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# Event-related potentials accompanying motor preparation and stimulus expectancy in the young, young-old and oldest-old

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## Abstract

Although aging is accompanied by neurobiological changes and increased susceptibility to many neurological disorders, little is known about neurophysiological changes that start in old age. Here, neurophysiological changes during old age were assessed by recording brain potentials associated with motor preparation and stimulus expectancy (contingent negative variation, CNV) in young-old (60–69), oldest-old (85–98), and young (17–23) subjects. Individual trials began by a button press, followed 2.5 s later by either a low or high pitch tone. In the "motor" condition subjects responded following high pitch tones ($P = 0.20$); in the "non-motor" condition subjects did not respond. Motor condition CNV amplitudes in the oldest old were more positive than the young and young-old groups, which were similar. In the non-motor condition, the young-old and oldest-old had similar CNV amplitudes that were positive in polarity, and were significantly different from young subjects. Motor potentials before button presses that started the trials were comparable among groups. Results show that neural activity associated with motor preparation and stimulus expectancy changes during advanced age, and that group differences can be modulated by task requirements.

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*Keywords:* Contingent negative variation; CNV; Readiness potential; SPN; P50; Go/no-go

## 1. Introduction

Aging is accompanied by substantial changes in neurobiological and cognitive function. Some measures exhibit monotonic changes as a function of age, such as reductions in processing speed inferred from behavioral measures [6,58] and latency of certain brain potentials (P300) [21,27,46]. Other measures accelerate with increasing age, such as various tests of fluid intelligence [34], fine motor control [61] and possibly white matter integrity [44] cf. [1,64]. The incidence of Alzheimer's disease increases exponentially after approximately age 60 [31], but may decline in the early 90s [40]. Neurological disorders such as Parkinson's disease [40] and stroke [54] also show a substantially increased incidence after age 60.

Taken together, the above findings demonstrate that different cognitive and neurobiological factors exhibit a variety of temporal patterns during the development of age-related changes, and that some changes may only become apparent in early old age. In contrast, experimental studies of aging often define the effects of aging by comparing one group of older subjects, typically ranging between ages 60 and 80, with young college students. Although this approach captures important age-related differences, it cannot evaluate the development of changes within old age. An experimental design using two older groups at age extremes (early old age, late old age) is useful because it can define neurobiological changes that occur during old age, identify variables associated with preservation of cognitive abilities, and can provide data to distinguish neurological disorders from what is nominally considered healthy aging.

The purpose of this study was to define changes in brain activity occurring between young adulthood, early old age, and late old age. Differences between groups of young (17–23 years) young-old (60–69 years), and oldest-old (85–98 years) subjects were evaluated using a self-paced contingent negative variation (CNV) task. The CNV is a well-studied brain potential that develops during a short (∼1–5 s) interval between two task-relevant stimuli, with the second "imperative" stimulus typically requiring a motor response [7,68]. The CNV occurring just before the imperative stimulus, often called the "late CNV" to distinguish it from potentials elicited by the first stimulus, is

Table 1
Demographic information

| | Young | Young-old | Oldest-old |
|---|---|---|---|
| n | 12 | 12 | 12 |
| Age | 20.2 ± 2.0 (17–23) | 65.8 ± 2.6 (61–69) | 90.6 ± 3.8 (85–98) |
| Education | 14.2 ± 1.6 | 15.3 ± 3.2 | 15.7 ± 1.9 |
| M/F | 6/6 | 5/7 | 6/6 |

*Note*: values are mean ± S.D. Age ranges are shown in the parentheses.

generated by a network of cortical and subcortical structures that includes prefrontal, posterior parietal, temporal, premotor, primary motor and somatosensory cortex, and the basal ganglia [4,19,23,25,55]. Among these regions some exhibit large structural changes with age, such as prefrontal cortex, while other regions, such as primary motor cortex, show slight changes with age [49,50]. Thus, the study of the CNV could provide information relevant for defining the performance of neural networks that utilize structures differentially affected by aging. Previous studies that compared late CNV amplitudes in young and older subjects reported similar [16,24,66] or somewhat smaller [36,39] amplitudes for older relative to young subjects.

In addition to examining CNV changes during old age, the present study also evaluated age differences as a function of task by contrasting conditions that did or did not require motor preparation. It was predicted that age differences would be greater and/or more likely in the condition that does not require motor preparation. Presumably, when motor preparation is required the CNV would largely reflect activity generated by regions especially important for motor preparation, such as supplementary motor, premotor, and primary motor cortex; regions that do not show major structural changes with age [49].

## 2. Methods

### 2.1. Subjects

There were three groups of subjects in this experiment (young, young-old, and oldest-old; see Table 1). Young subjects were UC Irvine undergraduates who received course credit for their participation in the experiment. Subjects in the young-old and oldest-old groups were recruited from the Successful Aging Program and the Center for Aging Research and Education at UC Irvine.

Ten out of 12 young-old subjects and 9/12 subjects in the oldest-old group were given the same battery of neuropsychological tests (see [20] for details). All older subjects given neuropsychological tests performed within normal limits. Results from selected tests are shown in Table 2. Episodic memory was assessed using the WMS-III logical memory subtest [70] and the CERAD word list learning task [41]. Language tests included the 30-item version of the Boston naming Test [30] and controlled oral word association (FAS fluency)[62]. Executive function was tested with the trailmaking tests A and B [51]. Visual-spatial skills were evaluated with the WAIS-III block design test [69]. The mini-mental state examination [17] was used as a

Table 2
Neuropsychological test results

| | Young-old (n = 10) | Oldest-old (n = 9) | P values (t-tests) |
|---|---|---|---|
| CERAD word list | | | |
| 5 min delayed recall | 8.1 ± 1.2 | 5.8 ± 2.5 | <0.03 |
| 30 min delayed recall | 7.7 ± 0.7 | 6.0 ± 2.6 | ns |
| 5 min delayed recognition | 20.0 ± 0.0 | 19.9 ± 0.3 | ns |
| 30 min delayed recognition | 19.9 ± 0.3 | 18.6 ± 2.6 | ns |
| WMS-III logical memory | | | |
| Immediate recall | 41.8 ± 10.0 | 38.0 ± 8.7 | ns |
| Delayed recall | 26.6 ± 7.0 | 22.4 ± 8.2 | ns |
| Boston naming test | 28.5 ± 1.3 | 26.7 ± 2.5 | ns |
| FAS verbal fluency | 49.7 ± 9.4 | 49.4 ± 14.8 | ns |
| WAIS-III block design | 34.1 ± 9.9 | 32.1 ± 14.4 | ns |
| Trailmaking test A (s) | 30.8 ± 14.2 | 60.1 ± 33.6 | <0.03 |
| Trailmaking test B (s)[a] | 72.7 ± 14.5 | 123.4 ± 35.1 | <0.01 |
| MMSE[b] | 29.3 ± 0.8 | 28.5 ± 1.4 | ns |
| Geriatric depression rating scale | 1.0 ± 2.0 | 1.0 ± 1.1 | ns |

*Note*: neuropsychological results presented above were from subgroups of subjects that were given a standard test battery. All values are raw scores (mean ± S.D.).

