



Chronic stroke and aging: The impact of acoustic stimulus intensity on fractionated reaction time

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ABSTRACT

In control samples, intense acoustic “go” stimuli accelerate the central and peripheral motor processes that compose simple reaction time movements. The goal of the current study was to determine whether movements that are initiated to intense acoustic cues facilitate simple reaction times in (1) adults with chronic stroke as compared to age matched controls and (2) in older as compared to younger adults. EMG and force data were collected from three groups (stroke, older adults, and younger adults) during a ballistic wrist and finger extension task. Movements were made to the onset of 80 dB and 107 dB acoustic cues and simple reaction times were fractionated into premotor and motor components. The present findings offer two important contributions to the literature. First, increases in stimulus intensity led to faster motor times in the impaired limb of stroke subjects. Second, increased stimulus intensity led to faster premotor reaction times across all groups, although an age rather than a stroke-specific motor deficit was evidenced, with the younger control group displaying significantly faster premotor times. Findings are integrated with previous evidence concerning post stroke corticospinal tract integrity and are interpreted via mechanisms which address stroke and age-related changes in motoneurons and activity in motor units.

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Chronic unilateral motor dysfunctions in the upper extremity severely limit instrumental movements of daily living [1]. However, empirical evidence from multiple treatment interventions indicates that many stroke survivors are able to regain voluntary control after a considerable amount of movement-based activity [6–9]. Indeed, neural plasticity in chronic stroke is at the forefront of relearning voluntary movements. Identifying viable variables that facilitate voluntary movements in chronic stroke remains a focus of considerable interest.

Over a century ago, researchers discovered that increases in stimulus intensity lead to a reduction in reaction time (RT) [28]. Quicker RT under these conditions is thought to reflect accelerated sensory and perceptual processing manifested in the presence of more intense physical stimuli [18]. More recent evidence confirmed that during movement planning, simple premotor RTs are significantly faster when an unexpected intense acoustic stimulus replaces or accompanies a visual ‘go’ signal [e.g., 4,5,24]. For instance, Carlsen et al. [4] reported that premotor RTs progressively decreased across dB levels (83 dB, 93 dB, 103 dB, 113 dB, 123 dB)

in healthy young adults, reaching asymptote at 113 dB. Notably, however, when intense acoustic cues elicited a startle response (as indexed via muscle activity in the sternocleidomastoid), the authors argued that the *startle circuit* was activated, leading to the conclusion that the startle circuit is distinct from other circuits underlying stimulus intensity effects.

Extending the implications of this work, recent evidence indicates that movements are facilitated by the presentation of startle cues among a sample of stroke patients [16,22]. Rothwell [22] reported data from eight stroke participants in which preplanned movements of the wrist and ankle were executed to the onset of a loud acoustic stimulus. EMG amplitudes were greater and the onset latency of movement was much shorter following the loud acoustic stimulus than when voluntary movements were made alone, or when unplanned movements were executed to the startle cue. Further, Jankelowitz and Colebatch [16] presented auditory cues at 120 dB and reported that approximately one quarter of the patients tested had exaggerated startle responses in the biceps of the clinically affected side. Together these data suggest that intense startle triggering acoustic cues facilitate activity in the motor system. However, each of these protocols used startle eliciting acoustic cues and did not investigate whether sub-startle stimulus intensity effects [4,11] were evident in prepared voluntary movements post stroke. As such, the primary aim in the current study was to determine the extent of intensity related facilitation post stroke.

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Table 1
Stroke participant characteristics.

Sex	Age (years)	Hand dominance	Side of lesion	Impaired side	Months since stroke	# Strokes	Box and Blocks ^a recovery ratio (%)
M	75	RH	R	LH	82	1	17/51 = 33
M	72	RH	L	RH	136	1	26/70 = 37
M	63	RH	L	RH	168	1	21/77 = 27
M	75	RH	R	LH	84	1	2/54 = 4
M	67	RH	R	LH	36	1	52/58 = 90
M	59	RH	R	LH	95	1	14/42 = 33
M	76	RH	R	LH	90	1	21/48 = 44
F	68	RH	R	LH	43	1	66/68 = 97
M	50	RH	L	RH	113	2 ^b	2/56 = 4

^a # Blocks moved by each limb. Recovery ratio = (# impaired/# unimpaired) × 100.

^b Both strokes were in the left hemisphere.

