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Age-related differences in muscle recruitment and reaction-time performance



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ABSTRACT

Previously, we showed that prolonged reaction-time (RT) in older persons is related to increased antagonist muscle co-activation, occurring already before movement onset. Here, we studied whether a difference in temporal agonist and antagonist muscle activation exists between young and older persons during an RT-test. We studied Mm. Biceps (antagonist muscle) & Triceps (agonist muscle) Brachii activation time by sEMG in 60 young (26 ± 3 years) and 64 older (80 ± 6 years) community-dwelling subjects during a simple point-to-point RT-test (moving a finger using standardized elbow-extension from one pushbutton to another following a visual stimulus). RT was divided in pre-movement-time (PMT, time for stimulus processing) and movement-time (MT, time for motor response completion). Muscle activation time 1) following stimulus onset (PMAT) and 2) before movement onset (MAT) was calculated. PMAT for both muscles was significantly longer for the older subjects compared to the young (258 \pm 53 ms versus 224 \pm 37 ms, p = 0.042 for Biceps and 280 \pm 70 ms versus 218 \pm 43 ms for Triceps, p < 0.01). Longer agonist muscle PMAT was significantly related to worse PMT and RT in young (respectively r = 0.76 & r = 0.68, p < 0.001) and elderly (respectively r = 0.42 & r = 0.40, p = 0.001). In the older subjects we also found that the antagonist muscle activated significantly earlier than the agonist muscle (-22 ± 55 ms, p = 0.003). We conclude that in older persons, besides the previously reported increased antagonist muscle co-activation, the muscle firing sequence is also profoundly altered. This is characterized by a delayed muscle activation following stimulus onset, and a significantly earlier recruitment of the antagonist muscle before movement onset.

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1. Introduction

Increase of the reaction time (RT) is a factor that contributes to slower motor performance at higher age. RT can be divided into premovement time (PMT, the time to process a stimulus and initiate a response) and movement time (MT, the time to execute the response, involving motor activity) (Roberts and Pallier, 2001). Although

Abbreviations: ADL, Activities of Daily Life; bADL, Dependency for basic activities of daily life; iADL, Dependency for instrumental activities of daily life; ADS, Activity Dimensions Summary score; MMSE, Mini Mental State Examination; MVC, Maximal Isometric Voluntary Contraction; MT, Movement time; MAT, Movement activation time; MAT, Activation time of the muscle relative to movement onset of the *i-th* MT period; PMT, Pre-movement time of the *i-th* RT trial; PMAT, Pre-movement activation time; PMAT, Activation time of the muscle relative to stimulus onset of the *i-th* PMT period; %PMAT, PMAT expressed as a percentage of PMT; RT, Reaction time; YPAS, Yale Physical Activity Scale.

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age-related decreases in cognitive functioning are known to result in slower processing speed and increase in RT. slowing is also observed in cognitively intact elderly persons (Gorus et al., 2006). Previously, Bautmans et al. reported a significantly (p < 0.001) longer RT (+32%) in older subjects (80 \pm 5 years) compared to young controls (26 \pm 3 years) during a simple (upper-limb) point-to-point RT-test. The difference between young and old participants was 2,4-fold higher for MT compared to PMT (Bautmans et al., 2011). This is in line with other RT studies (Gorus et al., 2006; Rossit and Harvey, 2008; Wolkorte et al., 2014) showing that the age-related increase of RT in healthy and cognitively intact older persons is most pronounced during the movement phase of the RT task. Interestingly, Bautmans et al. have shown that in older persons, longer RT was significantly (p = 0.001) related to a higher early co-activation of the antagonist muscle during the PMT, i.e. before the start of the movement. On the one hand, a higher co-activation of the antagonist muscle in older persons can improve joint stability as a compensation for age-related muscle weakness (Hortobagyi and DeVita, 2000), but on the other hand it will counteract

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and lower the net force exerted by the agonist muscle (Macaluso et al., 2002; Holsgaard-Larsen et al., 2011).