[a] One oldest-old subject did not perform trailmaking test, Part B.

[b] MMSE: mini-mental state exam. For MMSE, n = 12 for the oldest-old.

screening test for dementia, and all subjects (10 young-old and 12 oldest-old) scored ≥27 out of 30 possible points.

The remaining oldest-old subjects ($n = 3$) received the mini-mental status exam; and of these subjects two were given a different set of neuropsychological tests than was described above. Two subjects in the young-old group who are active in the University did not receive neuropsychological testing. All subjects were right handed except for one in the oldest-old group. Subjects signed informed consent forms and were tested according to a protocol approved by the UC Irvine Institutional Review Board.

## 2.2. Behavioral task

Subjects were seated in a comfortable chair inside a sound-attenuating, electrically shielded chamber and held a small button box in their right hand. A series of trials were performed, with each trial beginning when the subject pushed a "start" button with their right thumb. The button press was followed 2.5 s later by the presentation of either a 2,000 Hz (target) or 1,000 Hz (non-target) pure tone (100 ms duration, 5 ms rise/fall times). The auditory stimuli were presented through two speakers placed ~0.75 m in front of the subject at ~70 dB SPL, measured from where the subject sat. The sequence of tones was randomly presented (20% targets, 80% non-targets), with the restriction that at least one, but no more than nine, non-targets were presented between successive targets.

There were two experimental conditions (motor, non-motor; see Fig. 1). In the motor condition subjects responded to targets by pressing a button with their right thumb, and did not respond to non-targets. Subjects were instructed to make their response rapidly while maintaining a high level of accuracy. After waiting at least 4.0 s after stimulus presentation subjects pressed, the start button again to begin the next trial. In the non-motor condition, subjects were instructed to attend to the auditory stimulus, but were not instructed to respond to either stimulus. To verify that subjects were attending to the stimuli, on 10% of trials a visual query was randomly presented on a monitor in front of the subject 4.0 s after stimulus presentation (Fig. 1). The query asked whether the previous stimulus was a target, and the subjects responded by pressing one of two buttons, labeled 'yes' and 'no', with their right thumb. After responding to the query, subjects waited at least 4.0 s before initiating the next trial with a button press. In both conditions, subjects were asked to refrain from blinking between the initial button press (to start the trial) until ~1 s after the stimulus was presented. Depending on the amount of time subjects waited between trials, each block lasted ~6–8 min. Subjects were given a short practice block to familiarize themselves with the task, which also helped the subjects to relax and tended to minimize nervous blinking. To minimize lateral eye movements subjects viewed either a fixation point on the monitor in front of them (non-motor task) or a magazine picture (motor task). Verbal feedback was pro-
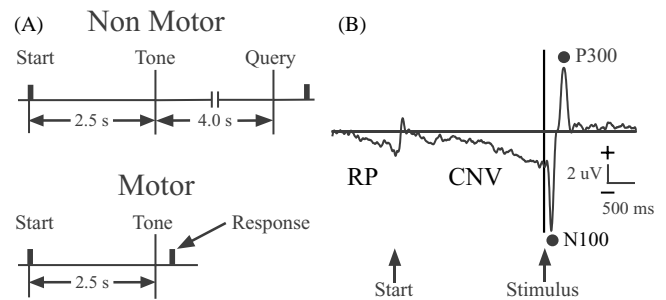


Fig. 1. Schematic diagram of trials from motor and non-motor conditions (A). Each trial began when the subject pressed a start button, which was followed 2.5 s later by the presentation of either a low pitch non-target (1000 Hz) or high pitch target tone (2000 Hz). In the motor condition (lower left panel) subjects pressed a button in response to targets. In the non-motor condition (upper left panel), subjects did not respond to the stimuli, but on 10% of the trials a visual query was presented 4.0 s after the tone. In response to the query subjects indicated by button press whether the previous stimulus was a target or non-target tone. (B) Potentials from the motor condition (DC-16 Hz filtering) in the young group to illustrate the measured components. Arrows indicate when subjects pushed a button to begin each trial ("Start") and when the subsequent tone was presented ("Tone"). The readiness potential developed prior to the start button press, and was followed by the contingent negative variation (CNV) which progressively increased in amplitude up until the stimulus was presented. The N100 and P300 post-stimulus potentials elicited by the stimulus are also shown. The P50 and P200 components were too small to be visualized at this scale.

vided to ensure that the subjects consistently waited at least 4 s between trials. Occasional button presses before the 4-s waiting period had elapsed led to a 4-s timeout period, after which time the subjects could start the next trial. The subjects reported that they could clearly detect the auditory stimuli, and all performed the task accurately (see Section 3).

A total of 80–160 trials were given in two to four blocks (40 trials/block) for each experimental condition (motor, non-motor). The purpose of using more than two blocks per condition in some subjects was to ensure that there were enough trials for a reliable event-related potential average. The non-motor condition was always performed before the motor condition to avoid the possibility of carryover effects from the motor condition to the non-motor condition.

The main procedural difference between this study and previous CNV studies was that in a typical CNV task a pair of stimuli (S1, S2) are separated by a foreperiod lasting ~1–5 s [7,68]. In contrast, in the current study a button press was substituted for the first stimulus. There were three reasons for making this change. First, the main objective of this study was to examine potentials during the foreperiod (i.e. CNV) that are associated with activity within a widespread cortical network. The initial sensory response to S1 was of less interest, and age differences were examined for potentials elicited by the tone following the initial button press. Second, a negative slow wave (the readiness potential) that develops before voluntary movement, in this instance before the "start" button press, could be assessed. The readiness potential provided a useful comparison measure for the CNV

because it reflects motor preparatory activity that is not associated with preparation for an upcoming cued response or attentional changes associated with stimulus expectancy. Finally, it was assumed that the likelihood of finding group differences that were secondary to differences in vigilance would be reduced if each subject could control when to begin each trial.