The second goal of the current study was to determine the extent of intensity related facilitation in the aging motor system. Simple RT responses begin to steadily slow once a person reaches 30 years of age, and continue to slow throughout the remaining lifespan [12]. Evidence suggests that age-related changes in the organization of the motor system are such that as age progresses, so too does the level/intensity of stimulation that the motor system requires to achieve the same outcome. For instance, Pitcher and colleagues used TMS to demonstrate that increased stimulus intensities were necessary to induce equivalent amplitude MEPs in older as compared to younger adults [21]. To date, although independent studies suggest that stimulus intensity is negatively associated with RT across age ranges [4,11,22], the impact of stimulus intensity on the RTs of varying age groups has not been tested in one study.

The present experiment quantified the effect of acoustic stimulus intensity (80 dB and 107 dB) on initiating upper extremity movements in chronic stroke, while comparing these effects with younger and older healthy adult control groups. Consistent with contemporary and classic fractionated RT studies [3,4,10,11,26], we calculated two traditional components: (a) a central index; represented by premotor RT, and (b) a peripheral index; represented by motor time. Three hypotheses were tested: (1) Premotor RT and motor time displayed by the impaired limb of the stroke group will be slowest compared to all other Group × Limb × Stimulus Intensity conditions. (2) Premotor RT and motor time will be faster to 107 dB cues as compared to 80 dB cues for each limb across group. (3) The younger control group will display faster premotor RT and motor time when compared to the stroke and older control group.

Table 1 shows the demographic characteristics of the stroke group. Admission criteria for the stroke group were: (1) diagnosis of no more than two strokes; (2) a lower limit of 10° of voluntary wrist/fingers extension from an 80° wrist flexed position; (3) the absence of other neurological deficits; (4) normal or corrected to normal vision and hearing; (5) Mini-Mental State Examination (MMSE) score ≥24. All participants in the older control group ($N=6$, 5 males, Mean Age = 64.60, SD = 10.45) and the younger control group ($N=9$, 8 males, Mean Age = 19.63, SD = .74) self-reported right-hand dominance, no central nervous system disorders that would affect movement, and normal or corrected to normal vision and hearing.

The study was conducted in accordance with the Declaration of Helsinki and all procedures were carried out with an adequate understanding by participants. All subjects read and signed an approved Institutional Review Board informed consent.

During each trial, participants were required to respond as quickly as possible to an acoustic stimulus (50 ms cue delivered binaurally through headphones) by initiating an isometric bimanual contraction of the wrist and finger extensor muscles against two independent load cells (left/right limb) (see Fig. 1). No participants were instructed to control the duration or amplitude of their brief contractions.

Participants completed a total of 64 experimental trials: 24 trials in which an 80 dB cue was presented, 24 trials in which a 107 dB cue was presented, and 16 trials in which no cue was presented (catch trials). Catch trials were included to prevent habituation and anticipation. The order of the trials was randomized and manipulated for each participant to ensure that the same condition (i.e., 80 dB, 107 dB, or catch) was not presented more than twice in succession. The beginning of each trial and the cue to get ready to respond was demarcated by the onset of a visual stimulus which remained on the screen for 6 s.¹ Acoustic stimuli were presented randomly between intervals of 2–4 s after trial onset. Intertrial intervals were 10–14 s.

EMG surface electrodes (silver–silver chloride electrodes, 1 cm in diameter and 2 cm apart with an epoxy-mounted preamplifier) were placed over the belly of the extensor digitorum communis and extensor carpi ulnaris muscles of the left and right arms. To index force generation during each wrist/finger extension, two 75 lb load cells embedded in cushioned platforms were altered in height to accommodate individual hand sizes. Upper limb EMG (bandpass filter 1–500 Hz) and force data were amplified by 5 K and collected at 1000 Hz via Biopac software (3.8.1, Biopac Systems Inc., Goleta, CA, USA). Trial onset/offset and auditory stimuli were controlled via a custom Labview program. Data were streamed to disk for offline analyses.

After answering questions and obtaining informed consent, participants sat in a comfortable chair positioned 1.0 m from a 19 in. LCD presentation screen. Force platform heights were adjusted, load cells were calibrated, and EMG sensors were attached to the forearm muscles. Following calibration, participants were familiarized to the protocol by completing 4 practice trials (1 × 107 dB, 2 × 80 dB, and 1 catch). At the end of testing, hands were removed from the force platforms, EMG sensors were removed, and participants were debriefed.