A supplementary element that can contribute to a longer RT in the elderly is an altered firing sequence of agonist and antagonist muscles. In healthy subjects a smooth, single-joint voluntary movement is usually characterized by a triphasic muscle activation pattern, consisting of an initial burst of agonist muscle activity (AG1), followed by a burst in antagonist muscle activity (ANT) and a second agonist burst (AG2) respectively (Hallett et al., 1975; Berardelli et al., 1996). It is assumed that AG1 provides the impulsive force to start the movement, that ANT halts the movement at the desired end-point, and that AG2 damps down the effect of ANT at the end of the movement (Berardelli et al., 1996). Pfann et al. (2004) reported that with slower movement speed older persons consistently show a more biphasic muscle activation pattern (an initial agonist muscle burst followed by an antagonist muscle burst) in point-to-point movements. However, age-related changes in muscle activation pattern are barely understood, and its relation to RT remains unclear. Therefore we investigated the difference in agonist and antagonist muscle activation pattern between elderly and young healthy subjects during a point-to-point RT test. We hypothesized that the increased antagonist muscle co-activation at the early phase of the RT task described previously in older persons (Bautmans et al., 2011) would be accompanied by an early activation of the antagonist muscle, and a delayed agonist muscle activation. Here, we found that in the aged the firing sequence is profoundly altered, characterized by a delayed muscle activation following stimulus onset, and a significantly earlier recruitment of the antagonist muscle before movement onset.

2. Methods

2.1. Participants

Participants and measurement procedures have been described previously in detail (Bautmans et al., 2011). In summary, 124 apparently healthy subjects participated in our study, among whom were 60 young subjects (30 male, 30 female, aged 26 \pm 3 years) and 64 community-dwelling elderly (32 male, 32 female, aged 80 ± 6 years). The participants were recruited via the university community, seniors associations, poster and flyer advertisements, and mailings. Subjects were excluded when presenting functional disability of the dominant upper extremity (paresis/paralysis, tremor or recent surgery), cognitive decline (Mini Mental State Examination (MMSE) score < 24/30 (Folstein, Folstein et al., 1975)), neurologic disorders, acute or uncontrolled conditions, or chronic inflammatory pathology. According to the present guidelines (Ferrucci et al., 2004), stable morbidity was not an exclusion criterion per se for older participants. None of the participants was involved in a specific training program or a trained master athlete. In this way a representative older population was obtained. The study was approved by the Medical Ethics Committees of the Universitair Ziekenhuis Brussel (Belgium) and the Erasmus Universitair Medisch Centrum Rotterdam (The Netherlands); and all participants gave written informed consent.

2.2. Measurements

2.2.1. Clinical characteristics

Height and weight were measured, and self-reported morbidity and medication use were recorded. All participants completed the Yale Physical Activity Survey (YPAS) questionnaire and the Activity Dimensions Summary score (YPAS-ADS) was calculated, reflecting the subject's physical activity (vigorous activity, leisure walking, moving, standing and sitting) over the last month on a scale from 0 (no activity at all) to 177 (maximal activity) (Dipietro et al., 1993). For descriptive purposes dependency for basic activities of daily life (bADL) was rated using a 6-item scale (bathing, dressing, transfers, use of toilet, continence and eating)

as described by Katz et al. (1963), complemented by orientation in time and place. Each item was scored from 1 (completely independent or no problem in orientation) to 4 (completely dependent or completely disoriented). Dependency for instrumental ADL (iADL) was evaluated using a 9-item questionnaire (telephone use, transportation, shopping, food preparation, housekeeping, handy-man work, laundry, medication use and handling finances) following Lawton et al. (1982). Each item was scored from 1 (completely dependent) to 3 (completely independent). Cognitive functioning was assessed using the Mini Mental State Examination (MMSE) (Folstein, Folstein et al., 1975). MMSE-scores > 23/30 were considered as normal.

2.2.2. Reaction time test

A detailed description of the experimental setup can be found in our previous report (Bautmans et al., 2011). The participants performed the RT-test which was preceded by a familiarization session (consisting in 15 trials). Simple, point-to-point RT was assessed using a modified van Zomeren RT-device as described previously (Gorus et al., 2006). Briefly, the device consists of a control panel (connected to a computer) with a central ready button around which eight pushbuttons (that can be illuminated) are arranged in a semicircle. The subject was positioned in front of a horizontally placed control panel with the trunk stabilized to the chair's back support using a belt (eliminating trunk movement). The elbow rested on an articulating elbow support, thus allowing unrestricted elbow extension movement (in a horizontal plane) and maximally reducing postural activity of Mm. Biceps & Triceps Brachii at rest. The position of the control panel was adjusted in order to obtain 60° abduction in the shoulder and 100° elbow extension (when target pushbutton pressed). Movements of the upper arm and hand were monitored using ADXL202 uniaxial piezo-resistive accelerometers (Analog devices, Breda, The Netherlands, adapted by Temec Instruments, Kerkrade, The Netherlands), attached with adhesive tape on the lateral epicondyle (one accelerometer, directed towards the target pushbutton in horizontal plane) and on the processus styloideus of the ulna (three accelerometers, X-axis directed towards the target pushbutton in horizontal plane, Y- and Z-axis perpendicular to respectively X- and Y-axis).