### 2.3. Electrophysiological recordings

Subjects were seated in an electrically shielded, acoustic isolation chamber. Brain electrical activity was recorded from 10 Ag/AgCl electrodes places at the Fz, Cz, Pz, Oz, F3, C3, P3, F4, C4 and P4 sites according to the 10/20 system [29]. Electrodes placed on the left and right mastoid served as references in a linked mastoid configuration. Two electrodes were placed above and below the eye to monitor eye movements, and one electrode was placed on the forehead to serve as the ground. Electrode impedances were $<5\,k\Omega$, and were occasionally checked during the recording session. The EEG and EOG were digitized (500 Hz), amplified, and filtered (DC-100 Hz). EEG, EOG, and stimulus-triggered responses were acquired continuously and later processed off-line. An eyeblink correction algorithm was used to correct for eye artifacts [22], then individual sweeps were visually inspected for artifacts before being accepted into the evoked potential average. Sweeps were automatically rejected if the voltage in any channel exceeded $150\,\mu V$ and only trials with correct responses were included in the event-related potential averages.

### 2.4. Data analysis

Behavioral measures in the motor condition included reaction time relative to stimulus onset, accuracy (correct responses to target stimuli), and false alarms (incorrect responses to non-targets). For the non-motor condition, accuracy was measured by the percentage of correct responses to the query.

The EEG was digitally filtered using FFT and inverse FFT procedures, and filter settings were adjusted depending on the component of interest. The EEG was low pass filtered (DC-3 Hz, 12 dB/octave) when measuring slow waves. For event-related potentials elicited by auditory stimuli (P50, N100, P200, and P300) the potentials were bandpass filtered (0.1–16 Hz, 12 dB/octave).

Amplitude of the readiness potential was measured using a 250 ms time window lasting from $-250$ to 0 ms before the button press. The CNV developed after resolution of the readiness potential and before the onset of the tone stimulus. Amplitudes of the late portion of the CNV were measured using a 250 ms time window ($-250$ to 0 ms) before stimulus presentation. As shown in the Results section, in some conditions the "CNV" had a positive polarity. For simplicity and comparison with previous studies the term "CNV", contingent negative variation, was retained even when the

potentials were positive in polarity. Readiness potential and CNV amplitudes were defined relative to a 100 ms baseline period from $-3.5$ to $-3.4$ before stimulus presentation. EEG sweeps for trials having non-target and target stimuli were included in event-related potential averages examining prestimulus potentials.

Auditory stimuli elicited three transient components (P50, N100, P200) that were followed by a positive component (P300). Event-related potentials elicited by auditory stimuli were compiled to non-target trials. Event-related potentials for targets were not averaged separately because there were too few target stimuli to construct reliable averages. Peak latencies were calculated relative to stimulus onset and amplitudes of stimulus evoked potentials were defined relative to a 100 ms prestimulus baseline period. The P50 peak was defined as the largest positive peak between 30 and 70 ms after stimulus onset. The N100 was defined as the maximum negativity between 80 and 180 ms, while the P200 was defined as the maximum positivity between 150 and 250 ms. P300 peaks were defined as the largest positive peak between 250 and 600 ms.

### 2.5. Statistical analysis

Data were analyzed using *t*-tests and repeated measures analysis of variance (ANOVA). Because the main objective of this study was to evaluate the effects of aging during early old age (young-old) and advanced old age (oldest-old), two separate group comparisons were performed: young versus young-old and young-old versus oldest-old. ANOVA factors included group (young, young-old, and oldest-old), condition (motor, non-motor), and electrode site (Fz, Cz, Pz, Oz, F3, C3, P3, F4, C4, P4). Scalp topography differences between groups were assessed using normalized values [38]. The Greenhouse–Geiser correction was applied to control for type I error when appropriate. When Greenhouse–Geiser corrections were utilized the adjusted *P*-values were reported. Post hoc testing utilized Tukey tests and single-sample *t*-tests. Statistical significance was set at $P < 0.05$.

## 3. Results

### 3.1. Behavior

In the motor condition median reaction times were significantly different between the young and young-old ($t_{(22)} = 2.7$; $P < 0.02$), but not between the young-old and oldest-old (Table 3). The variability in reaction times within individual subjects increased in the oldest-old, indicated by a significant difference in reaction time standard deviations among the young-old and oldest-old ($t_{(22)} = 2.4$; $P < 0.03$). Reaction time variability was also assessed by calculating the coefficient of variation (standard deviation/mean reaction time) for each individual, which controls for variability

Table 3
Behavioral results

| | Young | Young-old | Oldest-old |
|---|---|---|---|
| Reaction time (ms)[a] | 297.8 ± 30.0 | 440.0 ± 42.9 | 498.1 ± 38.9 |
| SD reaction time[b] | 96.7 ± 14.7 | 135.6 ± 16.6 | 246.3 ± 42.6 |
| CV[b] | 0.30 ± 0.03 | 0.29 ± 0.03 | 0.43 ± 0.05 |
| Accuracy: motor (%) | 98.8 ± 0.3 | 98.5 ± 0.4 | 94.7 ± 4.1 |
| Accuracy: non motor (%) | 98.4 ± 0.5 | 96.6 ± 1.2 | 92.2 ± 0.5 |
| False alarms: motor (%) | 1.1 ± 0.3 | 1.2 ± 0.5 | 1.6 ± 0.7 |
| MMSE (maximum 30) | – | 29.3 ± 0.3 | 28.8 ± 0.3 |

Notes: Significant group effects ($P < 0.05$): [a] = young vs. young-old, [b] = young-old vs. oldest-old. CV: coefficient of variation (reaction time S.D./mean reaction time). S.D.: standard deviation. False alarms indicate responses to non-target stimuli. MMSE: mini-mental state exam.

due to overall reaction time differences. The coefficient of variation also showed a significant difference between the young-old and oldest-old groups ($t_{(22)} = 2.2$; $P < 0.04$), with greater variability in the oldest-old. Standard deviations and coefficients of variation were not significantly different between the young and young-old groups. There were no significant differences between groups in accuracy or false alarms for either the motor or non-motor conditions.

Neuropsychological test results in subsets of young-old ($n = 10$) and oldest-old ($n = 9$) subjects were comparable, with no significant group differences on most tests (Table 2). The only exceptions were small group differences in CERAD word list 5 min delayed recall and the trailmaking test (A and B).

### 3.2. Event-related potentials

Grand average potentials are shown in Fig. 1B to illustrate the components that were analyzed. A negative readiness potential developed before the button press that started the trial. After the positive resolution of the readiness potential a negative-going slow potential (CNV) developed until the onset of the stimulus. Tone stimuli then elicited a series of components having latencies between ~50 and 400 ms (P50, N100, P200, P300). Because there were few target stimuli (4/block), differences between non-target and target stimuli will not be examined.

