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Running Head: Age and the motor system

Age effects on the asymmetry of the motor system: evidence from cortical oscillatory activity

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Abstract

Functional hemispheric asymmetry can be lost with aging. In this electroencephalographic study, we assessed hemispheric asymmetries in regulating motor responses by analyzing oscillatory brain activity during a go/nogo task in younger and older right-handed participants. Three conditions were embedded in the task: go, high-conflict and low-conflict nogo. The hand used to respond to go stimuli was varied block-wise. Independently of the go/nogo conditions and responding hand, young participants showed asymmetric desynchronizations in the mu (10 Hz) and beta (18-22 Hz) frequency bands that was stronger in the scalp sensorimotor region contralateral to the hand used for the go responses, while older adults showed a more symmetric pattern of desynchronization. These findings indicate that a loss of hemispheric asymmetry is a hallmark of the aging motor system, consistent with a decline of inter-hemispheric motor inhibition in normal aging.

Keywords: Time-frequency Analysis, Event-Related Desynchronization, Normal Aging, Motor System, Hemispheric Asymmetry, Go/nogo.

A motor response is usually the main dependent variable in studies investigating cognitive decline in aging. It is therefore critical to understand how the motor function changes with age, in order to dissociate motor dysfunctions from other types of cognitive impairment. Impaired motor performance is indeed a typical finding in studies on normal aging (Inuggi et al., in press; Mattay et al., 2002; Smith et al., 1999; Vallesi, McIntosh & Stuss, 2009b; Welford, 1988). A better understanding of the chances in the motor system may provide some hint on the mechanisms underlying this decline.

In healthy young adults, neural activity in the ipsilateral primary motor cortex (M1) is typically inhibited by the contralateral M1 during unimanual movements, especially during movements of the dominant hand, as assessed with Transcranial Magnetic Stimulation (TMS) (Ghacibeh et al., 2007; Leocani, Cohen, Wassermann, Ikoma, & Hallett, 2000). This pattern is progressively attenuated with age (Talelli, Waddingham, Ewas, Rothwell, & Ward, 2008b), as also reflected in functional imaging studies by less ipsilateral deactivation with advancing age (Naccarato et al., 2006; Ward & Frackowiak, 2003; Ward, Swayne, & Newton, 2008).

Functional reorganization of the central motor networks with aging (Kido, Tanaka, & Stein, 2004; Minati, Grisoli, & Bruzzone, 2007; Ward & Frackowiak, 2003) can lead to a more extensive, and less selective, recruitment of neural populations (Inuggi et al., in press). A more symmetric pattern of motor activation for unimanual movements with age could be due to an enhanced local connectivity within and between the primary motor cortices, secondary to an age-related dysfunction in the inhibitory circuits in the aging motor cortex (Peinemann, Lehner, Conrad, & Siebner, 2001; see also Talelli, Ewas, Waddingham, Rothwell, & Ward, 2008a). However, these studies only tested movements with the dominant hand.

An alternative hypothesis is that increased local connectivity between the primary motor cortices (leading to more symmetric activation patterns) may compensate for a decreased long-range functional connectivity within cortico-striatal and cortico-cerebellar (Taniwaki et al., 2007) or cortico-cortical loops (Wu et al., 2007) in the aging motor system.

The aim of the present study is to contribute to this debate by investigating age-related differences in cortical oscillatory rhythms over time (event-related spectral perturbations) recorded by electroencephalography (EEG). In healthy young adults performing pre-cued movements, event-related desynchronizations (ERDs) in the mu (~10 Hz) and beta (~20 Hz) frequency bands (Pfurtscheller, 1977; Pfurtscheller, 1981) initially occur contralaterally to the hand to be moved and become bilateral towards the movement execution. The most likely neural source of these frequency components is in the hand primary motor area, slightly more anterior for beta than for mu rhythm (Pfurtscheller, Pregenzer, Neuper, 1994). Pre-movement ERD is considered a correlate of motor cortical preparatory activity (Pfurtscheller & Berghold, 1989).

ERDs over sensorimotor areas occur not only for stimuli requiring a response, but also for trials that require a suppression of a motor response (nogo trials) during precued (Babiloni et al., 2004; Filipovic, Jahanshahi, & Rothwell, 2001) and uncued (Leocani, Toro, Zhuang, Gerloff, & Hallett, 2001) go/nogo tasks, although the former study only reported alpha (mu) ERDs and the latter beta ERDs. The fact that ERDs for nogo stimuli last less than those for go stimuli in cued paradigms (Leocani et al., 2001) suggests that, even in nogo trials, they indicate partial motor activation rather than response suppression. Extrapolating from the above reviewed evidence that older adults have a less efficient inter-hemispheric motor inhibition, it can be predicted that they shall show a more symmetric pattern of ERDs over left and right motor scalp regions than younger controls during both go and nogo trials. We advanced previous research by exploring the following aspects:

(i) By manipulating the responding hand block-wise, we tested whether a lack of motor asymmetry generally occurs with age for movements with both hands (see Ward & Frackowiak, 2003, for fMRI evidence), or if it is more prominent for the dominant (right) hand. Age-related motor asymmetries in ERDs have been assessed before using the dominant hand only (e.g., Talelli et al., 2008a);

(ii) We tested whether possible age-related differences can be generalized to conditions in which no overt motor execution occurs (nogo trials).

(iii) Two types of nogo trials were used with different degrees of cognitive interference (high, low), in order to explore possible effects of cognitive demands on age-related changes in ERDs, since it has been shown that demanding task conditions are associated with neural over-recruitment in aging (e.g., Vallesi, McIntosh, & Stuss, in press).

