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Behavioural Brain Research xxx (2004) xxx–xxx
BEHAVIOURAL BRAIN RESEARCH
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Research report

Human cortical rhythms during visual delayed choice reaction time tasks A high-resolution EEG study on normal aging

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Received 1 October 2003; received in revised form 5 December 2003; accepted 6 December 2003

Abstract

Neuroimaging cognitive study of aging requires simple tasks ensuring a high rate of correct performances even in stressful neurophysiological settings. Here two simple delayed choice reaction time tasks were used to unveil event-related desynchronization (ERD) of theta (4–6 Hz) and alpha (6–12 Hz) electroencephalographic rhythms across normal aging. In the first condition, a cue stimulus (one bit) was memorized along a brief delay period (3.5–5.5 s). The explicit demand was visuo-spatial, but the retention could be also based on phonological and somatomotor coding. In the second condition, the cue stimulus remained available along the delay period. Correct performances were higher than 95% in both groups and tasks, although they were significantly better in young than elderly subjects ($P < 0.03$). During the delay period, theta and alpha ERD accompanying correct responses were recognized in the two groups, the alpha ERD being stronger and prolonged during the memory than non-memory task. On the other hand, the fronto-parietal theta and parietal alpha ERD were stronger in young than elderly subjects during both tasks. Notably, the frontal alpha ERD was negligible in elderly subjects. In conclusion, the present simple tasks unveiled in elderly compared to young subjects (i) a weaker involvement of (para)hippocampal-cortical circuits as revealed by theta ERD and (ii) a weaker involvement of "executive" thalamo-cortical circuits as revealed by frontal alpha ERD. These effects might worsen behavioral performances to the simple cognitive tasks with age. The present protocol is promising for the neuroimaging study of pathological aging.

Keywords: Short-term memory; Delayed choice reaction time; Aging; Cerebral cortex; Electroencephalography (EEG); Theta rhythm; Alpha rhythm; Event-related desynchronization/synchronization (ERD/ERS)

1. Introduction

Normal aging is accompanied by a slower information processing and by a decline of short-term memory (STM; [1]), which would be reflected in the "on-line" retention or manipulation of information [2–6]. The normal aging also affects the spatial pattern of fronto-parietal cortical activity, as revealed by a previous study on electroencephalographic (EEG) rhythms [7]. In that study, subjects performed easy and difficult versions of a spatial "matched-to-sample" task. In the easy version, the subjects matched the current letter position with a prefixed position. In the difficult version ("n-back" variant), the current letter position was matched with that cued two trials back (i.e. continuous updating). As a striking result, young but not elderly subjects displayed an increase of the frontal midline theta rhythm (about 4–7 Hz) proportional to the memory load. Indeed, the theta power typically increases during mental efforts, possibly as an effect of a fronto-hippocampal drive [7–10].

As another evidence of that study [7], young adults showed a parallel decrease of the parietal alpha power

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doi:10.1016/j.bbr.2003.12.012

(about 8–12 Hz) as a function of the memory load. In elderly subjects, the decrement of the alpha power also involved the frontal regions. These results unveiled that normal aging affected the alpha power during heavy memory loads, possibly due to a thalamo-cortical desynchronizing drive recruiting cortical neuronal resources [8–11].

With respect to "match-to-sample" and "n-back" STM tasks, the delayed reaction time tasks include no on-line probe stimulus to be matched with the memorized cue [12–15]. Subject has to retain an association of cue stimulus-motor response along a brief delay period ending with a go stimulus. Thanks to its simplicity, the delayed reaction time task has been successfully used for the study of cognitive processes in Schizophrenia and aging [14,16–18].

Cortical EEG rhythms during delayed reaction time tasks have been recently explored in young but not elderly subjects [19,20]. During the delay period of a Go/Nogo task, the fronto-parietal alpha power (8–12 Hz) gradually decreased [19]. In another experiment, subjects had to remember the spatial feature of a cue stimulus along the delay period [20]. Theta (4–6 Hz) and alpha (6–8 Hz) power decreased in fronto-parietal areas, more during the STM than control condition. These results were surprising since the theta power usually increases during mental effort and high memory load [7–10].

Here two simple delayed reaction time tasks were used to unveil changes of fronto-parietal theta (4–6 Hz) and alpha (6–12 Hz) EEG rhythms across normal aging. In the first condition, a simple cue stimulus (one bit) was memorized along a brief delay period (3.5–5.5 s). The explicit demand was visuo-spatial, but the retention could be also based on phonological and somatomotor coding. Of note, only one bit of information had to be retained. In the second condition, the cue stimulus remained available along the delay period. The aim was to evaluate the fronto-parietal cognitive processes (theta and alpha oscillations) during cognitive tasks simpler than those previously used in aging research [7,21,22], in the perspective of early dementia studies.

2. Materials and methods

2.1. Subjects

The experiments were performed in two groups of healthy, right-handed (Edinburgh Inventory) volunteers. The group of the young adults (N young) consisted of 16 subjects with a mean age of 33.5 years (±1.5 standard error (S.E.); 7 females and 9 males), while the group of the elderly adults (N old) consisted of 16 subjects with a mean age of 66.4 years (±2.34 S.E.; 7 females and 9 males). All subjects had no previous history of neurological or psychiatric diseases as revealed by an accurate medical examination. Furthermore, they presented no sign of mild cognitive impairments as assessed by a standard neuropsychological testing. Finally, all subjects gave their informed written consent according to the declaration of Helsinki and the local institutional ethics committee approved general procedures.