### 3.3. Readiness potential

Readiness potentials developing before the button press that started each trial are shown in Figs. 2–5. Amplitudes of the readiness potential were assessed using separate 2 (group) × 2 (condition) × 2 (site: C3, C4) ANOVAs to compare young versus young-old and youngest-old versus oldest-old. There were significant effects of site for both the young versus young-old ($F_{(1,22)} = 25.4$; $P < 0.001$) and young-old versus oldest-old ($F_{(1,22)} = 32.2$; $P < 0.001$). In both comparisons amplitudes at C3 were larger than C4, a result consistent with previous work showing larger readiness potential amplitudes at sites contralateral to the finger that was moved [13,60]. For the young-old versus oldest-old comparison there was also a significant group × site interac-

tion ($F_{(1,22)} = 5.2$; $P < 0.04$), indicating larger amplitudes at C3 in the young-old compared to the old-old group (−3.0 ± 0.7 versus −1.9 ± 0.4 μV, respectively) but similar amplitudes at C4 (−0.7 ± 0.4 versus −1.0 ± 0.3 μV, respectively). These findings indicate that the readiness potential was, in general, comparable in amplitude and lateralization among all groups, with the exception of somewhat larger amplitudes at C3 in the young-old relative to the old-old group.

#### 3.3.1. Contingent negative variation: young versus young-old

Grand average potentials in young and young-old groups are shown in Fig. 2 (motor condition) and Fig. 3 (non-motor condition). A 2 (group) × 2 (condition) × 10 (site) ANOVA had significant main effects of group ($F_{(1,22)} = 7.6$; $P <$
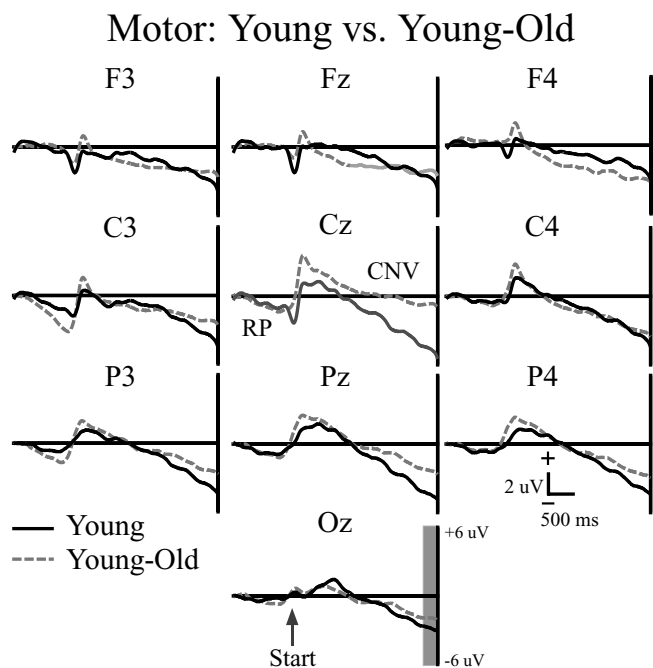


Fig. 2. Grand average potentials for young and young-old in the motor condition. There were no overall group differences in CNV amplitude, but topographic analysis indicated less positive amplitudes in the young-old for a subset of sites, primarily Cz. Arrow indicates the button press to start each trial. Vertical line indicates stimulus onset and the gray shading represents the 250 ms window used to quantify the CNV.
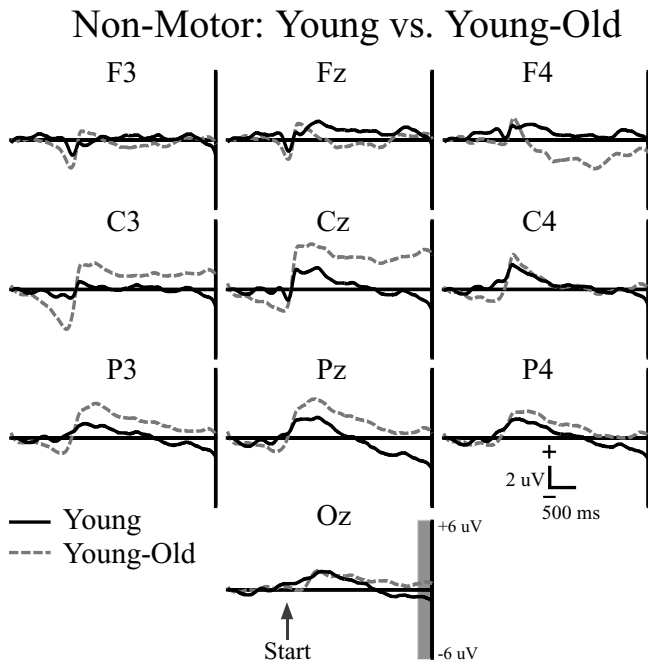
## Non-Motor: Young vs. Young-Old



Fig. 3. Grand average potentials for young and young-old in the non-motor condition. A significant group main effect indicated more positive CNV amplitudes in young-old relative to young subjects. Readiness potential amplitudes before the start button press were not significantly different between groups, although the grand average readiness potential was larger in the young-old, especially at C3, due to a few subjects with large potentials in the young-old and small amplitudes in the young. Arrow indicates the button press to start each trial. Vertical line indicates stimulus onset and the gray shading represents the 250 ms window used to quantify the CNV.