Method

Participants

Sixteen healthy older (8 females; mean age: 72 years, range: 60-81) and 22 younger (10 females; mean age: 26 years, range: 19-36) volunteers gave their informed consent prior to their inclusion in the study. The participants had normal or corrected-to-normal vision and reported no history of neurological or psychiatric disorders. The two groups were matched for handedness, since all were right-handed, with the average Edinburgh Handedness Inventory score (Oldfield, 1971) being 92 (range: 70-100) and 87 (range: 40-100), for the older and younger groups, respectively. Inclusion criteria for the older group included the absence of dementia, as assessed with the Mini-Mental-State-Examination (threshold score > 27). All subjects received 20 dollars for participating in the experimental session. The study, which has been conducted according to the 1964 Declaration of Helsinki, was previously approved by the Baycrest Research Ethics Board.

Material and Task

Participants were tested individually in a sound-attenuated semi-dark room following the montage of a 64-channel electroencephalographic cap. Visual stimuli were presented through a computer display at a distance of ~60 cm.

The task was a modified version of that used in our previous works (Vallesi, Stuss, McIntosh, & Picton, 2009c; Vallesi, McIntosh, Alexander, & Stuss, 2009a). Here, the hand used for go responses was varied between blocks instead of being the dominant hand only. Go/nogo stimuli were letters and numbers coloured in blue or red (50% each). For half of the subjects, go stimuli were “red O” and “blue X”, and nogo stimuli were either “blue O” and “red X” (high-conflict nogo) or red and blue numbers 2 and 3 (low-conflict nogo). The association between colour and go/nogo letters was opposite for the other half of the subjects.

At the beginning of each trial, a go/nogo stimulus was presented for 300 ms. A blank screen followed the stimulus offset for an interval that varied randomly between 2.4 and 4.4 sec. There were 4 blocks of trials. Each block consisted of 80 go (50%), 40 high-conflict nogo (25%) and 40 low-conflict nogo (25%) stimuli. Stimulus types were presented in a random fashion. Participants were instructed to press “B” on a computer keyboard when a go stimulus occurred, and not to respond to nogo stimuli. The right hand was used for the go responses in two consecutive blocks of trials, while the left hand was used in the other two blocks (order counterbalanced across subjects). Speed and accuracy were equally emphasized. Each block was preceded by 6 practice trials (not analysed). The experimental design consisted of a 2 hand (right, left) by 3 go/nogo condition (go, high-conflict nogo, low-conflict nogo) by 2 age (younger, older) design.

Behavioral data analysis

Practice trials, the first trial of each block, trials with go response latencies before 100 ms post-stimulus onset (anticipations) and after 2000 ms post-stimulus onset (delayed responses) were discarded from further analyses. Response times (RTs) to go stimuli were submitted to a 2x2 mixed ANOVA with age as the between subjects factor and responding hand as the within-subject factor. Accuracy data of the two age-groups were compared using non-parametric Kolmogorov-Smirnov tests separately for each hand and each go/nogo category.

Electrophysiological recording and pre-processing

Scalp voltages were recorded using NeuroScan 4.0 and two SynAmps amplifiers. Sixty-four channel ElectroCaps (10/20 system) were used including two pairs of ocular sites on the outer canthi and infra-orbital ridges. Electrode impedance was kept under 5 kΩ. Continuous EEG was digitized (sampling frequency: 250 Hz) through a 0.01–100 Hz band-pass filter.

For each subject, continuous data were off-line re-referenced to an average reference and epoched into -0.5 to 2.1 sec trials (time-locked to the stimulus onset occurring at 0 sec) which were concatenated. An Independent Component Analysis (ICA) was run on the concatenated epochs and eye movements and other major artifacts detected by visual inspection as independent ICA components were removed, as implemented in EEGLAB (Delorme & Makeig, 2004).

Event-related spectral perturbations (ERSP)

ERSP were calculated on artefact-free trials (re-epoched from -0.5 to 1.5 sec) with correct go/nogo responses according to the 6 conditions (2 responding hand x 3 go/nogo type). Since errors were not frequent, we could not analyze ERSP for error trials. ERSP were obtained with EEGLAB (Delorme & Makeig, 2004) by computing the power spectrum over a sliding latency window on each epoch and normalizing each of them by its respective pre-stimulus mean baseline spectra and then performing averaging across data trials. For each epoch, frequencies were estimated from 4 to 50 Hz (with a step of ~1 Hz between consecutive frequencies) using a Morlet wavelet transform (Bertrand et al., 1994; Goupillaud, Grossman & Morlet, 1984). The cycle number increased from 3 at the lowest frequency (4 Hz) to 18.75 at the highest frequency (50 Hz), to obtain a finer frequency resolution at higher frequencies than with other approaches such as the Short-Time Fourier Transform (Delorme & Makeig, 2004). The size of the sliding window was 209 samples (836 ms). Two hundred spectral time-points were generated from 178 to 1178 ms. The average number of trials for go and nogo stimuli was 150 (70–160) and 74 (36–80), respectively, with no difference between the two age groups. Although it is difficult to separate motor-related EEG activity from sensory-related activity due to trial-by-trial RT variability, stimulus-locked averages were used instead of response-locked ones in order to compare both go and nogo stimuli, since the latter did not require movement execution (see Leocani et al., 2001).