Two dependent variables were calculated for each trial: premotor RT and motor time. Calculations were derived from onset of muscle contractions and force production. Baseline EMG and force scores were calculated for each trial (mean score during the 150 ms preceding acoustic stimulus onset). Onset of muscle contraction was identified by locating the first time point (after presentation of the acoustic cue) where EMG signal amplitude was greater than double the baseline value [27]. Thus, premotor RT equaled the elapsed time from the onset of the acoustic cue until the initiation of muscle contraction [27]. The onset of force production was identified as the first time point where force data exceeded double the force baseline value. Motor time was then calculated as the duration of time from muscle contraction to force onset [19].

¹ Visual stimuli were a range of emotional and neutral pictures. No significant between group findings for picture content were evidenced and so data were collapsed across the picture content condition for brevity. The interested reader is directed to reference [10,11] which addressed picture content, stimulus intensity, and fractionated RT in healthy young adults.

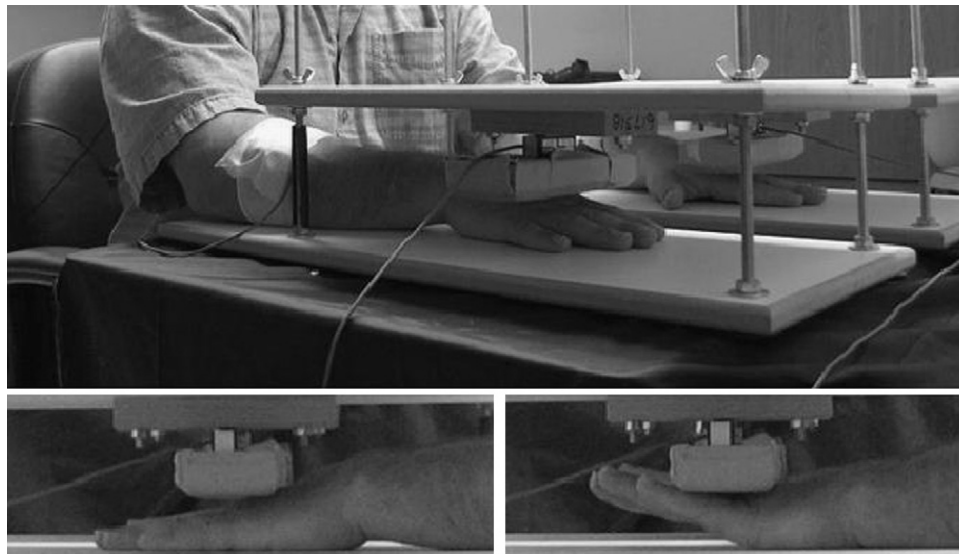


Fig. 1. Experimental setup. Top: postures of arms, forearms, and shoulders before and during the task. Bottom left: posture of hands relative to load cells during movement preparation and ITI. Bottom right: posture of hands relative to load cells during movement execution.

Summary statistics for each acoustic cue were created by averaging premotor RT and motor time for each group (stroke, older control and younger control) and for each limb (impaired, unimpaired). For the control groups, the impaired limb corresponded to their non-dominant limb and the unimpaired limb was matched to their dominant limb.

Premotor RT and motor time were each analyzed in a separate mixed design Group (3: stroke, older control, younger control) \times Limb (2: impaired, unimpaired) \times Stimulus Intensity (2: 80 dB, 107 dB) analysis of variance (ANOVA) with repeated measures on the last two factors. Tukey–Kramer's follow-up procedure was used when appropriate.

Table 2 shows premotor RT data for each group and both limbs as a function of stimulus intensity levels. The three-way ANOVA indicated two significant main effects: (1) Group, $F(1, 20) = 4.19$, $p = .030$, $\eta^2 = .30$ and (2) Stimulus Intensity, $F(1, 20) = 18.32$, $p < .001$, $\eta^2 = .48$. Post hoc analyses on the group main effect revealed that the younger control group displayed faster premotor RTs relative to the older control group and the stroke group (younger control: $M = 195.81$ ms, $SE = 17.55$; older control: $M = 256.76$ ms, $SE = 20.26$; stroke: $M = 259.97$ ms, $SE = 16.54$). In addition, the stimulus intensity findings indicated faster premotor RTs for the 107 dB acoustic cues ($M = 218.14$ ms, $SE = 12.07$) as compared to 80 dB acoustic cues ($M = 256.89$ ms, $SE = 10.00$). The main effect of limb and all interactions failed to reach significance ($p > .05$).