2.2. Experimental tasks

Subjects were seated in a comfortable reclining armchair, placed in a dimly-lit, sound-damped, and electrically-shielded room. They kept their forearms resting on armchairs, with right index finger resting between two buttons spaced 6 cm each other. A computer monitor was placed in front of them (about 100 cm). The STM task (Fig. 1) comprised a sequence of baseline stimulus (0.7° cross at the center of the monitor), visual warning stimulus (the cross was surrounded by a circle for 1 s), visual cue stimulus (two vertical bars large about 2° and height 2.5–7° for 2 s), delay period (blank screen for 3.5–5.5 s), go stimulus (the circle appeared again for 1 s), and right finger movement to press the proper button of a custom-made device. This device had two large buttons distant about 10 cm each other, which were electronically connected to the mouse of the computer giving the visual stimuli. Subjects had to click left mouse button if the taller bar (cue stimulus) was at the left monitor side, whereas they had to click the right mouse button if the taller bar was at the right monitor side. In the no STM (NSTM) condition, the visual cue stimulus was delivered up to the go stimulus. Two trial blocks for each condition were pseudo-randomly intermingled (block = 50 single trials; 2 min pause). Subjects were told in advance if the block was NSTM or STM. In the perspective of future dementia

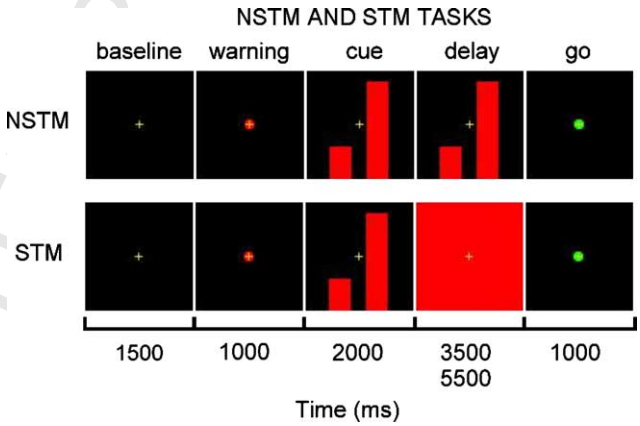

Fig. 1. Set up and experimental tasks. The experiment included two variants (conditions) of the delayed choice reaction time tasks. The sequence of events for the condition of STM was as follows: (i) a cross at the center of the monitor as a visual warning stimulus lasting 1 s, (ii) a couple of vertical bars as a visual cue stimulus lasting 2 s, (iii) a blank screen as a delay period lasting 3.5–5.5 s, (iv) a circle at the center of the monitor as a go stimulus lasting 1 s, and (v) a finger movement as a motor response. Subjects had to click either left button of a home-made device if the taller bar was at the left monitor side or right button if the taller bar was at the right monitor side. This device had two large buttons distant about 10 cm each other, which were electronically connected to the mouse of the computer giving the visual stimuli. Compared to the STM task, the condition with no memory load (NSTM) had visual cue stimuli lasting up to the go stimulus.

studies, subjects were free to use any memorization strategy including visuo-spatial imagery, somatomotor preparation, and mental "phonological" coding and rehearsal. Before the recording session, a training of about 10 min familiarized the subjects with the experimental apparatus and tasks.

2.3. EEG recordings

EEG data were recorded (0.1–60 Hz bandpass; 256 Hz sampling frequency) with a 46 tin electrode cap referenced to linked ears. The electrodes were disposed according to an augmented 10–20 system (Table 1) and electrode impedance was kept lower than 5 kΩ. The position of the electrodes and landmarks was digitized.

Electrooculogram (0.1–60 Hz bandpass; 256 Hz sampling frequency) and surface electromyographic activity of bilateral extensor digitorum muscles (1–60 Hz bandpass; 256 Hz sampling frequency) were also collected. Electrooculogram monitored blinking or eye movements, whereas electromyogram monitored the voluntary movements as well as involuntary mirror movements and muscle activations.

2.4. Off-line preliminary data analysis

Two experimenters rejected EEG single trials associated with wrong behavioral performance, mirror or involuntary finger movements (less than 5%), slight muscle activation, and instrumental artifacts.

The spatial resolution of the artifact-free EEG data was enhanced by surface Laplacian estimation (regularized 3-D spline function [23,24]). The surface Laplacian estimation acts as a spatial filter that reduces head volume conductor effects and annuls electrode reference influence [23,25].

The single trial analysis was carefully repeated on the Laplacian-transformed EEG data, to discard the single trials contaminated by residual computational artifacts. In 4 out of 16 subjects (2 females and 2 males) for each group, the number of artifact-free EEG single trials was insufficient (i.e. lower than 20% of the individual data set). Consequently, the EEG data of 12 subjects (5 females and 7 males) for each group were further considered for the final data analysis.

For the young subjects, the mean of the individual artifact-free EEG data was of 82 (±12 S.E.) single trials for the NSTM condition and of 68 (±10 S.E.) single trials for the STM condition. For the elderly subjects, these means were of 63 (±7 S.E.) single trials for the NSTM condition and of 56 (±8 S.E.) single trials for the STM condition (no statistical difference; $F(1, 22) = 1.46$; $P < 0.25$). Motor reaction time after the go stimulus was computed for all artifact-free EEG single trials.