For the present purposes, data concerning the mu (centred at 10 Hz) and beta (18-22 Hz) bands recorded from electrodes C3 and C4 are reported, similar to previous studies (Leocani et al., 2001; Pfurtscheller, 1977). These electrodes detect ERSP from the hand sensorimotor regions (Pfurtscheller et al., 1994). To reduce the variability between adjacent sampling points and the number of multiple comparisons, consecutive values were averaged in time-windows of 54 ms (see Leocani et al., 2001). To focus on ERDs, we analysed the 5 time-windows between 162 and 432 ms, that is around the occurrence of mu and beta ERDs (see Figure 2). Mixed ANOVAs with a 2 (age: younger, older) x 3 (condition: go, high-conflict nogo, low-conflict nogo) x 2 (responding hand: left, right) x 2 (electrode: C3, C4) design were conducted for mu and beta ERD, separately for each time-window, with age as a between-subjects variable and the others as within-subject variables. A Bonferroni correction was applied for multiple comparison correction.

To investigate whether the pattern of ERD symmetry was compensatory or detrimental for performance with aging, we used Pearson correlation analyses comparing, for the go trials, RTs and the C3-C4 difference in mu or beta ERDs, for the left and the right hand blocks and for each of the 5 time-windows, separately.

Results

Behavioral results. Table 1 reports RTs and error percentage. Go responses were slower in the older than in the young group [$F(1,36)=5.1$, $p<.05$]. Go responses tended to be slower with the left hand than with the right hand [$F(1,36)=3.2$, $p=.08$]. A lack of a clear right-hand advantage is in line with previous literature on simple, choice and go RTs (Annett & Annett, 1979; Goodin, Aminoff, Ortiz, & Chequer, 1996; Leocani et al., 2001). No interaction was observed between responding hand and age ($p>.26$). False alarms were much more frequent for high-conflict (4.5%) than for low-conflict (0.2%) nogo conditions. Kolmogorov-Smirnov tests for each hand and go/nogo category showed that there was no age difference for accuracy on any experimental condition (for all, $p > .1$).

---Insert Table 1 about here---

ERSPs for the whole computed bandwidth (4-50 Hz) are shown in Figure 1.

---Insert Figure 1 about here---

Mu ERDs. Mu ERDs are displayed in Figure 2. A condition main effect was observed for all the time-windows analyzed [162-432 ms; for all, $Fs(2,72)=38\text{-}80$, Bonferroni corrected $ps<.001$], indicating that mu ERDs were strongest for the go condition and lowest for the low-conflict nogo condition. This effect was followed up with post-hoc Bonferroni corrections, which showed that, apart from a tendency in the comparison between go and high-conflict nogo trials in the 162 ms time-window ($p=.086$), each condition was always significantly different from each other (for all, $ps<.002$). An electrode by hand interaction was significant in the 162-324 time-windows [for all, $Fs(1,36)=8\text{-}18$, corrected $ps<.03$], and a trend in the 324-378 ms time-window (corrected $p=.055$), indicating that ERDs were more pronounced in the electrode contralateral to the responding hand.

Importantly, the age by electrode by hand interaction showed a tendency in the 216-270 ms time-window (corrected $p=.06$) and was significant in the three time-windows between 270 and 432 ms [for all, $Fs(1,36)=12\text{-}16$, corrected $ps<.005$]. This effect indicated that, while the younger group had more pronounced mu ERDs in the electrode contralateral to the side of the go response, the older group had similar ERDs for both electrodes C3 and C4, regardless of the go response side. Importantly, this interaction occurred for all the three conditions, since no interaction with the condition was observed. To follow up this 3-way interaction we run separate 2x2x3 repeated measures ANOVAs for each group with electrode, hand and condition as the repeated measures. For the younger group, the crossover electrode by hand interaction was significant [for each of the three time-windows between 270 and 432 ms: $Fs(1, 21)>18$, $ps<.001$], confirming the asymmetric recruitment of the contralateral motor region according to the responding hand. Conversely, this interaction was not significant for the older group [Fs(1, 15)<1.2, ps>.28].

---*Insert Figure 2 about here*---

Beta ERDs. Beta ERDs are reported in Figure 3. Beta ERD modulations were basically similar to those observed in the mu band. A hand main effect was observed in the ANOVAs on the 162-216 time window [F(1,36)=14, corrected p < .005]. This indicated that beta ERDs were stronger for the left hand blocks in this early time-window. A condition main effect was also observed for all the time-windows analyzed [162-432 ms; for all, Fs(2,72)=60-83, corrected ps<.001], indicating that ERDs were strongest for the go condition and lowest for the low-conflict nogo condition. Bonferroni analyses showed that, apart from the comparison between go and high-conflict nogo in the 162 ms time-window (p=.11), each condition was always significantly different from each other (for all, ps<.001). An electrode by hand interaction was observed in the 162-324 time-windows [for all, Fs(1,36)=9-39, corrected ps<.001], indicating that ERDs were more pronounced in the electrode contralateral to the responding hand.

An age by electrode by hand interaction occurred in the two time-windows between 162 and 270 ms [for both, Fs(1,36)=8-9, corrected ps<.05]. This interaction indicated that, while the younger group showed the cross-over electrode by hand interaction, this interaction was attenuated or absent in the older group. As for the mu rhythm, this interaction occurred for all the three conditions, since no interaction with the condition was observed. This 3-way interaction was followed up by separate 2x2x3 repeated measures ANOVAs for each group with electrode, hand and condition as the repeated measures. For the younger group, the electrode by hand interaction was significant [for each of the two time-windows between 162 and 270 ms: Fs(1, 21)>12.9, ps<.0017]. In opposition, this interaction was not significant for the older group [Fs(1, 15)<3.7, ps>.07].

Finally, an age main effect was obtained in the 324-378 ms time-window [$F(1,36)=9$, corrected $p = .025$], indicating that beta ERDs lasted longer in the older group, a result which fits with the pattern of longer RTs with age.