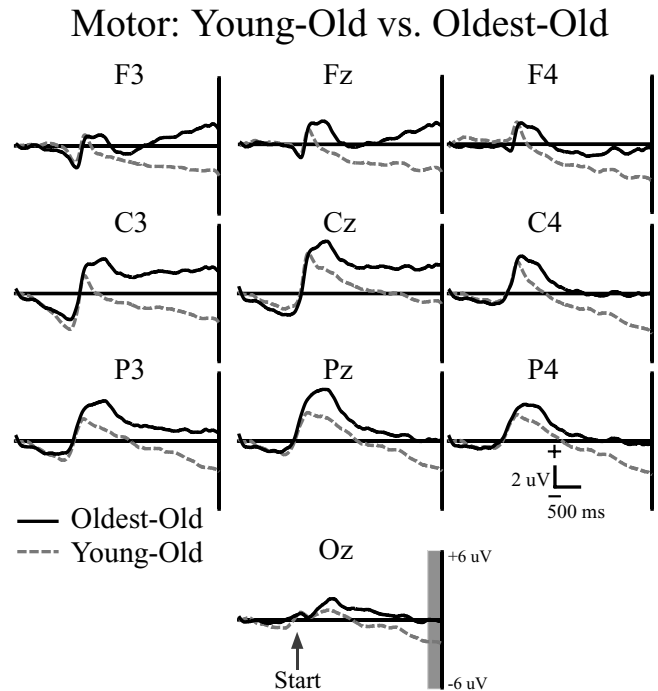## Motor: Young-Old vs. Oldest-Old



Fig. 4. Grand average potentials for young-old and oldest-old groups in the motor condition. Arrow indicates the button press to start each trial. A significant main effect of group showed that CNV amplitudes were more positive in the oldest-old than in the young-old group. Vertical line indicates stimulus onset and the gray shading represents the 250 ms window used to quantify the CNV.
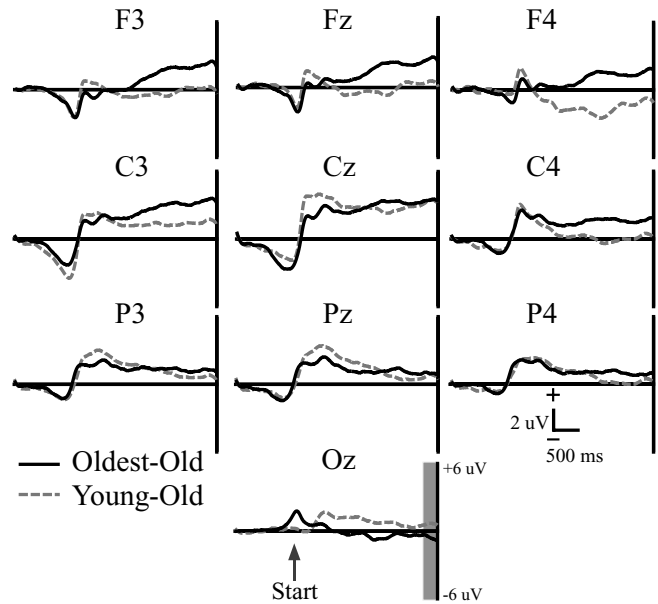
## Non-Motor: Young-Old vs. Oldest-Old



Fig. 5. Grand average potentials for young-old and oldest-old groups in the non-motor condition. The main effect of group was not significant, but separate analysis of frontal sites (Fz, F3, F4) showed a significant group difference, with more positive potentials in the oldest-old. Vertical line indicates stimulus onset and the gray shading represents the 250 ms window used to quantify the CNV.

0.02), condition ($F_{(1,22)} = 32.6$; $P < 0.001$), and a significant group × site interaction ($F_{(9,198)} = 5.3$; $P < 0.001$). CNV amplitudes were larger in the young relative to young-old ($-2.2 \pm 0.4$ and $-0.8 \pm 0.4\,\mu V$, respectively), and larger in the motor versus non-motor condition ($-2.9 \pm 0.4$ versus $0.0 \pm 0.3\,\mu V$, respectively). Topographic differences were further assessed using normalized amplitude values. A 2 (group) × 2 (condition) × 10 (site) ANOVA indicated a significant group × site interaction ($F_{(9,198)} = 4.1$; $P < 0.001$). In both conditions, normalized group differences were most pronounced at Cz and, to a lesser degree, the Pz, C3, and C4 sites, which corresponds to the greater positivity at these sites in the young-old compared to the young (Figs. 2 and 3).

Group differences were evaluated in greater detail by conducting separate 2 (group) × 10 (site) ANOVAs for the motor and non-motor conditions. In the motor condition, there was a significant group × site interaction ($F_{(9,198)} = 2.8$; $P < 0.03$), but the main effect of group did not attain significance ($P > 0.15$). In contrast, in the non-motor condition there was a significant group effect ($F_{(1,22)} = 8.1$; $P < 0.01$) in addition to a significant group × site interaction ($F_{(9,198)} = 5.1$; $P < 0.001$). These results indicate that CNV amplitudes in the young-old group were significantly

smaller than young subjects in the non-motor condition, but were comparable in the motor condition. Group differences were most evident at left and midline centro-parietal sites in the non-motor condition, and to a lesser degree in the motor condition.

To determine if CNV amplitudes were significantly different from $0 \mu V$ in the non-motor condition, one-sample $t$-tests were conducted at individual electrode sites in each group. In young subjects, three sites attained significance (Cz, Pz, P4: $P$ values $< 0.05$), and one site (Pz) was $<0.01$ (Bonferroni correction for multiple comparisons). In the young-old, one site was significantly different from $0 \mu V$ (Cz: $P < 0.01$), and the polarity was positive. Thus, in the non-motor condition, the CNV was generally not evident except at a few posterior sites in young subjects and by a positive potential at Cz in young-old subjects.

### 3.3.2. Contingent negative variation: young-old versus oldest-old

Grand average potentials in young-old and oldest-old groups are shown in the motor (Fig. 4) and non-motor (Fig. 5) conditions. CNV amplitudes were analyzed using a 2 (group) $\times$ 2 (condition) $\times$ 10 (site) ANOVA. There were significant effects of group ($F_{(1,22)} = 10.3$; $P < 0.01$), condition ($F_{(1,22)} = 20.7$; $P < 0.001$), site ($F_{(9,198)} = 9.2$; $P < 0.001$), and a significant group $\times$ site interaction ($F_{(9,198)} = 2.3$; $P < 0.03$). Amplitudes were more negative in the young-old relative to oldest-old ($-0.8 \pm 0.4$ versus $1.5 \pm 0.6 \mu V$), and were more negative in the motor ($-0.7 \pm 0.5 \mu V$) compared to the non-motor ($1.4 \pm 0.4 \mu V$) condition. Topographic differences were further evaluated using normalized values. A 2 (group) $\times$ 2 (condition) $\times$ 10 (site) ANOVA did not indicate significant group $\times$ site or group $\times$ condition $\times$ site interactions ($P$ values $> 0.09$). The lack of a significant group $\times$ site interaction using normalized values suggests that the significant group $\times$ site interaction using absolute amplitudes may be due, in part, to group differences in overall strength of cortical sources generating the scalp potentials rather than a difference in the configuration of sources [38].