Table 1
List including 46 electrodes (augmented 10–20 system) used for the present experiments

Electrodes
Fp1, Fp2
AF7, AFz, AF8
F7, F5, F3, F1, Fz, F2, F4, F6, F8
FC3, FCZ, FC4
T7, C5, C3, C1, Cz, C2, C4, C6, T8
TP7, CP3, CPz, CP4, TP8
P7, P5, P3, P1, Pz, P2, P4, P6, P8
PO7, POz, PO8
O1, Oz, O2

The position of the labels in the list roughly represents the position of the corresponding electrodes over the scalp. Of note, hyphen between two electrode labels indicates that the electrode is located halfway the two labeled electrodes.

2.5. Determination of individual theta and alpha bands

The power spectrum analysis was based on a standard FFT approach using Welch technique and Hanning windowing function. For the determination of the individual theta and alpha bands, an anchor frequency was selected according to literature guidelines; it is called the individual alpha frequency (IAF) peak [26–28]. Practically, the IAF was defined as the frequency showing the higher power density in the 6–12 Hz spectrum. With reference to the IAF, the frequency bands of interest were as follows: theta as IAF − 6 to IAF − 4 Hz, alpha 1 as IAF − 4 Hz to IAF − 2 Hz, alpha 2 as IAF − 2 Hz to IAF, and alpha 3 as IAF to IAF + 2 Hz (Fig. 2).

2.6. Computation of event-related desynchronization/synchronization (ERD/ERS)

To quantify the event-related changes of EEG power, we used the popular procedure called event-related desynchronization/synchronization (ERD/ERS; [29–31]). The ERD/ERS of the individual theta, alpha 1, alpha 2 and alpha 3 bands was computed as follows. Laplacian EEG time se-

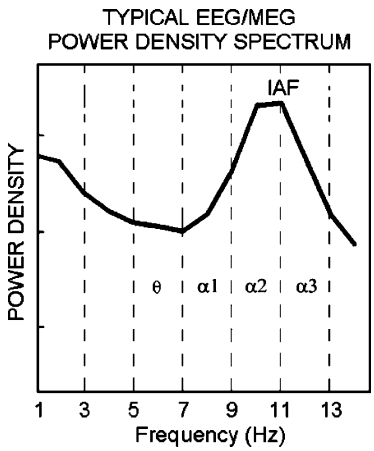

Fig. 2. Model of a typical frequency spectrum computed from EEG (or magnetoencephalographic, MEG) data. Frequency bands of interest were theta, alpha 1, alpha 2 and alpha 3, which were computed according to a well-known procedure based on the detection of IAF peak (see Section 2 for further explanations).

ries were bandpassed (Bartlett function), squared, averaged across 120-ms periods (to 8 samples/s), and averaged across all single trials. The ERD/ERS was defined as the percentage decrement/increment of the power density at the "event" compared to a "pre-event" baseline (from −2 to −1 s).

A spline interpolating function [32] determined the individual ERD/ERS values at theoretical 46 sites of augmented 10–20 system. These electrodes were displaced over a 3-D head model approximating each individual head model. This template model was constructed based on the magnetic resonance data of 152 subjects, digitized at Brain Imaging Center of the Montreal Neurological Institute (SPM96).

2.7. Measurement of ERD/ERS latency and amplitude

The latency of the ERD/ERS peaks was measured for the theta, alpha 1, alpha 2, and alpha 3 with respect to the zerotime, taken as the onset of the cue stimulus. The ERD and ERS peaks were independently recognized by two experimenters within frontal and parietal regions of interest (ROIs). These ROIs included (i) F5, F3 and F1 electrodes for the left prefrontal region or FL, (ii) F6, F4 and F2 electrodes for the right prefrontal region or FR, (iii) C3 and C1 for the left central region or CL, (iv) C4 and C2 for the right central regions or CR, (v) P5, P3 and P1 electrodes for the left posterior parietal region or PL, and (vi) P6, P4 and P2 electrodes for the right posterior parietal region or PR.

The ERD/ERS amplitude was automatically measured for each experimental condition at each of the 46 electrodes. The ROI having the maximal ERD/ERS values was considered as a reference for the latency of the topographical mapping.

2.8. Statistical analysis

Statistical comparisons were performed by ANOVA for repeated measures. Mauchley's test evaluated the sphericity assumption and the correction of the degrees of freedom was made by Greenhouse-Geisser procedure. Duncan test was used for post hoc comparisons ($P < 0.05$).

The ANOVA dependent variables for the evaluation of the behavior were the percent of correct responses and the type of errors. For the percent of correct responses, the factors were Group (N young, N old) and Condition (NSTM, STM). For the errors, the factors were Group (N young, N old), Condition (NSTM, STM) and Error type (Wrong responses, Anticipated response, Delayed response). For the movement reaction time, the ANOVA design comprised the factors Group (N young, N old) and Condition (NSTM, STM).

For the evaluation of the ERD/ERS latency, the ANOVA analysis used the factors Group (N young, N old), Condition (NSTM, STM), and Time (peaks).

For the evaluation of the ERD/ERS amplitude, the ERD/ERS values at the electrodes belonging to the same ROI were averaged. The mean ERD/ERS value served as an input for two ANOVA analyses for repeated measures. The ANOVA for the theta band included the factors Group (N young, N old), Condition (STM, STM), ROI (FL, FR, CL, CR, PL, PR), and Time period (peaks), while the ANOVA for the alpha bands included the factors Group (N young, N old), Condition (NSTM, STM), Band (Alpha 1, Alpha 2, Alpha 3), ROI (FL, FR, CL, CR, PL, PR), and Time period (peaks). The percent of the correct responses was used as covariate, to exclude that a different percentage of the correct responses could influence the ERD/ERS results.