---*Insert Figure 3 about here*---

Pearson correlations between RT in the go condition and the C3-C4 ERD difference in the mu or beta rhythm for the left and the right hand blocks and for each of the 5 time-windows analyzed were never significant (for all, $p > .1$).

Discussion

The present study shows that normal aging is associated with a symmetric pattern of mu and beta ERDs in the scalp sensorimotor regions during a go/nogo task. This pattern contrasts with that observed in younger adults, who showed more pronounced mu and beta ERDs in the scalp motor region contralateral to the hand associated to the go response, regardless of whether this was the dominant or the non-dominant hand.

ERDs over the scalp motor regions were observed in all the go/nogo conditions, although they were strongest for the go condition and weakest for the low-conflict nogo condition. This finding is compatible with the view that ERDs indicate cortical activation irrespective of whether the intended cognitive process involves the selection or the suppression of a response (Filipovic et al., 2001). However, it is plausible that, given the generally early onset of the ERDs, they indicate a motor pre-activation rather than motor suppression also during nogo trials.

Importantly, the more symmetric pattern of mu and beta ERDs with aging for all conditions suggests that this is a general hallmark of the aging motor system that is independent of the specific motor demands (see Labyt, Cassim, Szurhaj, Bourriez, & Derambure, 2006), since it was associated not only to the execution of a motor response (go stimuli), or to high cognitive demands (high-conflict nogo stimuli), but also to the motor activation/inhibition for stimuli that produce low levels of interference (as demonstrated by performance at ceiling; also see Vallesi et al., 2009a; Vallesi, Hasher & Stuss, in press).

These findings complement and extend previous literature, showing that the ipsilateral M1 is less deactivated during unimanual movements with advancing age (Ward & Frackowiak, 2003; Naccarato et al., 2006; Ward et al., 2008) in conditions where the overt movement should not be executed (nogo). The underlying mechanism for this phenomenon may involve changes in inter-hemispheric connections between the motor cortices, as assessed with TMS (Talelli, et al., 2008a; 2008b). However, these previous studies only tested movements with the dominant hand. The present study extends these results to the non-dominant hand, since it demonstrated a similar symmetric pattern with both hands using a complementary technique such as event-related spectral perturbations.

The present results also corroborate previous studies showing that normal aging is associated with a more widespread bilateral pattern of mu ERDs (Derambure et al., 1993). They also extend the finding of this bilateral pattern with aging to the beta band. Thus, although the two frequency bands probably have partially different functional meanings, with the beta band more closely related to motor control (Kuhlman, 1978) and with more anterior neural sources in the precentral sulcus than the mu-rhythm (Pfurtscheller et al., 1994), similar age effects occur on both of them.

In the present study, ERDs occurred much earlier than go-RTs. This finding is in agreement with the fact that the onset of mu and beta ERDs largely precedes cortico-spinal activation, as assessed with self-paced movements (Chen, Yaseen, Cohen, & Hallett, 1998). It is also possible that, in the present paradigm, stimulus-locked averaging emphasizes the processes linked to the stimulus processing more than the response-related processes (therefore being closer in time with the stimulus rather than with the response). However, this procedure was necessary to compare go conditions that required a response with nogo conditions which did not require a response (i.e., no response-locked averaging was possible).

Another possibility is that a mechanism reflected by the mu and beta ERDs is the initial selection of the relevant motor cortex at least in younger adults soon after the stimulus onset. The potential response side is known a priori in the paradigm adopted here (responding hand varied block-wise), and participants had to decide later whether to execute this response or not according to the nature of the go/nogo stimulus. The preparation and execution of the movement are then delayed until a go/nogo decision is reached, and are not entirely reflected in the stimulus-locked mu/beta ERDs.

In contrast to the asymmetric pattern of motor ERDs in the younger group, older adults pre-activated both motor regions (vs. the contralateral only) and for a longer period of time than younger controls. This symmetric pattern of motor cortex activation can be due to a compensatory mechanism for the progressive loss of cortico-spinal motoneurons with age (Eisen, Entezari-Taher, & Stewart, 1996), or for a decrease of long-range connectivity with other regions of the motor loops (Taniwaki et al., 2007; Wu et al., 2007). However, it is not clear from the present results whether these changes have a compensatory nature. They do not appear to promote better performance with aging, since no correlation between the degree of symmetry in ERDs and speed in go trials was found here (for all, $p > .1$). It seems therefore more likely that this *symmetrization* is due to a loss of inter-hemispheric inhibition (Talelli et al., 2008a). However, further studies using different paradigms and higher sample sizes are necessary to further explore the behavioral consequences of this loss of motor asymmetry.

The symmetric ERDs are in contrast to the lateralized readiness potential (LRP) data reported in a previous study, which showed that older adults prepared a lateralized motor response not only for go stimuli, but also, in contrast to younger controls, for high- and low-conflict nogo stimuli (Vallesi & Stuss, 2010). These data, as well as previous ones (De Jong, Gladwin, & 't Hart, 2006), suggest that the ERDs and the LRP might measure dissociable processes.

In conclusion, the present go/nogo study demonstrates that mu and beta ERDs recorded over the scalp sensorimotor regions become more symmetric with advancing age. This pattern is in line with an inefficient interhemispheric inhibition which produces an age-related loss of hemispheric specialization in the motor cortex.

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Disclosure Statement for Authors

Authors state that there are no actual or potential conflicts of interest.

References

Annett, M. & Annett, J. (1979). Individual differences in right and left reaction time. Br.J Psychol., 70, 393-404.