Group differences were assessed in greater detail by conducting separate 2 (group) $\times$ 10 (site) ANOVAs for the motor and non-motor conditions. In the motor condition, there were significant effects of group ($F_{(1,22)} = 12.3$; $P < 0.01$) and site ($F_{(9,198)} = 4.7$; $P < 0.001$), but the group $\times$ site interaction was not significant. For the non-motor condition, there was not a significant group effect. The effects of site ($F_{(9,198)} = 9.6$; $P < 0.001$) and the group $\times$ site interaction ($F_{(9,198)} = 2.7$; $P < 0.04$) were significant. To determine if CNV amplitudes in the oldest-old were significantly different from $0 \mu V$ in the motor and non-motor conditions one-sample t-tests were conducted at individual electrode sites in each group. In the motor condition, two sites attained significance (F3, Cz: $P < 0.05$), and neither $P$ value was $<0.01$. For the non-motor condition all sites were significantly different from $0 \mu V$ except Pz, Oz, and

P3; F3, C3, Cz and C4 were $<0.01$ (Bonferroni corrected for multiple comparisons). Thus, for the oldest-old, the CNV was positive in polarity, particularly in the non-motor condition.

In summary, the findings suggest that in the young-old group CNV amplitudes were similar to young subjects in the motor condition and similar to oldest-old subjects in the non-motor condition. CNV amplitudes in the three groups are plotted in Fig. 6 (motor condition) and 7 (non-motor condition). To further illustrate these results, similarity of CNV amplitudes in the young-old group relative to the young and oldest-old were quantified by expressing amplitudes in the young-old as a percentage of the range between young (0%) to oldest-old (100%) for each site and condition. In the motor condition only 1/10 sites (Cz) was $>50\%$ in the young-old, while in the non-motor condition 5/9 sites were $>50\%$. Note that nine sites were compared in the non-motor condition because mean young-old amplitudes were slightly more positive than the young and oldest old groups at Oz in the non-motor condition.
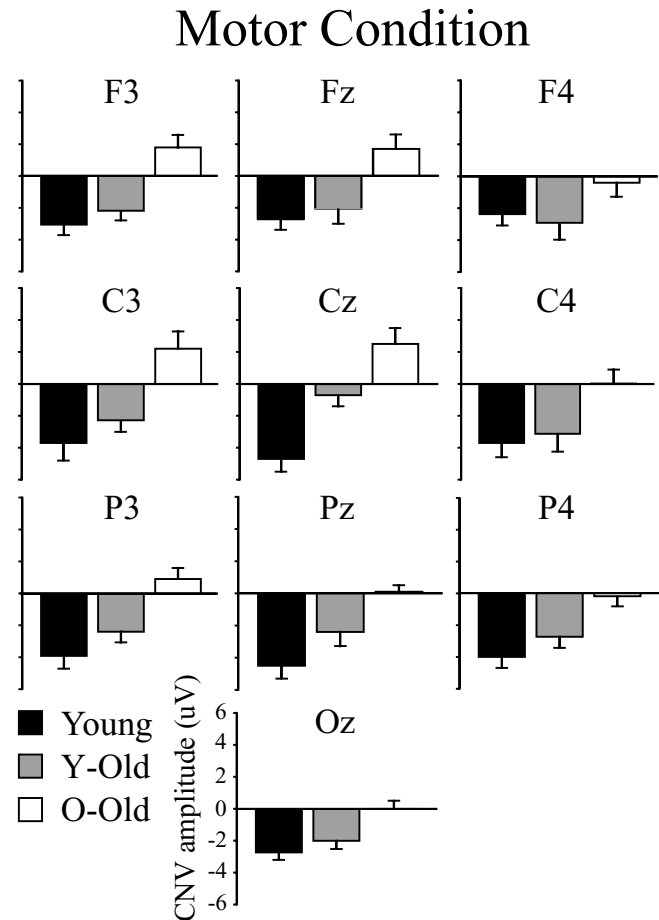


Fig. 6. Mean CNV amplitudes in the motor condition. With the exception of Cz, CNV amplitudes in the young-old were similar to the young. Amplitudes of the young and young-old were more negative compared with the oldest-old group. Y-old: young-old; O-old: oldest-old.
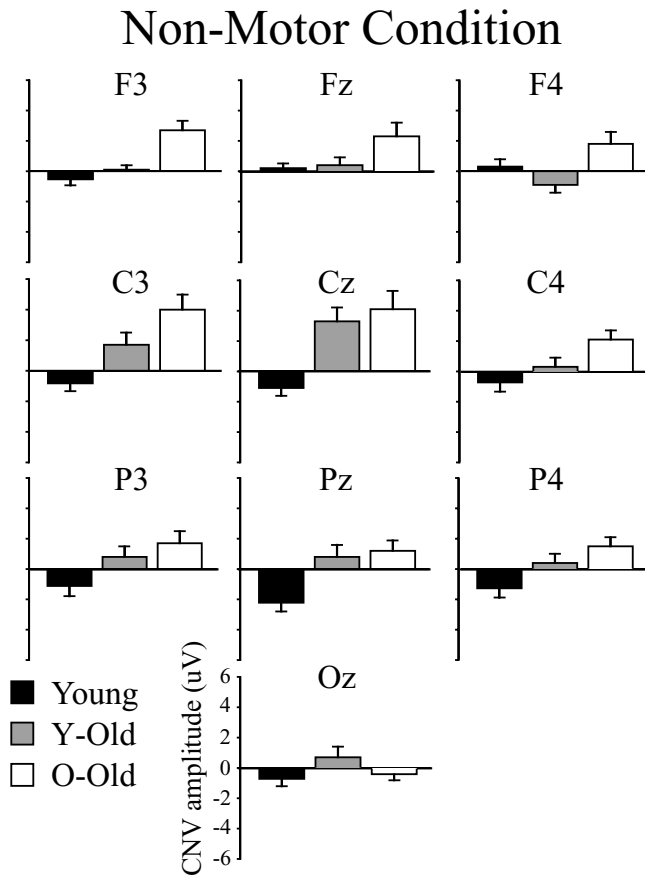
## Non-Motor Condition



Fig. 7. Mean CNV amplitudes in the motor condition. At frontal sites amplitudes for both the young and young-old were not significantly different from 0 μV, but the oldest-old group exhibited a positive-going CNV. At midline and left central and parietal sites (Cz, Pz, C3, P3) CNV amplitudes in young-old oldest-old were similar and positive in polarity, in contrast to young subjects who had small negative amplitudes. Y-old: young-old; O-Old: oldest-old.