3. Results

3.1. Behavioral results

The NSTM and STM tasks were performed with a high amount of correct responses (>95%). ANOVA analysis showed a main statistical effect for Group ($F(1, 22) = 5.37$; MSe = 10.91; $P < 0.03$) indicating that the young subjects (NSTM, 97.5 ± 0.7% S.E.; STM, 97.1 ± 0.3% S.E.) performed better than the elderly subjects (NSTM,

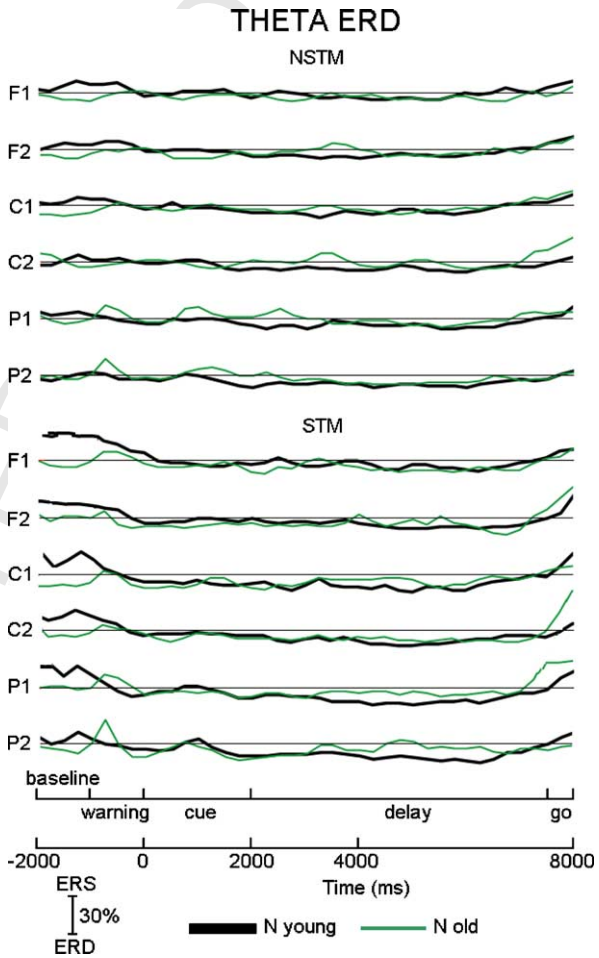

Fig. 3. The grand average waveforms of the theta ERD during the NSTM and STM conditions in the young (N young) and elderly (N old) subjects. These waveforms refer to representative frontal, central and parietal electrode sites.

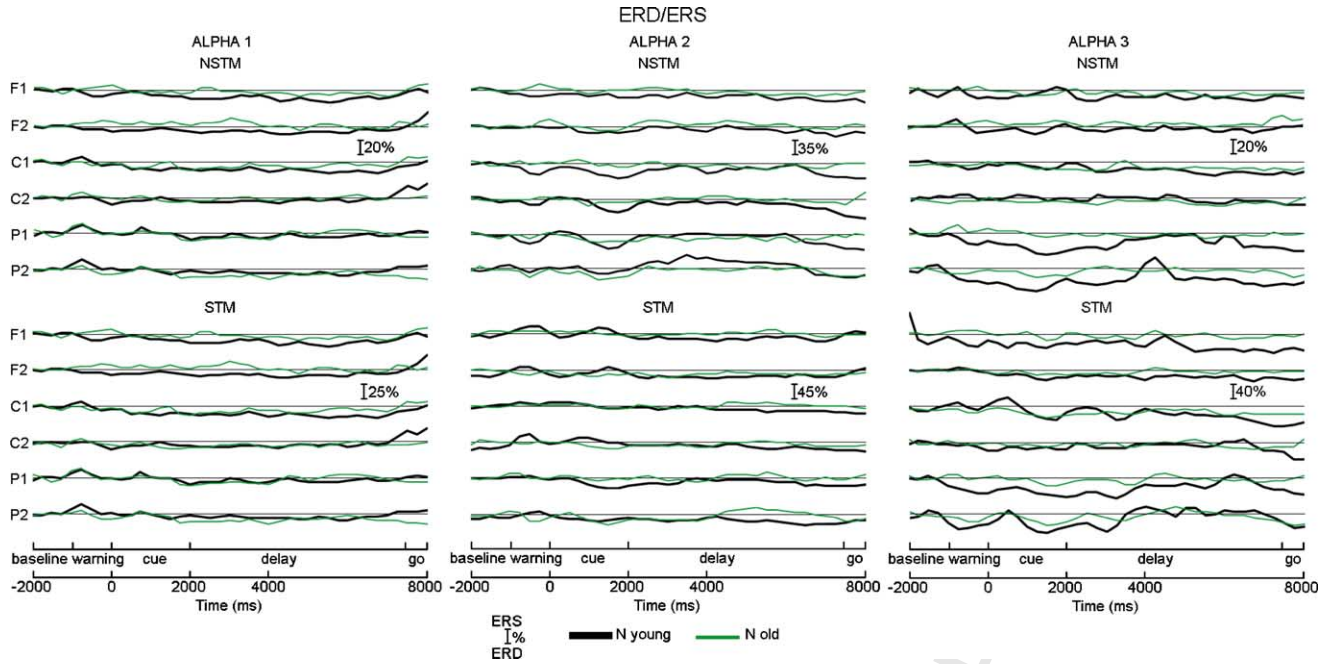

Fig. 4. The grand average waveforms of the alpha 1, alpha 2 and alpha 3 ERD/ERS during the NSTM and STM conditions. These waveforms refer to representative frontal, central and parietal electrode sites in the young (N young) and elderly (N old) subjects.