During the RT-test, subjects had to hold down the central ready button to trigger stimulus onset; stimulus offset was attained by pressing the illuminated target button. The RT-assessment protocol in this study consisted in a simple, non-choice RT-test during which always the same target button was used (the fourth or fifth pushbutton for respectively left- and right-handed subjects; 13 cm distance between central ready and target button). Participants were instructed to respond as quickly and accurately as possible and, after response offset, to return immediately to the central pushbutton, thereby triggering the stimulus onset for the next trial. Tasks were made self-paced, meaning that the next inter-stimulus interval (randomly fluctuating between 3 to 6 s) only started after the participant has returned to the central pushbutton. PMT was defined as the interval between stimulus onset and the moment when the subject releases the central button; and MT as the time needed to move the finger to the peripheral response button (using standardized elbow-extension, involving M. Triceps Brachii contraction) (see online Supplementary Material for pictures of the different phases of the RT test). The activity of the central and target pushbuttons were synchronously sampled at 12500 Hz, together with the accelerometers' signals and sEMG of the Mm Biceps & Triceps Brachii (see Fig. 1), and stored on a personal computer for further analysis.

2.2.3. Surface electromyography and signal processing

Self-adhesive pre-gelled electrodes (Ag/Cl, 10 mm diameter, 20 mm inter-electrode distance) were placed over the M. Biceps Brachii Caput Breve, M. Triceps Brachii Caput Longum and one reference electrode on the spinal processus of the seventh cervical vertebra (the skin was cleaned using pure alcohol and shaved when necessary) according to

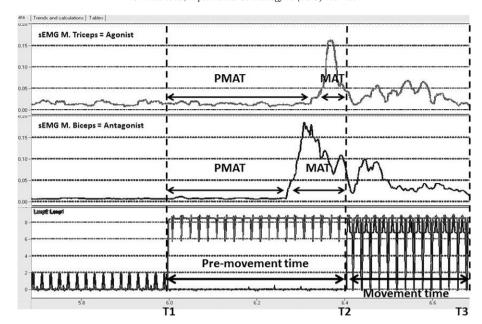


Fig. 1. Signal plot during RT. Representative plot of synchronously sampled sEMG of Mm. Biceps & Triceps Brachii (for illustrative purposes full-wave rectified and RMS-smoothed over 2 ms) and signals of the pushbuttons during a single RT-stimulus in a female participant aged 85 years. PMAT = pre-movement activation time, MAT = movement activation time, T1 = illumination of target pushbutton (visual stimulus, start of PMT), T2 = release of the central ready pushbutton (end of PMT and start of MT), T3 = pressing the target pushbutton (end of MT).

the SENIAM-recommendations (Hermens et al., 2000). sEMG sensors were connected to a universal amplifier (MPAQ, IDEE/Maastricht Instruments, Maastricht, The Netherlands) using shielded wires in order to avoid movement artifacts. All raw sEMG signals were simultaneously sampled at 12500 Hz (Butterworth 4th order, band-pass 10–5000 Hz and notch-filtered) and stored on a personal computer.