Analysis of the motor times indicated that reliable main effects for each factor were superseded by three significant two-way interactions: (1) Group \times Limb, $F(2, 20) = 9.29$, $p = .001$, $\eta^2 = .48$, (2) Group \times Stimulus Intensity, $F(2, 20) = 12.63$, $p < .001$, $\eta^2 = .56$, (3) Limb \times Stimulus Intensity, $F(1, 20) = 20.13$, $p < .001$, $\eta^2 = .50$. Moreover, our findings were further qualified by a reliable Group \times Limb \times Stimulus Intensity interaction, $F(2, 20) = 3.75$, $p = .041$, $\eta^2 = .27$. The significant three-way interaction confirmed our prediction that motor times would be slowest for the impaired limb of the stroke group at 80 dB relative to all other conditions. In addition, motor times were slower for the impaired limb of the stroke group to 107 dB cues relative to all other conditions, aside from the unimpaired limb of the stroke group at 80 dB and the impaired limb of the younger group at 80 dB. Finally, motor times were faster for the unimpaired limb of the younger control group following 107 dB cues as compared to the impaired limb of the younger control group at 80 dB and the unimpaired limb of the stroke group at 80 dB.

The primary goal of the current study was to determine whether movements that are initiated to intense acoustic cues would facilitate central and peripheral motor processes in adults with chronic stroke, particularly in their impaired limb. A secondary aim was to assess the impact of acoustic stimulus intensity on voluntary movements in the aging motor system. The present findings offer two important contributions to the literature.

Table 2

Mean (and SD) premotor RTs and motor times to 80 dB and 107 dB acoustic cues for the impaired and unimpaired limb for each group.

Group-limb	Premotor RT (ms)		Ratio ^a	Motor time (ms)		Ratio ^a
	80 dB Mean (SD)	107 dB Mean (SD)		80 dB Mean (SD)	107 dB Mean (SD)	
Young						
Unimpaired	227.73 (45.28)	169.82 (47.21)	134.10	35.16 (10.14)	31.32 (7.61)	112.22
Impaired	221.81 (41.76)	163.88 (44.69)	135.34	42.67 (15.67)	35.00 (10.58)	121.92
Old						
Unimpaired	271.73 (70.45)	246.88 (71.45)	110.06	40.63 (21.39)	41.90 (19.63)	96.97
Impaired	256.12 (49.76)	252.33 (73.88)	101.50	37.97 (13.01)	36.03 (8.44)	105.40
Stroke						
Unimpaired	267.73 (47.81)	224.47 (65.14)	119.28	42.74 (10.26)	37.80 (7.90)	113.04
Impaired	296.22 (57.93)	251.47 (64.98)	117.80	69.43 (14.14)	53.53 (14.80)	129.71

Note: for the younger and older control groups the unimpaired limb corresponds to the dominant limb and the impaired limb corresponds to the non-dominant limb.

^a Ratio columns for both premotor and motor times represent an index of stimulus intensity: Ratio = (80 dB/107 dB) \times 100.

First, an age effect rather than a stroke-specific effect was responsible for slower premotor RTs, with the younger control group displaying faster premotor RTs relative to both older groups. Indeed, the similarity between the older control group and the stroke group suggests that the corticospinal tracts (CST) of participants in the chronic stroke group were largely intact. Second, increases in stimulus intensity resulted in faster motor times in the impaired limb of chronic stroke participants. Although a similar pattern was evidenced in the premotor RT data, the trend was not significant. We therefore suggest that whereas mild/moderate upper limb motor deficits following stroke are reflected in both central and peripheral processes, the deficit appears to be more clearly distinguishable in peripheral motor processes (i.e., motor time). Each of these findings is elaborated further.

Analyses corroborated an age-related slowing of premotor RT [12,21] with no differences between the chronic stroke and the older control group emerging. In the current sample of stroke participants, therefore, signal conduction speed from the brain to the periphery was not significantly compromised as compared to the older control group. Although we accept that unequal group sizes and the relatively small sample size may have been partly responsible, our robust effect sizes suggest that a more plausible explanation may reside in the characteristics of our stroke group. All stroke participants were required to demonstrate partial movement prior to inclusion (i.e., 10° of initial movement), which was further qualified by our Box and Block tests derived recovery index which showed some level of recovery in all participants. Each of these indices, coupled with the premotor RT data, suggest that the corticospinal tract in the stroke group was largely intact. Hence, although recovery rates (as indexed by the Box and Block test) indicated mild/moderate severity, our findings suggest that premotor RT may function independently from the efficacy of performing a functional motor task (i.e., picking up, moving, and releasing a block).