95.2 ± 0.7% S.E.; STM, 95.7 ± 0.9% S.E.). The ANOVA analysis also pointed to a statistical interaction ($F(2, 44) = 10.96$; MSe = 2.22; $P < 0.0001$) among the factors Group (N young, N old), Condition (NSTM, STM) and Error Type (Wrong responses, Anticipated response, Delayed response). During the NSTM condition, the elderly subjects performed more anticipated responses than the young subjects did ($P < 0.005$). Furthermore, they performed more delayed responses than the young subjects did during the STM condition ($P < 0.0005$).

The ANOVA analysis of the reaction time showed neither a main statistical effect for Group ($P = 0.08$) nor a statistical interaction between the factors Group and Condition ($P = 0.45$). On the contrary, the ANOVA results pointed to a main statistical effect for Condition ($F(1, 22) = 7.67$; $P = 0.01$). In both groups, the reaction time was longer for the STM (547–650 ms) than NSTM (521–604 ms) condition. Of note, there was no difference in reaction time between groups even with the statistical analysis performed in the NSTM and STM considered separately ($P = 0.07$ and 0.09, respectively).

3.2. Temporal evolution of ERD/"ERS" peaks

Figs. 3 and 4 show the group ERD/ERS waveforms of the theta, alpha 1, alpha 2, and alpha 3 during the NSTM and STM conditions for the two groups. These waveforms refer to representative frontal, central, and parietal electrodes.

Table 2
Mean latency (±S.E.) of theta, alpha 1, alpha 2, and alpha 3 event-ERD/ERS peaks

	T1		T2	
	N young, mean (±S.E.)	N old, mean (±S.E.)	N young, mean (±S.E.)	N old, mean (±S.E.)
NSTM				
Theta	4477 (±280)	4166 (±233)	–	–
Alpha 1	2292 (±101)	2437 (±172)	4396 (±198)	3792 (±224)
Alpha 2	2479 (±219)	2229 (±117)	4145 (±264)	4000 (±306)
Alpha 3	2562 (±148)	2500 (±190)	4708 (±153)	3750 (±185)
STM				
Theta	4613 (±236)	4208 (±212)	–	–
Alpha 1	2958 (±252)	2521 (±161)	4771 (±239)	3770 (±249)
Alpha 2	3042 (±144)	3000 (±204)	4729 (±170)	4700 (±97)
Alpha 3	2812 (±180)	3167 (±227)	4500 (±169)	4687 (±88)

These peaks refer to both STM and NSTM conditions for the young (N young) and elderly (N old) subjects. Zerotime indicates the onset of the visual cue stimulus (i.e. two vertical bars).

Substantial alpha and theta ERS values were observed during the warning and cue periods, as a possible effect of the visual evoked potentials. During the period of interest (delay period), the theta waveforms showed a long lasting ERD having maximal amplitude at parietal electrodes. On the other hand, the alpha ERD/ERS waveforms disclosed an ERD peak (T1) followed by a reduced ERD or a true ERS peak (T2). For sake of brevity, we called "ERS" peaks both reduced ERD and true ERS. Both theta and alpha ERD values were maximal during the delay period of the STM condition.

Table 2 reports the mean (±S.E.) latency of the theta and alpha ERD/ERS during the delay period. The only statistical difference was that the alpha ERD/ERS peak was later for the young than elderly subjects (main effect Group, $F(1, 22) = 5.14$; $P < 0.03$).

3.3. Spatial distribution of ERD/"ERS" peaks

Figs. 5 and 6 illustrate the topographical maps of the theta and alpha ERD/"ERS" peaks during the delay period. The theta ERD peak was widely distributed over the scalp, the amplitude being stronger in the young than elderly subjects. On the other hand, the alpha ERD (time 1, T1) was maximum in bilateral central and parietal areas in both groups. This central-parietal alpha ERD was stronger in young than elderly subjects. Topographically, it was preponderant on the left hemisphere in young subjects and more bilaterally represented in elderly subjects. Furthermore, a frontal alpha ERD was recognized especially in the young subjects. Afterwards (time 2, T2), the ERD values reduced over the whole scalp in both groups. Finally, the alpha central-parietal "ERS" (time 2, T2) was stronger in the elderly than young subjects.

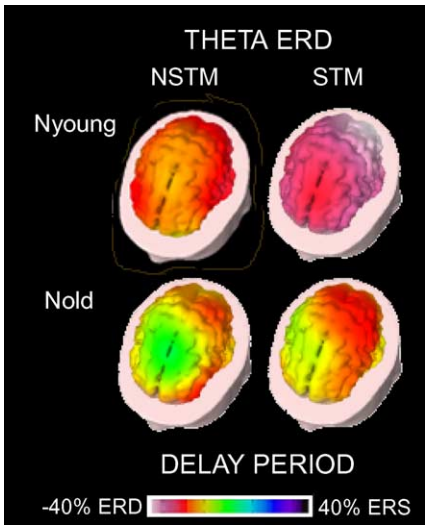

Fig. 5. Three-dimensional color maps of the theta ERD peak during the delay period of the NSTM and the STM conditions in the young (N young) and elderly (N old) subjects. The data refer to those illustrated in Fig. 3. Color scale: maximum ERD and ERS are coded in white and violet, respectively. The maximal (%) value of the ERD/ERS is reported.