Signal processing was performed using data-acquisition software (IdeeQ version 2.9b3, IDEE/Maastricht Instruments, Maastricht, The Netherlands). For the RT-test, 28 stimuli were generated by the test device. When errors occurred (i.e. when MT > 3 s) the system automatically generated a replacement stimulus. Additionally, an observer recorded the wrongly executed trials during the RT-test (e.g. when the subject missed the target pushbutton or made aberrant movements with the arm). The correctly executed trials were confirmed by offline visual inspection of the accelerometer signals. For each participant, at least 23 correctly executed trials (stimuli) were available for data analysis. Median RT, PMT and MT were calculated based on the first available 23 trials, as described previously (Bautmans et al., 2011). The raw sEMG signals of the Mm. Biceps and Triceps Brachii were full-wave rectified and RMS-smoothed over 20 ms. For each RT-trial, the onset of muscle activation was determined as the time point at which the sEMG amplitude exceeded the peak value of the rest sEMG signal (calculated over 250 ms preceding visual onset of the first sEMG burst). For each of the 23 RT-trials, muscle activation time relative to stimulus onset (premovement activation time, PMAT), and relative to movement onset (movement activation time, MAT) were calculated (see Fig. 1), and expressed as mean values, computed as:

$$\begin{aligned} & \text{Muscle PMAT } &= \frac{1}{23} * \sum_{2i=1}^{23} \textit{PMAT}_i \\ & \text{Muscle MAT } &= \frac{1}{23} * \sum_{i=1}^{23} \textit{MAT}_i. \end{aligned}$$

Similarly, PMAT was expressed as a percentage of PMT (%PMAT) for each of the 23 RT-trials, and expressed as mean value, computed as

Muscle %PMAT =
$$\frac{1}{23} * \sum_{i=1}^{23} \frac{PMAT_i}{PMT_i}$$
.

2.3. Statistical analysis

Statistical analysis was performed using IBM SPSS statistics 22.0.0. Differences according to age-groups (young versus old), as well as the interaction with gender, were analyzed for all continuous outcome measures using two-way Analysis Of Variance (ANOVA). Since bADL, iADL and MMSE are expressed on ordinal scales, as well as to reduce potential bias due to possible outliers, Spearman's Rho correlation coefficients were computed to analyze relations of muscle activation with PMT, MT, RT and clinical characteristics. Significance was set a priori at $p < 0.05. \ \,$

3. Results

The clinical characteristics of the participants are reported in detail elsewhere (Bautmans et al., 2011). Briefly, none of the older participants showed problematic MMSE or dependency scores and no significant difference was found in physical activity (based on the YPAS-ADS) between both groups (see Table 1).

For both M. Biceps Brachii (acting as an antagonist during the RTtest) and M. Triceps Brachii (acting as an agonist during the RT-test) PMAT was significantly longer in the old subjects compared to the young (258 \pm 53 ms versus 224 \pm 37 ms, p = 0.042 for Biceps and 280 \pm 70 ms versus 218 \pm 43 ms for Triceps, p < 0.01) (see Fig. 2). The elderly thus showed a delayed muscle activation in these muscles compared to the young. Longer M. Triceps Brachii PMAT was significantly related to worse PMT & total RT in young (respectively r = 0.76 & r =0.68, p < 0.001) and elderly (respectively $r = 0.42 \ \& \ r = 0.40$, p = 0.001). For neither M. Biceps nor for M. Triceps Brachii PMAT, MAT and %PMAT, significant relationships were found with cognition (MMSE-score), dependency (bADL and iADL), physical activity (YPAS-ADS), morbidity or medication use; neither in the elderly nor in the young participants separately. M. Biceps Brachii MAT was significantly longer in elderly than in young (65 \pm 42 ms versus 50 \pm 36, p = 0.01) whereas for the M. Triceps Brachii MAT no significant difference was found (43 \pm 63 ms in elderly versus 57 \pm 27 ms in young, p = 0.652) (see Fig. 2). The mean difference in MAT between M. Biceps Brachii and M. Triceps Brachii in the young ones was 6 \pm

Table 1 Participants' characteristics.

Parameter	Young subjects (N = 60)	Old subjects $(N = 64)$
Female	50%	50%
Age (years)*	26.0 ± 3.0	79.6 ± 4.5
MMSE (score: 0-30)	-	28.6 ± 1.5
bADL-dependency (score: 8-32)	-	8.3 ± 0.6
iADL-dependency (score: 9-27)	-	26.0 ± 1.8
YPAS-ADS (score: 0-177)	55.1 ± 20.5	49.6 ± 32.8
PMT (ms)*	269.5 ± 29.1	310.6 ± 41.2
MT (ms)*	176.7 ± 33.6	277.7 ± 73.2
RT (ms)*	450.5 ± 54.2	595.2 ± 102.3

Mean \pm SD. *Significant difference between young and old subjects (p < 0.01, two-way ANOVA, no significant interaction with gender); MMSE = Mini-Mental-State examination; bADL & iADL = respectively basic and instrumental activities of daily life; YPAS-ADS = Activity Dimensions Summary score of the Yale Physical Activity Survey; PMT = pre-movement time; MT = movement time; RT = total reaction time.

