localization of psychological processes in man. Br Med Bull 27:272–277

Missonnier P, Leonards U, Gold G, Palix J, Ibanez V, Giannakopoulos P (2003) A new electrophysiological index for working memory load in humans. Neuroreport 14:1451–1455

Missonnier P, Gold G, Leonards U, Costa-Fazio L, Michel JP, Ibanez V, Giannakopoulos P (2004) Aging and working memory: early deficits in EEG activation of posterior cortical areas. J Neural Transm 111:1141–1154

Missonnier P, Gold G, Fazio-Costa L, Michel JP, Mulligan R, Michon A, Ibanez V, Giannakopoulos P (2005) Early event-related potential changes during working memory activation predict rapid decline in mild cognitive impairment. J Gerontol A Biol Sci Med Sci 60:660–666

Onofrj M, Thomas A, Iacono D, D'Andreamatteo G, Paci C (2001) Age-related changes of evoked potentials. Neurophysiol Clin 31:83–103

Onton J, Delorme A, Makeig S (2005) Frontal midline EEG dynamics during working memory. Neuroimage 27:341–356

Palva S, Palva JM (2007) New vistas for alpha-frequency band oscillations. Trends Neurosci 30:150–158

Pesonen M, Hämäläinen H, Krause CM (2007) Brain oscillatory 4–30 Hz responses during a visual n-back memory task with varying memory load. Brain Res 1138:171–177

Poeck K (1985) Clues to the Nature of disruption to limb Praxis. In: Roy EA (ed) Neuropsychological studies of apraxia and related disorders. Elsevier, Amsterdam, pp 99–109

Raghavachari S, Kahana MJ, Rizzuto DS, Caplan JB, Kirschen MP, Bourgeois B, Madsen JR, Lisman JE (2001) Gating of human theta oscillations by a working memory task. J Neurosci 21:3175–3183

Rajah MN, McIntosh AR (2008) Age-related differences in brain activity during verbal recency memory. Brain Res 1199:111–125

Reitan RM (1958) Validity of the Trail Making Test as an indicator of organic brain damage. Percept Mot Skills 8:271–276

Reuter-Lorenz P (2002) New visions of the aging mind and brain. Trends Cogn Sci 6:394

Reuter-Lorenz PA, Jonides J, Smith EE, Hartley A, Miller A, Marshuetz C, Koeppe RA (2000) Age differences in the frontal lateralization of verbal and spatial working memory revealed by PET. J Cogn Neurosci 12:174–187

Richard CC, Veltmeyer MD, Hamilton RJ, Simms E, Paul R, Hermens D, Gordon E (2004) Spontaneous alpha peak frequency predicts working memory performance across the age span. Int J Psychophysiol 53:1–9

Rugg MD, Mark RE, Gilchrist J, Roberts RC (1997) ERP repetition effects in indirect and direct tasks: effects of age and interitem lag. Psychophysiology 34:572–586

Rypma B, D'Esposito M (2000) Isolating the neural mechanisms of age-related changes in human working memory. Nat Neurosci 3:509–515

Sauseng P, Klimesch W, Doppelmayr M, Pecherstorfer T, Freunberger R, Hanslmayr S (2005) EEG alpha synchronization and functional coupling during top-down processing in a working memory task. Hum Brain Mapp 26:148–155

Schnider A, Hanlon RE, Alexander DN, Benson DF (1997) Ideomotor apraxia: behavioral dimensions and neuroanatomical basis. Brain Lang 58:125–136

Stern Y (2009) Cognitive reserve. Neuropsychologia 47:2015–2028

Van der Linden M, Collette F, Seron X (1999) Adaptation française de la procédure de Grober et Buschke. Solal, Marseille

Wager TD, Smith EE (2003) Neuroimaging studies of working memory: a meta-analysis. Cogn Affect Behav Neurosci 3:255–274

Wechsler D (1955) Manual for the Wechsler adult intelligence scale. Psychological Corporation, New York

Wechsler D (1981) Manual for the Wechsler adult intelligence scale-revised. Psychological Corporation, New York