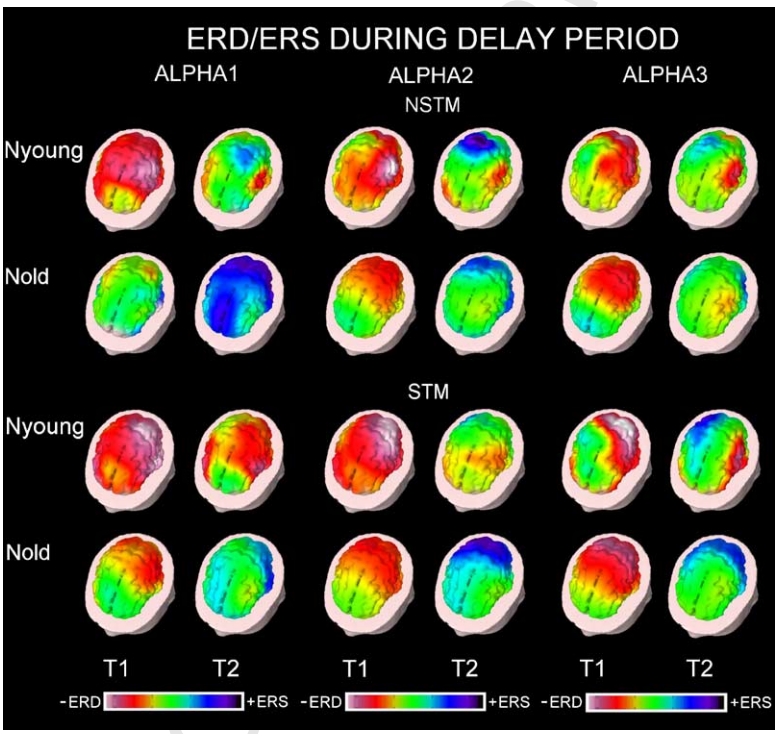

Fig. 6. Three-dimensional color maps of group alpha 1, alpha 2 and alpha 3 ERD peak (T1) and ERS peak (T2) during the delay period during the NSTM and STM conditions in the young (N young) and elderly (N old) subjects. The data refer to those illustrated in Fig. 4 and the color scale is as in Fig. 5. The maximal ERD/ERS values were ±36% for the alpha 1, ±45% for the alpha 2, and ±42% for the alpha 3.

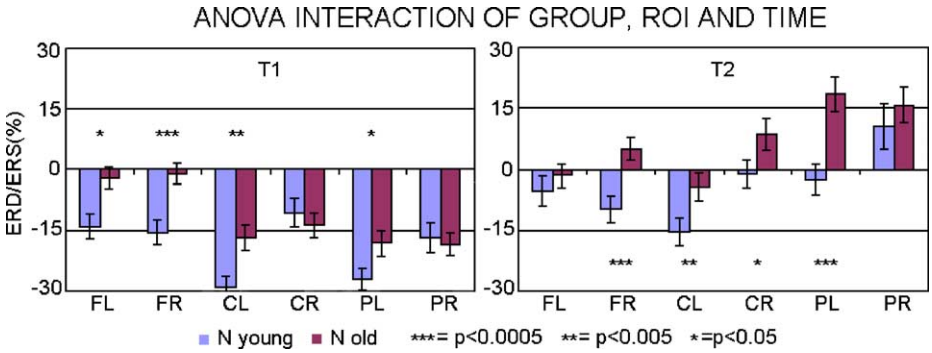

Fig. 7. Means across subjects (±S.E.) of the ERD/ERS amplitude as provided by the ANOVA design. In particular, these means refer to a statistical interaction among the factors Group (N young, N old), Region of interest (left frontal, right frontal, left central, right central, left parietal, right parietal), and Time period (ERD peak or T1, "ERS" peak or T2). The results of Duncan post hoc testing are indicated by asterisks.

3.4. Statistical analysis of ERD/"ERS"

The first ANCOVA analysis (percentage of correct responses as a covariate) pointed to a stronger theta ERD peak (delay period) in the young than elderly subjects (main effect Group, $F(1, 20) = 5.75$; MSe = 1500; $P < 0.03$).

The second ANCOVA analysis (percentage of correct responses as a covariate) for the alpha ERD/"ERS" peaks (delay period) showed a statistical interaction ($F(5, 110) = 2.23$; MSe = 424; $P < 0.05$) among the factors Group (N young, N old), ROI (FL, FR, CR, CL, PL, PR) and Time (T1 at ERD peak, T2 at "ERS" peak). Fig. 7 illustrates the means (±S.E.) of the ERD/"ERS" representing these statistical results. Duncan post hoc testing of this interaction indicated that the ERD peak (T1) was stronger in the young than elderly subjects in left frontal ($P < 0.02$), right frontal ($P < 0.0003$), left central ($P < 0.002$), and left parietal ($P < 0.02$). Instead, the "ERS" peak (T2) was stronger in the elderly than young subjects in right frontal ($P < 0.0002$), left central ($P < 0.006$), right central ($P < 0.02$) and left parietal ($P < 0.00002$) areas. Concerning the hemispherical alpha ERD asymmetry shown in Fig. 6, young subjects presented an alpha ERD peak (T1) stronger in left than right central area ($P < 0.0001$) and in left than right parietal area ($P < 0.006$). On the contrary, the alpha ERD peak (T1) showed no statistical significant difference between left and right central-parietal areas in the elderly subjects.