Babiloni, C., Brancucci, A., Arendt-Nielsen, L., Babiloni, F., Capotosto, P., Carducci, F., Cincotti, F., Romano, L., Chen, A.C., Rossini, P.M. (2004). Alpha event-related desynchronization preceding a go/no-go task: a high-resolution EEG study. Neuropsychology, 18, 719-728.

Bertrand, O., Bohorquez, J., Pemier, J., 1994. Time–frequency digital filtering based on an invertible wavelet transform: an application to evoked potentials. IEEE Trans. Biomed. Eng., 41, 77-88.

Chen, R., Yaseen, Z., Cohen, L. G., & Hallett, M. (1998). Time course of corticospinal excitability in reaction time and self-paced movements. Ann.Neurol., 44, 317-325.

De Jong, R., Gladwin, T. E., & 't Hart, B. M. (2006). Movement-related EEG indices of preparation in task switching and motor control. Brain Res., 1105, 73-82.

Delorme, A. & Makeig, S. (2004). EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. J Neurosci.Methods, 134, 9-21.

Derambure, P., Defebvre, L., Dujardin, K., Bourriez, J. L., Jacquesson, J. M., Destee, A., Guieu, J.D. (1993). Effect of aging on the spatio-temporal pattern of event-related desynchronization during a voluntary movement. Electroencephalogr.Clin Neurophysiol., 89, 197-203.

Eisen, A., Entezari-Taher, M., & Stewart, H. (1996). Cortical projections to spinal motoneurons: changes with aging and amyotrophic lateral sclerosis. Neurology, 46, 1396-1404.

Filipovic, S. R., Jahanshahi, M., & Rothwell, J. C. (2001). Uncoupling of contingent negative variation and alpha band event-related desynchronization in a go/no-go task. Clin Neurophysiol., 112, 1307-1315.

Ghacibeh, G. A., Mirpuri, R., Drago, V., Jeong, Y., Heilman, K. M., & Triggs, W. J. (2007). Ipsilateral motor activation during unimanual and bimanual motor tasks. Clin Neurophysiol., 118, 325-332.

Goodin, D. S., Aminoff, M. J., Ortiz, T. A., & Chequer, R. S. (1996). Response times and handedness in simple reaction-time tasks. Exp.Brain Res., 109, 117-126.

Goupillaud, P., Grossman, A. & Morlet J. (1984). Cycle-Octave and Related Transforms in Seismic Signal Analysis. Geoexploration, 23, 85-102.

Inuggi, A., Amato, N., Magnani, G., Gonzalez-Rosa, J. J., Chieffo, R., Comi, G., & Leocani,L. (in press). Cortical control of unilateral simple movement in healthy aging. Neurobiol.Aging. DOI: 10.1016/j.neurobiolaging.2009.02.020

Kido, A., Tanaka, N., & Stein, R. B. (2004). Spinal excitation and inhibition decrease as humans age. Can.J Physiol Pharmacol., 82, 238-248.

Labyt, E., Cassim, F., Szurhaj, W., Bourriez, J. L., & Derambure, P. (2006). Oscillatory cortical activity related to voluntary muscle relaxation: influence of normal aging. Clin Neurophysiol., 117, 1922-1930.

Leocani, L., Cohen, L. G., Wassermann, E. M., Ikoma, K., & Hallett, M. (2000). Human corticospinal excitability evaluated with transcranial magnetic stimulation during different reaction time paradigms. Brain, 123 (Pt 6), 1161-1173.

Leocani, L., Toro, C., Zhuang, P., Gerloff, C., & Hallett, M. (2001). Event-related desynchronization in reaction time paradigms: a comparison with event-related potentials and corticospinal excitability. Clin Neurophysiol., 112, 923-930.

Mattay, V.S., Fera, F., Tessitore, A., Hariri, A.R., Das, S., Callicott, J.H., Weinberger, D.R.(2002). Neurophysiological correlates of age-related changes in human motor function. Neurology, 58, 630-635.

Minati, L., Grisoli, M., & Bruzzone, M. G. (2007). MR spectroscopy, functional MRI, and diffusion-tensor imaging in the aging brain: a conceptual review. J Geriatr.Psychiatry Neurol., 20, 3-21.

Naccarato, M., Calautti, C., Jones, P. S., Day, D. J., Carpenter, T. A., & Baron, J. C. (2006). Does healthy aging affect the hemispheric activation balance during paced index-to-thumb opposition task? An fMRI study. Neuroimage, 32, 1250-1256.

Oldfield, R. C. (1971). The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia, 9, 97-113.

Peinemann, A., Lehner, C., Conrad, B., & Siebner, H. R. (2001). Age-related decrease in paired-pulse intracortical inhibition in the human primary motor cortex. Neurosci.Lett., 313, 33-36.

Pfurtscheller, G. (1977). Graphical display and statistical evaluation of event-related desynchronization (ERD). Electroencephalogr.Clin Neurophysiol., 43, 757-760.

Pfurtscheller, G. (1981). Central beta rhythm during sensorimotor activities in man. Electroencephalogr.Clin Neurophysiol., 51, 253-264.

Pfurtscheller, G. & Berghold, A. (1989). Patterns of cortical activation during planning of voluntary movement. Electroencephalogr.Clin Neurophysiol., 72, 250-258.

Pfurtscheller, G., Pregenzer, M., Neuper, C., 1994. Visualization of sensorimotor areas involved in preparation for hand movement based on classification of mu and central beta rhythms in single EEG trials in man. Neurosci. Lett. 181, 43-46.

Smith, C.D., Umberger, G.H., Manning, E.L., Slevin, J.T., Wekstein, D.R., Schmitt, F.A., Markesbery, W.R., Zhang, Z., Gerhardt, G.A., Krvscio, R.J., Gash, D.M. (1999). Critical decline in fine motor hand movements in human aging. Neurology, 53, 1458-1461.