Using a goal directed force pulse task, Ward et al. [25] demonstrated that the integrity of the CST post stroke negatively correlates with the recruitment of secondary motor areas. However, given that ~30% of the corticospinal tract fibers originate in primary motor cortex, 30% from the premotor cortex and ~40% from the somatosensory cortex [13,15,17], we suggest that premotor RT may be more affected by CST integrity as compared to the extent of post stroke cortical reorganization from primary to secondary motor areas. In the current study, the task was a simple RT response to an auditory stimulus with no limitations placed on task duration, strength, or complexity. As such, our data show that cortical motor areas and the CST were able to transfer a simple go signal from the brain to the periphery without any significant temporal deficit (relative to age-matched controls). However, our findings do not permit us to speculate on whether the group differences/similarities were driven by a reorganization of the motor system post stroke, or whether the initial stroke location spared these systems. Nevertheless, how CST integrity and motor cortex reorganization alter the speed of muscle activity onset as compared to the quality and complexity of the functional movement that may follow is important to establish and a topic for future investigation.

The impact of stroke and stimulus intensity on motor time was consistent with our first hypothesis. Specifically, the more intense 107 dB acoustic cue decreased motor times of the impaired limb to a similar level as the unimpaired limb at 80 dB. With regard to the impact of a cerebral infarction on peripheral motor processes, previous evidence has shown that: (a) the number of electrically excitable motor axons is reduced [2], (b) the range of motoneuron recruitment forces is compressed [14], (c) the ability to increase motor unit discharge rate during voluntary force increases is diminished [14], and (d) fewer high threshold motor units are recruited on the impaired as compared to the non-impaired side [20]. Collectively, the consequences of these changes in the peripheral system

may lead to a reduction in the efficiency of a muscle contraction, an increase in effort and fatigue, and a sense of weakness for force generation [14]. However, given that motor units can be driven to fire at higher frequencies after a period of audiovisual feedback training [23], we postulate that in the current study an increase in auditory stimulus intensity may have partially offset the deficits that manifest as a result of one or a potential combination of these factors.

Aside from the robust effect of stimulus intensity on the impaired limb of the stroke group, the facilitatory effect of stimulus intensity was generally less pronounced in older as compared to younger participants. This finding complements previous evidence which has shown that increased stimulus intensities are necessary to induce equivalent amplitude MEPs in older as compared to younger adults [21]. Pitcher and colleagues offer two potential mechanisms that may underlie their age-related findings, each of which can be extrapolated to the current data. Fewer spinal motoneurons may have been activated synchronously in the older as compared to the younger participants. Conversely, older participants may have engaged a similar quantity of motoneurons, but in a less synchronous manner. In the current study, either of these mechanisms may have been responsible for the aging effect as well as the lack of a stimulus intensity effect in older participants. More specifically, whereas the 27 dB increase in stimulus intensity led to reliable reductions in premotor RT and motor time in the younger group, this increase in intensity was not large enough to elicit reliable changes in the older control group or the unimpaired limb of the stroke group.

Importantly, the stimulus intensity effect was only evidenced in motor times of the impaired limb of the stroke group, suggesting that the stimulus intensity levels used in the current study may offset stroke related peripheral slowing but not an age-related slowing of central motor processes. Whether increasing stimulus intensity would impact an age-related slowing of central motor processes, and whether the intensity of an auditory startle eliciting stimulus would be greater in older as compared to younger adults has not been empirically tested. Moreover, the suggestion that the startle circuit is distinct from the circuit that mediates stimulus intensity effects [4] makes further investigation of this issue all the more compelling.

We offer four suggestions to extend the current line of research: (a) manipulation of a broader range of stimulus intensities; (b) focus on upper and lower extremity motor function; (c) record EMG data from the sternocleidomastoid and orbicularis oculi muscles to control for trials in which a startle response is elicited [4]; and (d) index and correlate CST integrity and primary/secondary motor cortex reorganization with RT measures in addition to functional measures.

In conclusion, deficits in premotor RT should not be assumed post stroke even when functional tasks show mild/moderate impairment. Indeed, results from the current stroke group suggest a level of independence between the central and peripheral motor systems and their susceptibility to stimulus intensity effects of movement initiating cues. We emphasize, however, that the current results and subsequent conclusions may well be qualified by stroke lesion location and should not be generalized to all chronic stroke patients. Finally, we did not find evidence to support the notion that increasing stimulus intensity can offset an age-related slowing of RT, although empirical tests that further manipulate increases in stimulus intensity are necessary to qualify this position.

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