The second ANCOVA analysis also pointed to a statistical interaction ($F(2, 44) = 3.95$; MSe = 688; $P < 0.025$) among the factors Condition (NSTM, STM), Band (Alpha 1, Alpha 2, Alpha 3), and Time (T1 or ERD peak, T2 or ERS peak). Duncan post hoc indicated that, regardless the subject group, the ERD peak (T1) was stronger during the STM than NSTM condition at alpha 2 ($P < 0.02$) and alpha 3 ($P < 0.05$). Finally, the amplitude of the ERD values at "ERS" peak (T2) was stronger during the STM than NSTM condition at alpha 1 ($P < 0.002$).

As a control, two ANOVA analyses demonstrated that the above findings were not due to a different baseline band power of the theta and alpha bands.

4. Discussion

4.1. Methodological remarks

Here young and elderly adults were given very simple variants of the delayed reaction time task in which only one bit of information had to be retained for few seconds. The rationale for a so simple cognitive demand is that the neurophysiological study in normal or pathological aging must be based on short and simple paradigms, in order to avoid fatigue/distraction and to maximize the correct responses. Indeed, several trials with correct performances are necessary for an acceptable signal-to-noise ratio of the neurophysiological signal.

In the present study, brain rhythms were investigated by the topographical mapping of the theta and alpha ERD/ERS. The procedure required no computational assumption such as the number of equivalent dipoles or regularization parameters [33] and was successfully applied in prior investigations [7,10,34–39]. As a limitation, ERD/ERS sources must be inferred with caution based on the topographical mapping. For example, surface Laplacian maxima could not fit the corresponding tangential cortical sources [23,32]. Here we accounted for such a limitation considering wide scalp frontal and parietal regions of interest. The Laplacian estimates at these regions could be roughly ascribed to underlying prefrontal and posterior parietal areas.

Here the determination of the individual theta and alpha bands followed the influential guidelines by Klimesch's group [26–28]. That approach has provided a body of evidence that the analysis of individual EEG frequency bands can disclose invaluable information on brain rhythmicity beyond standard definition of theta at 4–7 Hz and alpha at 8–12 Hz [27,40,41].

The present experimental design did not include any experimental manipulation to dissociate (i) visuo-spatial versus linguistic features of the cue stimulus [42,43], (ii) the retention process versus the selection of the memorized item for the motor response [44,45], and (iii) the effects of the different visual stimulations during the delay periods of the STM

(blank screen) versus NSTM (cue stimulus on the screen) conditions [34].

4.2. Normal aging affected behavioral performances

Young and elderly subjects performed the two delayed choice reaction time tasks with more than 95% of correct performances. A so high percentage is ideal for the study of brain rhythms, which requires a lot of EEG epochs associated with correct performances. Therefore, the present tasks could be used for neuroimaging cognitive studies in mild dementia.

Despite the globally good rate of correct responses, the two tasks were performed significantly better by the young (97.5%) than elderly (95.5%) subjects. In addition, the elderly subjects performed significantly more anticipated responses during the NSTM condition (as impulsive behavior) and more delayed responses during the STM condition (as a slowing of decisional and visuo-motor processes). This fits the known decline of correct cognitive performances across normal aging [7,46–50].

In this study, the normal aging did not affect motor reaction time, possibly due to the extreme task simplicity. In previous studies, more complex cognitive tasks using "match-to-sample" and "n-back" paradigms have unveiled a general slowing of cognitive processing and reaction time in elderly subjects, possibly due to the fact that decisional and visuo-motor processes were concentrated after the go stimuli [7,51].

4.3. Normal aging affected theta ERD

A widely distributed theta ERD was observed during the delay period of the two conditions (STM and NSTM). Notably, its amplitude was greater in the young than elderly subjects. Noteworthy, this theta ERD difference occurred regardless the slightly different behavioral performances between the two groups (i.e. better in the young than elderly subjects), which was used as a covariate in the statistical evaluation of the theta ERD. These results extend prior EEG evidence in young adults engaged in delayed tasks with a low memory load [20]. Furthermore, the results complement previous EEG evidence showing enlarged theta rhythms during "n-back" tasks with heavy memory loads [7,9,10]. Notably, the increment of the cortical theta is generally associated with the involvement of reciprocal cortico-(para)hippocampal loops during mental effort and memory workload [20,52–56]. In the same line, a reasonable view is that the decrement of the cortical theta reflects an inhibitory information processing throughout these loops. According to this view, the normal aging would be related to a less efficient inhibition of hippocampal-cortical circuits during simple cognitive tasks. An intriguing speculation is that cortical theta oscillations characterize the selective memorization processes as induced by delayed reaction time [20] respect to the massive memorization processes as induced by "n-back" tasks [7,9,10]. This speculation merits to be experimentally tested manipulating the amount and type of STM paradigms.