Talelli, P., Ewas, A., Waddingham, W., Rothwell, J.C., & Ward, N.S. (2008a). Neural correlates of age-related changes in cortical neurophysiology. Neuroimage, 40, 1772-1781.

Talelli, P., Waddingham, W., Ewas, A., Rothwell, J.C., & Ward, N.S. (2008b). The effect of age on task-related modulation of interhemispheric balance. Exp.Brain Res., 186, 59-66.

Taniwaki, T., Okayama, A., Yoshiura, T., Togao, O., Nakamura, Y., Yamasaki, T., Ogata, K., Shigeto, H., Ohyagi, Y., Kira, J., Tobimatsu, S. (2007). Age-related alterations of the functional interactions within the basal ganglia and cerebellar motor loops in vivo. Neuroimage, 36, 1263-1276.

Vallesi, A., Hasher, L., Stuss, D.T. (in press). Age-related changes in transfer costs: evidence from go/nogo tasks. Psychology and Aging. DOI: 10.1037/a0020300.

Vallesi, A., McIntosh, A. R., Alexander, M. P., & Stuss, D. T. (2009a). FMRI evidence of a functional network setting the criteria for withholding a response. Neuroimage, 45, 537-548.

Vallesi, A., McIntosh, A. R., & Stuss, D. T. (2009b). Temporal preparation in aging: a functional MRI study. Neuropsychologia, 47, 2876-2881.

Vallesi A., McIntosh A.R., Stuss D.T. (in press). Over-recruitment in the aging brain as a function of task demands: evidence for a compensatory view. Journal of Cognitive Neuroscience. DOI: 10.1162/jocn.2010.21490.

Vallesi, A., Stuss, D. T., McIntosh, A. R., & Picton, T. W. (2009c). Age-related differences in processing irrelevant information: evidence from event-related potentials. Neuropsychologia, 47, 577-586.

Vallesi, A., & Stuss D.T. (2010). Excessive sub-threshold motor preparation for non-target stimuli in normal aging. Neuroimage, 50, 1251-1257.

Ward, N. S. & Frackowiak, R. S. (2003). Age-related changes in the neural correlates of motor performance. Brain, 126, 873-888.

Ward, N. S., Swayne, O. B., & Newton, J. M. (2008). Age-dependent changes in the neural correlates of force modulation: an fMRI study. Neurobiol.Aging, 29, 1434-1446.

Welford, A. T. (1988). Reaction time, speed of performance, and age. Ann.N.Y.Acad.Sci., 515, 1-17.

Wu, T., Zang, Y., Wang, L., Long, X., Hallett, M., Chen, Y., Li, K., Chan, P. (2007). Aging influence on functional connectivity of the motor network in the resting state. Neurosci.Lett., 422, 164-168.

Table 1. Above: Average error percentage (and standard error of the mean) for each task condition and age group. Below: Average go-RT in ms (and standard error of the mean) for each responding hand and age group.

	Go		High-Conflict nogo		Low-conflict nogo	
Errors (%)	L	R	L	R	L	R
Younger	2.2 (0.7)	2.6 (0.9)	5.3 (0.8)	4.4 (0.8)	0.3 (0.1)	0.2 (0.1)
Older	1.6 (0.7)	1.9 (0.7)	4.1 (1)	4.3 (0.9)	0.1 (0.1)	0.2 (0.1)

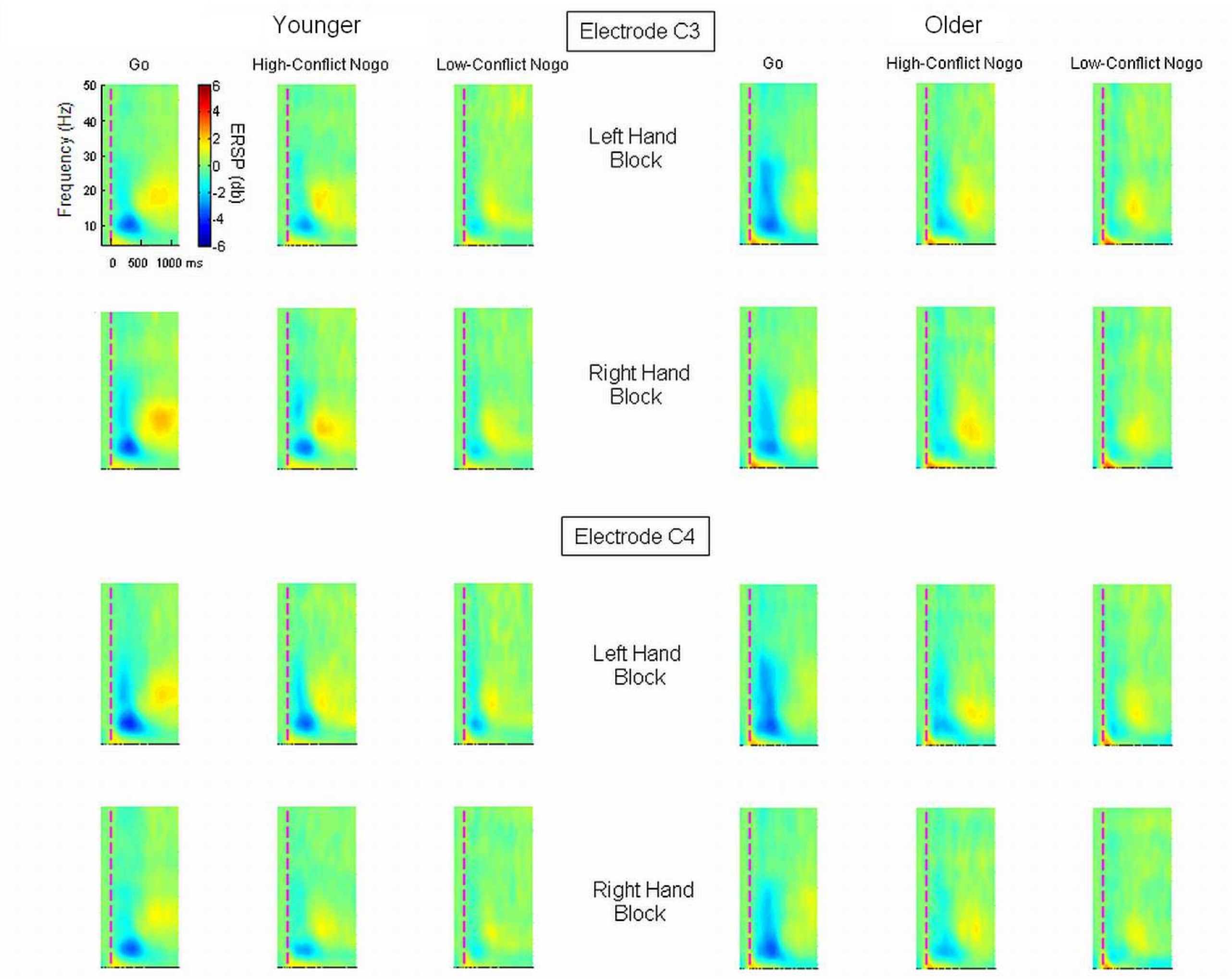
RT (ms)	L	R
Younger	643 (20)	639 (18)
Older	709 (19)	692 (17)