47 ms (p = 0.311), whereas for the elderly the difference was -22 ± 55 ms (p = 0.003). A positive difference means that the agonist muscle (M. Triceps Brachii) activates first, while a negative one means that the antagonist muscle (M. Biceps Brachii) activates first. No significant interaction with gender was found. The %PMAT (= PMAT/PMT) of M. Biceps Brachii was similar in both groups (80 \pm 13% in elderly versus 82 \pm 13% in young, p = 0.321) whereas the %PMAT of M. Triceps Brachii was significantly higher in elderly compared to young (87 \pm 21% versus 79 \pm 10%, p < 0.01) (see Fig. 3). Since total PMT corresponds to 100%, 87% PMAT of M. Triceps Brachii means that this muscle activates when 87% of the PMT is elapsed. Consequently, in elderly the M. Triceps Brachii activates at a later stage during the pre-movement phase compared with the young.

4. Discussion

In this experiment we explored the difference in agonist and antagonist muscle activation pattern between elderly and young healthy subjects during a point-to-point RT test. We hypothesized that the increased antagonist muscle co-activation at the early phase of the RT task that we described previously in older persons (Bautmans et al., 2011) would be accompanied by an early activation of the antagonist muscle and a delayed agonist muscle activation. Here, we found that in the aged the firing sequence of agonist and antagonist muscles is profoundly altered.

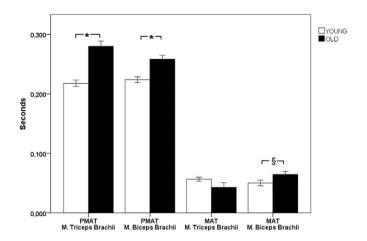


Fig. 2. Pre-movement activation time and movement activation time during point-to-point reaction time test. Significant difference between young and old subjects *p < 0.01, $\S p < 0.05$ (ANOVA, no interaction with gender); bars represent mean \pm SE (based on 23 trials); PMAT = pre-movement activation time; MAT = movement activation time.

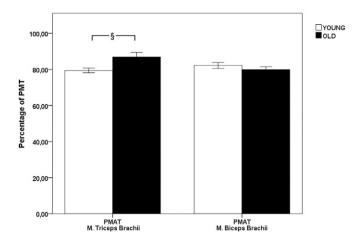


Fig. 3. Muscle pre-movement activation time as percentage of total pre-movement time during point-to-point reaction time test. Significant difference between young and old subjects p < 0.05 (ANOVA, no interaction with gender); bars represent mean \pm SE (based on 23 trials); PMAT = pre-movement activation time. PMT = pre-movement time.

A first important observation was a significantly delayed muscle activation following stimulus onset in the older participants. In fact, in the elderly PMAT was significantly longer for M. Biceps and M. Triceps Brachii compared to the young. The temporal delay in pre-movement activation of the agonist muscle (i.e. longer PMAT) confirms the results of Lewis and Brown (1994) who found a significantly longer agonist (in their study the M. Biceps Brachii) muscle activation time which was associated with a longer pre-movement time in elderly compared to younger subjects. We also found that longer agonist PMAT was significantly related to worse PMT and RT. In our RT-test, PMAT represents the time necessary for stimulus reception, integration and decision making in the central nervous system, preparation of the motor program, and sending motor commands to the muscles. Since subjects presenting MMSE-scores < 24/30 were excluded from our study, we believe that our results are not biased by dementia. As previously stated by Salthouse, "nearly all studies with reaction time tasks have found that young adults respond faster than older adults" (Salthouse, 2000); however, the psychophysiological and neurobiological mechanisms are not yet fully understood. In their literature review, Manini et al. (2013) recently described that the age-related alteration in communication from neuron to skeletal muscle can be due to a decline of dopaminergic neurotransmission and impairment of corticospinal excitability. In addition, in elderly persons motor- and cognition-related cortical and subcortical areas are over-activated when performing a motor task (Mattay et al., 2002; Nesselroade and Salthouse, 2004; Heuninckx et al., 2005; Seidler et al., 2010). Also it is observed that in elderly persons, movement preparation leads to additional cortical activity, which is most prominent in the prefrontal cortex (Vallesi et al., 2009; Berchicci et al., 2012). Preparation of movement is suggested to be less optimal in older subjects (Wolkorte et al., 2014).