### 3.3.3. Contingent negative variation: analysis of frontal sites

Examination of Figs. 6 and 7 suggests that CNVs at frontal sites (Fz, F3, F4) in the young and young-old groups were similar for both conditions, while amplitudes in the oldest-old were more positive than the young and young-old. The verify this impression the young versus young-old and young-old versus oldest-old groups were compared using 2 (group) × 2 (condition) × 3 (site: Fz, F3, F4) ANOVAs. For young versus young-old there was a significant effect of condition ($F_{(1,22)} = 34.7$; $P < 0.001$) but not for group ($P > 0.80$). In contrast, the young-old versus oldest-old comparison revealed significant effects for group ($F_{(1,22)} = 12.8$; $P < 0.01$), condition ($F_{(1,22)} = 14.1$; $P < 0.001$), and site ($F_{(2,44)} = 8.5$; $P < 0.001$). These results confirm that CNV amplitudes at frontal sites did not differ between the young and young-old in either condition, but were more positive in the oldest-old relative to the young-old in both conditions.
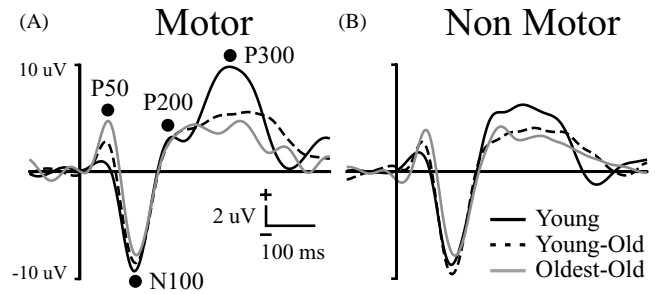


Fig. 8. Post-stimulus potentials in the young, young-old, and oldest-old in the motor (A) and non-motor (B) conditions to non-target tones. P50 amplitude was significantly different among the three groups, with progressive amplitude increases from young, young-old, and oldest-old groups, respectively. Note that the component labeled "P300" in response to non-target stimuli differs from the typical "P300" reported in the literature, which is elicited by target stimuli. Vertical lines indicate stimulus onset.

### 3.4. Post-stimulus potentials

Event-related potentials following presentation of non-target tones are shown in Fig. 8. Amplitudes and latencies of each component (P50, N100, P200, P300) were assessed using separate 2 (group) × 2 (condition) ANOVAs comparing young versus young-old and young-old versus oldest-old groups. For P50 amplitude there were no significant group effects among young and young-old groups ($P < 0.13$) or between young-old and oldest-old ($P < 0.07$). Although the grand average potentials show clear P50 amplitude differences between groups, there was substantial individual variability among subjects within each group, which accounts for the lack of significant group effects. A 3 (group) × 2 (condition) ANOVA, containing all three groups, did show a significant effect of group ($F_{(2,33)} = 6.0$; $P < 0.01$). Post hoc Tukey tests indicated significant differences between young and oldest-old groups. There were no significant effects on P50 latency, or amplitudes and latencies of the N100 and P200 for either set of group comparisons. Amplitude of the P300 increased from anterior to posterior sites, and was maximal at the Pz electrode, especially in young subjects. Analyses of peak P300 amplitude and latency used measures from the Pz site. For P300 amplitudes in the young versus young-old comparison there were significant effects of group ($F_{(1,22)} = 14.4$; $P < 0.01$) and condition ($F_{(1,22)} = 11.7$; $P < 0.01$), with smaller amplitudes in the non-motor condition. In the young-old versus oldest-old comparison there was a significant effect of condition ($F_{(1,22)} = 7.7$; $P < 0.03$). There were no significant group effects for P300 latency in either comparison.

## 4. Discussion

In this study overall CNV amplitudes were significantly different between the three age groups, and the group differences were modulated by task requirements. CNV

amplitudes in the young-old group were similar to the young in the motor condition, both of which were more negative than the oldest-old. In contrast, for the non-motor condition CNV amplitudes in the young-old were similar to the oldest-old, both of which were more positive than the young. In both conditions CNV amplitudes at frontal sites were similar for the young and young-old, and were more positive in the oldest-old. Findings will be discussed with respect to neurobiological changes occurring during aging and possible functional correlates, with an emphasis on changes that occur during old age.

### 4.1. Aging and the contingent negative variation component

In the context of tasks that provide information about an upcoming task-relevant stimulus (such as stimulus onset time and the required response), a diverse set of neurobiological mechanisms can be engaged to prepare for an upcoming stimulus to facilitate execution of the appropriate response [7,53]. Convergent evidence from human neuroimaging and animal studies indicates that preparation for an impending stimulus is associated with activities in prefrontal and premotor cortex acting in concert with posterior association regions [12,14,15,18,32,48,57,59]. The CNV prior to presentation of the second stimulus in a pair is generated by a network of cortical and subcortical structures including prefrontal, temporal, premotor, primary motor and somatosensory cortex [4,19,23,33,55], and the basal ganglia [3,26]. Potentials at central and parietal sites may also be associated with a subcomponent of the CNV that is present when subjects do not respond to the upcoming stimulus (termed stimulus preceding negativity (SPN)) [7,8,67].

Previous CNV studies comparing young and older subjects reported that CNV amplitudes before the imperative stimulus were similar [16,24,66] or somewhat smaller [36,39] in the older relative to young subjects. The absence of age effects in the motor condition for the young-old is consistent with previous studies having mean ages in the older group of ∼65 years [16,24,66]. A study using somewhat older elderly subjects [39] (mean age = 72, range 64–91) reported reductions in CNV amplitude at a frontal site, which is similar to the finding of smaller CNV amplitudes at frontal sites in the oldest-old group relative to the young and young-old in the motor condition.

For both sets of group comparisons the group × condition interaction in the omnibus ANOVA did not attain significance. However, follow-up ANOVA's within each condition were able to define significant group effects on CNV amplitude, with the young-old differing significantly from the oldest-old in the motor condition and from the young in the non-motor condition. The absence of group × condition interactions was largely attributable to a few sites in conditions not having significant group differences, where small differences were present. For young-old subjects in the motor condition CNV grand average amplitudes at left and midline centro-parietal sites were less than young sub-

jects. At frontal sites in the non-motor condition amplitudes in the young-old were at baseline compared with positive CNV amplitudes in the oldest-old. For young-old subjects in the motor condition the sites showing small group differences in the grand average potentials (C3, Cz, P3, Pz) are the same sites that were largely responsible for significant young versus young-old differences in the non-motor condition. Thus, there were indications of small, non-significant differences between the young and young-old at these sites in the motor condition, and the group differences were larger and attained significance in the non-motor condition.