4.4. Normal aging affected alpha ERD

During the early phase of the delay period, a bilateral alpha ERD was recognized in the two groups. The central-parietal alpha ERD was stronger in young than elderly subjects, regardless the STM or NSTM condition and the percentage of the correct performances used as a covariate in the statistical evaluation of the alpha ERD. Notably, the frontal alpha ERD was marked in young but not in elderly subjects. Indeed, the elderly subjects would rely mainly on visuo-spatial and sensorimotor abilities of central-parietal areas. Instead, the young adults would allocate more computational resources as revealed by the alpha ERD amplitude, especially in terms of the executive/control abilities of prefrontal areas. Even with simple cognitive demands, this could ensure to young subjects more correct responses, less "impulsive" responses, less delayed responses, and more prolonged cortical processing during the delay period (prolonged alpha ERD). The present results agree with previous evidence demonstrating less intense cortical responses to cognitive demands with age [57–61]. In particular, it has been repeatedly shown that alpha ERD topography is larger in young than elderly subjects involved in cognitive tasks [62,63]. On the other hand, the present results complement previous evidence showing an increase of the frontal alpha ERD in elderly subjects engaged in "n-back" tasks, which are much more demanding than the current ones [7].

During the late phase of the delay period, the central-parietal alpha ERD recovered much more in elderly than young subjects. This substantiates the explanation of the early alpha ERD, namely a more intense cortical information processing in young than elderly subjects. However, it should be made clear that the physiological mechanisms at the basis of that recovery is unclear based on the present data. Indeed, the second phase of the delay period was characterized by absolute ERS values or just a reduction of the ERD not reaching absolute ERS values. Therefore, it is not possible here to explain the alpha recovery in terms of active inhibition or removal of excitatory drive associated with GABA-ergic and glutamate-ergic processes, respectively. This issue should be addressed by future studies combining EEG data with those of paired transcranial magnetic stimulations according to a previous fruitful methodological approach [64–68].

The present alpha ERD could not dissociate the two main processes occurring during the delay period, namely the retention of the cue stimulus and the motor preparation [44]. Therefore, the influence of the motor preparation on the present results is an open issue to be addressed in future studies. At the present stage of research, we have reasons against and in favour of an important role of the motor processes

in the present results. "Against" reasons are the following. First of all, the motor preparation was paired for the NSTM and STM conditions, in which the time intervals, go stimulus, and motor demands were identical. Secondly, the delay period between the cue and go stimuli varied trial-by-trial (3.5–5.5 s), to discourage a pre-stimulus motor preparation. Thirdly, the alpha ERD did not progressively increase during the delay period as expected for a pure motor process. Indeed, the typical trend of the motor preparation is a progressive increase of the alpha ERD up to the movement execution [11,69]. On the other hand, the reason in favour of a role of the "motor process" is based on the strong alpha ERD in the central regions overlying sensorimotor areas for both young and elderly subjects. In particular, the central-parietal alpha ERD was prominent in the hemisphere contralateral to the movement in young but not in elderly subjects. This result is consistent with previous evidence of a less selective involvement of sensorimotor cortical networks with age [37,64,70,71].

In both groups, there was a stronger (6–12 Hz) and prolonged (6–8 Hz) alpha ERD during the STM than NSTM condition. According to the current view on brain rhythmicity, the low-band (6–10 Hz) and high-band (10–12 Hz) alpha ERD would indicate the prevalence of attentional and task-specific retention processes, respectively [11,27]. These findings integrate previous reports on the different modulation of low- and high-band alpha in young subjects, as a function of attentional cues, memory load, and intellectual ability [7,9–11,27,34].

4.5. Delayed choice reaction time and "working memory"

An open issue of the present study is whether the delayed choice reaction time paradigm can test "working memory" functions typically probed by "delayed match-to-sample" and "n-back" paradigms. Human "working memory" functions encompass (i) selective attention to current episodes, (ii) storage and rehearsal of visuo-spatial and phonological information, and (iii) active "executive" processes such as information manipulation and motor selection/inhibition [72,73]. During the delayed choice reaction time task, subjects retain one out of two possible responses ("left" or "right" side) and operate mild "executive" processes such as to refrain from impulse acts and to avoid proactive interference effects across trials. Of note, a recent EEG study considered the delayed reaction time task as probing "working memory" [20].

5. Conclusions

This high-resolution EEG study evaluated fronto-parietal cognitive processing along normal aging using two very simple delayed choice reaction time tasks (STM and NSTM). Correct performances were higher than 95% in both groups and tasks, although they were significantly better in young than elderly subjects ($P < 0.03$). During the delay period, theta and alpha ERD accompanying correct responses were recognized in the two groups, the alpha ERD being stronger and prolonged during the memory than non-memory task. On the other hand, the fronto-parietal theta and parietal alpha ERD were stronger in young than elderly subjects during both tasks. Notably, the frontal alpha ERD was negligible in elderly subjects. On the whole, the present simple tasks unveiled in elderly subjects (i) a weaker involvement of (para)hippocampal-cortical circuits as revealed by theta ERD and (ii) a weaker involvement of "executive" thalamo-cortical circuits as revealed by frontal alpha ERD. These effects might worsen behavioral performances to the simple cognitive tasks with age. The present protocol is promising for the neuroimaging study of pathological aging.

Acknowledgements

The authors thank Prof. Fabrizio Eusebi, Chairman of the Biophysics Group of Interest of Rome I University, for his continuous support. The research was granted by Telethon Onlus Foundation ("Progetto E.C0985") and Fatebenefratelli Association for Research (AfaR).

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