Secondly, we observed a significantly earlier recruitment of the antagonist muscle before movement onset in the elderly subjects compared to the young. In fact, MAT was significantly longer in the elderly compared to the young for the antagonist muscle (M. Biceps Brachii), but not for the agonist muscle (M. Triceps Brachii). Moreover, we found that %PMAT of M. Biceps was significantly smaller than %PMAT of M. Triceps, which means that in the elderly participants the antagonist muscle activated earlier than the agonist muscle in the premovement phase. Reduced reciprocal inhibition through the 1a inhibitory interneuron is a possible underlying mechanism for increased antagonist muscle activity observed in elderly persons (Hortobagyi and Devita, 2006). However this leaves unaddressed the timing issue. It is suggested that inaccuracies in the scaling of flexion, extension and co-activation commands may underlie the altered muscle activation

with aging (Hortobagyi and Devita, 2006). Early activation of the antagonist muscle (M. Biceps Brachii) may prolong the pre-movement phase (i.e. longer PMT). From a biomechanical point of view, the early (co-)activation of the antagonist muscle, before the start of the movement, may hinder the agonist muscle to generate force thus increasing the time necessary to start the movement task. Interestingly, Burke and Kamen (1996) found evidence that during a simple RT-test elderly persons need additional time to activate a sufficient number of alpha motor neurons to initiate a muscle contraction. Several authors have described that, compared to young persons, elderly show different motor strategies and associated brain activity (Bernard and Seidler, 2012; Heetkamp et al., 2014). In fact, the differences in co-activation of antagonist muscles during voluntary motor tasks might be related to age-related changes in activation and inhibition patterns at the cortical level. In a review of Papegaaij et al. (2014) it is speculated that the reduced cortical reciprocal inhibition plays a role in the increased antagonist muscle coactivation seen in elderly subjects. The authors describe that aging causes a reorganization of the cortical control of voluntary movement, which is characterized by an increase in brain activation and a decrease in cortical inhibition.

In our study, the participants had no functional disabilities in ADL. However, it cannot be excluded that this earlier activation of the antagonist muscle is more pronounced in disabled older persons. Future studies including physically impaired older persons are necessary to explore this aspect. However, the relevance of our findings with respect to function in older persons is supported by previous research. A significant relationship between RT-performance and physical functioning, dependency, fall-risk and mortality in elderly persons has been reported (Dhesi et al., 2002; Petrella et al., 2004; Metter et al., 2005). Interestingly, Pijnappels et al. showed that simple point-to-point RT performance (using a light as stimulus and a finger-press as response) was significantly related to balance, choice-stepping RT as well as the occurrence of multiple falls within 1 year follow-up in elderly retirement-village residents (Pijnappels et al., 2010). During the choice-stepping RT-test subjects were instructed to step on an illuminating panel (out of 4 placed in front and aside each foot) as quickly as possible (Pijnappels et al., 2010). Possibly, more pronounced disturbances in agonistantagonist muscle activation similar to the age-related changes we describe here might be related to increased fall risk in elderly persons.

Although the exact mechanisms of the age-related differences in muscle activation that we observed in our participants remain unclear, we have provided more insight in the presence of altered antagonist muscle co-activation during an RT-test, which might be responsible for increased RT in elderly persons. Since resistance training may decrease antagonist muscle co-activation (Arnold and Bautmans, 2014) and large effect sizes for improvement of response time during and following intermediate intensity exercise were described (McMorris et al., 2011), it would be worthwhile to investigate the effect of physical exercise on these temporal issues in agonist–antagonist recruitment during an RT-test and/or rapid movements.

5. Conclusions

We conclude that in elderly persons the muscle firing sequence is profoundly altered, characterized by a delayed muscle activation following stimulus onset, and a significantly earlier recruitment of the antagonist muscle before movement onset. Since our elderly participants were cognitively intact, the source of these alterations is probably located within the neuromuscular system, and might be a target for exercise interventions.

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