Unexpectedly, the CNV was positive in polarity in the oldest-old. Positive potentials are not likely due to artifacts, such as eyeblinks, because: (1) amplitudes were largest at central instead of frontal sites; (2) were larger in the non-motor versus motor condition; (3) an eyeblink correction routine was successfully performed; and (4) individual sweeps were visually inspected for artifacts. The present results cannot define the mechanism of polarity differences between groups because scalp event-related potential components can be the net result of simultaneous contributions from neural sources in multiple locations [42], and the present study was not designed to directly identify neural sources. Additional studies employing techniques such as high density electrode arrays and source modeling or functional neuroimaging would be useful for defining the mechanisms of polarity differences between groups. Although speculative, positive CNV polarities in the oldest-old may reflect age-related reductions in synapse number and changes in the structure of apical dendrites of pyramidal cells [45]. Negative slow potentials at scalp sites reflect, in part, activity from excitatory postsynaptic potentials generated at synapses on the apical dendrites of pyramidal cells [5]. Therefore, age-related changes in the number and/or configuration of cortical synapses may contribute to the positive CNV on the oldest-old.

In the non-motor condition, clear negative-going potentials, indicative of a stimulus preceding negativity, were not observed in the young-old but were present at three sites in the young (Cz, Pz, P4). A previous study using a visual stimulus discrimination task reported amplitude increases (i.e. greater negativity) of an SPN wave in older relative to young subjects [24]. Although the Hillman et al. [24] study and the current experiment both employed stimulus discrimination tasks, there were substantial differences in stimulus modality, timing between stimuli, use of self-paced trials versus experimenter determined trial onsets, and different data analysis procedures, which may be relevant to the different findings.

The non-motor condition required the subjects to remember the tone's pitch until the time when the query might be presented (4.0 s after stimulus presentation). Although the CNV occurred before tone presentation, the present results cannot rule out the possibility that the memory requirements in the non-motor conditions are relevant to group differences in CNV amplitude.

### 4.2. Task-dependent modulation of age effects in young-old subjects

Neuroimaging and behavioral studies indicate that the magnitude, or even the presence, of age-differences can be modulated by the specific task demands and strategies utilized by subjects (e.g. [11,35]. The current findings also showed a similar task-dependent interaction with age. In the motor condition CNV amplitudes in young-old subjects are similar to young subjects; in the non-motor condition they are most similar to the oldest-old. The present results cannot directly determine if task instructions modulated the activity of similar generators in each condition or if, instead, neural generators less affected by age were recruited in the motor condition. Because premotor and motor cortical regions are likely to be engaged in the motor condition but have a lesser role in the non-motor condition, at least some of the group differences as a function of task are likely attributable to selective use of regions important for motor preparation in the motor condition that are not strongly affected by age [49].

Subjects in all three groups performed at high levels of accuracy (>90% correct), which suggests that group differences in CNV results were not secondary to performance differences between groups. Moreover, in the motor condition, there is a double dissociation between reaction time and CNV amplitudes among the groups. Reaction time is significantly longer in young-old versus young subjects but CNV amplitudes are comparable. In contrast, reaction times in the young-old and oldest-old are similar but CNV amplitudes are significantly different. The combination of these results strongly suggests that group differences in CNV amplitude are not attributable to performance differences.

### 4.3. Self-paced readiness potential and aging

In contrast to the CNV results, readiness potential amplitudes preceding the self-paced button press that initiated each trial were not significantly different between age groups, a result consistent with previous findings using younger elderly subjects [60]. Thus, neurophysiological activity associated with motor preparation for voluntary movements, as defined by the readiness potential, is comparable across age groups. Group differences in the CNV but not the readiness potential are likely attributable to different, but overlapping, configurations of neural sources that contribute to both the CNV and the readiness potential [26]. The readiness potential is thought to be generated by a network of cortical and subcortical structures that includes the supplementary motor area (SMA) and premotor cortex, anterior cingulate gyrus, and basal ganglia, with additional activity in primary motor and somatosensory cortex contralateral to the effector shortly before a movement is made [28,52].

The presence of substantial group differences in CNV activity but not in the readiness potential may also reflect differences in the functional significance of these potentials.

The readiness potential, by definition, is a pre-movement event-related potential given that a response was actually made. In contrast, for go/no-go tasks the CNV is a pre-stimulus potential given that a response might be made, depending on the upcoming stimulus. Thus, differences between what the potential developed before (a movement versus a stimulus), and when the decision to respond was made (before the movement versus sometime after stimulus presentation) are important considerations for any comparison between the CNV and the readiness potential. For example, neural activity associated with working memory, attention, stimulus timing, or the information value of the upcoming stimulus may contribute to the CNV but not to the self-paced readiness potential [7].

Although the readiness potential does not appear to change substantially with age, an fMRI study examining age-related differences during unimanual paced movement reported larger magnitudes and spatial extent of activation in motor cortex and associated areas [37]. Mattay et al. [37] also reported ipsilateral motor cortical activations in older subjects that were not observed in young subjects, a result also observed using EEG measures [56]. Thus, aging may be associated with neural changes during movement, but these differences are not reflected by the self-paced readiness potential.

### 4.4. Post-stimulus event-related potentials

Amplitude of the P50 component increased significantly when analyzed across all three groups, with the smallest amplitudes in the young, intermediate in the young-old, and largest amplitudes in the oldest-old. Group effects when comparing two groups (young versus young-old and young-old versus oldest-old) did not attain significance, a result possibly due to insufficient statistical power related to individual differences in P50 amplitude within each group. Previous aging studies have also defined age-related increases in the amplitudes of middle latency potentials (Pa, Nb, Pb or P1) occurring during the same time period as the P50 [2,9,10,71].

The waveform labeled "P300" in this task, based on polarity and approximate latency, is probably not the same component as the P300 that is elicited by infrequent targets in standard target detection tasks [20,47,65]. In this study, the P300 was present to non-target stimuli, and more importantly did not show latency increases with age [21,27,46]. The P300 to non-targets is similar to a component previously described in a standard target detection task that progressively develops when several non-targets are presented in a row, and is larger when a motor response is required [63]. Targets in the current study most likely elicited the typical P300 components, but targets were not analyzed separately because there were not enough sweeps to adequately measure potentials in most individuals. A study assessing the P300 to targets in the oldest-old reported that P300 latency continues to increase with age in subjects over 90 [43].

In summary, the main findings showed that in the motor condition late CNV amplitudes in the oldest-old were more positive than CNVs in the young and young-old groups, which had similar amplitudes. In the non-motor condition the young-old and oldest-old groups had similar CNV amplitudes, and were significantly more positive than the CNV in young subjects. Amplitudes of the readiness potential that developed before the start of each trial were comparable among groups. Results show that neural activity associated with motor preparation and stimulus expectancy changes during advanced age, and that group differences can be modulated by task requirements.

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