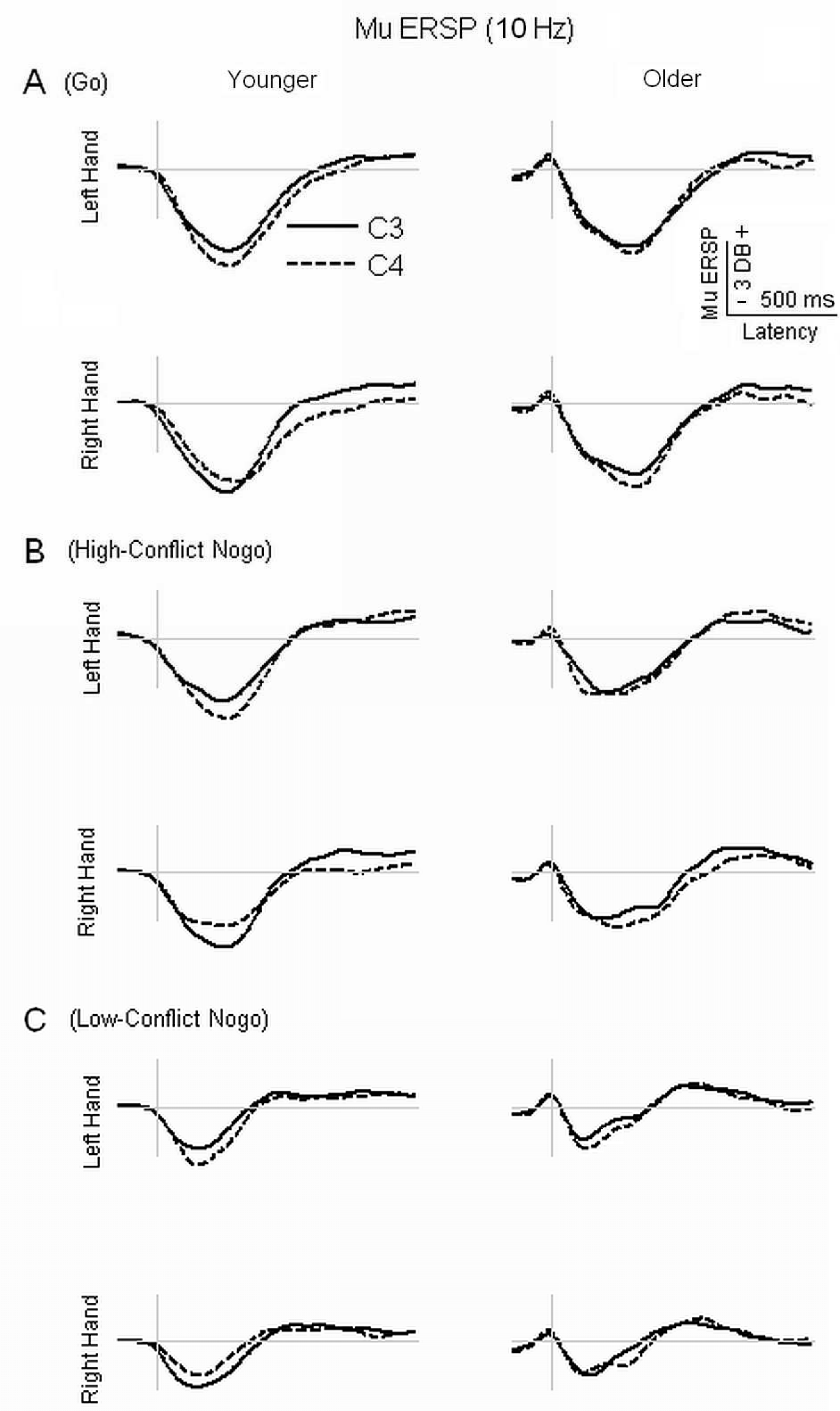
Figure Captions

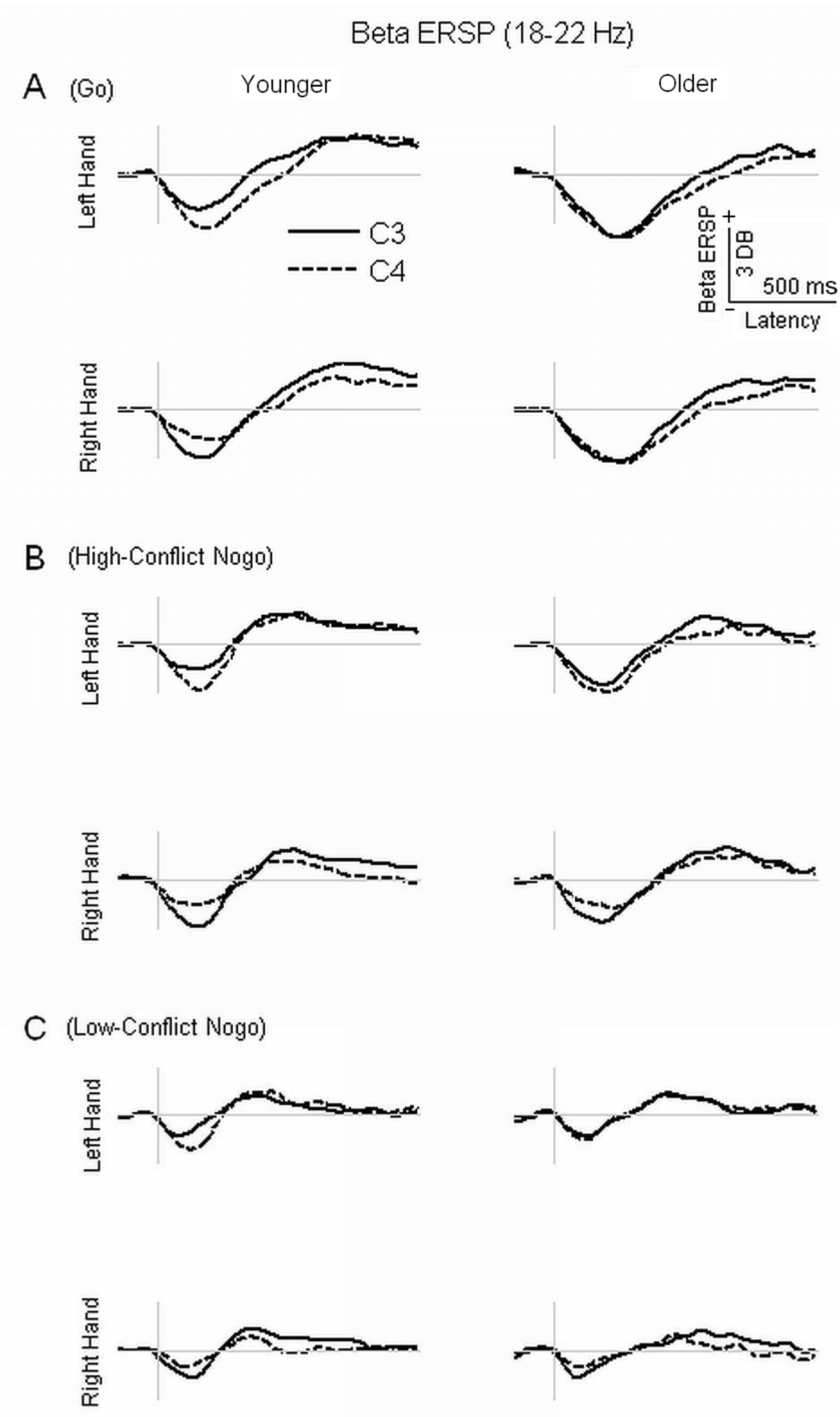
Figure 1. An over-view of the Event-Related Spectral Perturbations (ERSP) from 4 to 50 Hz according to age group (Younger, Older), condition (Go, High-Conflict Nogo, Low-Conflict Nogo), responding hand block (Left, Right), and electrode (C3, C4). Colour code indicates the power (in dB) at a given frequency and latency relative to the stimulus onset.

Figure 2. Event-Related spectral Perturbations (ERSP) in the mu band (10 Hz) for each electrode (C3, C4), responding hand blocks (right, left) and age group (younger, older). Panels A, B and C show data from the go, high-conflict nogo and low-conflict nogo conditions, respectively.

Figure 3. Event-Related spectral Perturbations (ERSP) in the beta band (18-22 Hz) for each electrode (C3, C4), responding hand blocks (right, left) and age group (younger, older). Panels A, B and C show data from the go, high-conflict nogo and low-conflict nogo conditions, respectively.


Younger
Electrode C3
Older
Go
High-Conflict Nogo
Low-Conflict Nogo
Go
High-Conflict Nogo
Low-Conflict Nogo
Frequency (Hz)
50
40
30
20
10
0 500 1000 ms
ERSP (db)
6
4
2
0
-2
-4
-6
Left Hand Block
Right Hand Block
Electrode C4
Left Hand Block
Right Hand Block


Mu ERSP (10 Hz)
A (Go)
Younger
Older
Left Hand
Right Hand
C3
C4
Mu ERSP
- 3 DB +
500 ms
Latency
B (High-Conflict Nogo)
Left Hand
Right Hand
C (Low-Conflict Nogo)
Left Hand
Right Hand


Beta ERSP (18-22 Hz)
A (Go)
Younger
Older
Left Hand
Right Hand
C3
C4
Beta ERSP
+
-
3 DB
500 ms
Latency
B (High-Conflict Nogo)
C (Low-Conflict Nogo)