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Short-interval intracortical inhibition and manual dexterity in healthy aging

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ABSTRACT

Short-interval intracortical inhibition (SICI) acting on the first dorsal interosseus was measured using paired-pulse transcranial magnetic stimulation (interstimulus interval = 2 ms) in samples of young and healthy older subjects and correlated with manual dexterity measured with the Purdue Pegboard test and two isometric force-matching tasks. There was an age-related decrease in SICI and an age-related decline in all dexterity measures. The level of SICI was not correlated with any of the dexterity measures, but the appearance of atypical facilitation (rather than inhibition) in some subjects was associated with impaired pegboard performance but not force-matching performance. We conclude that SICI at rest is reduced with healthy aging but this loss of SICI does not directly contribute to the loss of dexterity; a shift in the balance of facilitatory and inhibitory processes in motor cortex to facilitation might interfere with sequenced hand movements.

1. Introduction

The decline of motor function, including manual dexterity, with healthy aging has been well documented (see the review by Ward, 2006). While this decline is due in part to peripheral changes, such as sarcopenia and nerve conduction, interest has recently focused on functional changes in the cerebral cortex that might contribute (Hortobágyi and DeVita, 2006). More specifically, since fine motor control requires suppressing activation of muscles that are antagonistic or irrelevant to the movement, attention has been drawn to age-related changes of inhibitory processes in motor cortex that might diminish motor performance.

It is well established that coactivation of agonist and antagonist muscles, including intrinsic hand muscles, increases with aging (Burnett et al., 2000; Klass et al., 2007). While the increase in coactivation with aging has been thought of as a strategy to increase joint stiffness and thereby limit movement variability, it might also hamper dexterous hand movements. Increased coactivation with aging has been linked to an age-related loss of cortical reciprocal inhibition, shown by the loss of the inhibitory effect of electrical stimulation of afferents from a forearm flexor on the size of the motor evoked potential (MEP) elicited in a forearm extensor by transcranial magnetic stimulation (TMS) of motor cortex (Hortobágyi et al., 2006). TMS has also been used to investigate age-related changes in short-interval intracortical inhibition (SICI), an intracortical inhibitory process evident in the inhibitory effect of a conditioning TMS pulse (which is below the threshold intensity required to elicit an MEP) on the amplitude of the MEP elicited by a suprathreshold TMS pulse delivered from 1 to 6 ms after the conditioning pulse (Kujirai et al., 1993). SICI appears to play a role in manual dexterity through selective suppression of unwanted muscle activation (Stinear and Byblow, 2003), in a process of surround inhibition (Sohn and Hallett, 2004). The evidence on age-related changes in SICI is mixed: studies to date have reported less SICI at rest in an old than a young group (Peinemann et al., 2001), no difference in SICI between old and young groups (Oliviero et al., 2006), and more SICI in an old than a young group (Kossev et al., 2002; Smith et al., 2009; McGinley et al., 2010). No reported studies have investigated if SICI and manual dexterity are associated in a group including young and normally aging individuals. We therefore measured SICI in young and old subjects with larger samples than has been typical of previous research and examined the association of these measures with measures of manual dexterity from two different tasks.

2. Methods

2.1. Subjects

Data are reported for forty-nine healthy volunteers who participated in the study. There were 25 younger subjects (13 females) whose ages ranged from 18 to 29 years (median = 20 years) and 24 older subjects (13 females) whose ages ranged from 59 to 88 years (median = 68 years). The younger subjects were university students and the older subjects were recruited from the local community.

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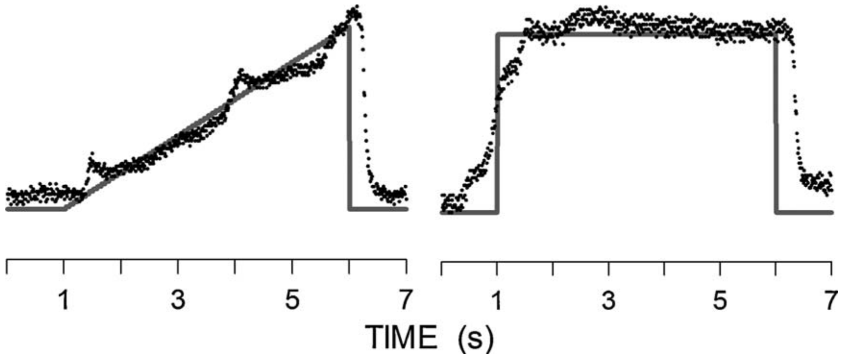

Fig. 1. Illustrative trials with a ramp target (left panel) and a square-wave target (right panel). The targets are shown as solid lines and the pinch forces as a series of points.

All subjects were self-reported right-handers and reported no motor or neurological impairment. To control for cognitive impairments that have been found to affect fine motor skill (Scherder et al., 2008) only those who scored within the normal range on the Montreal Cognitive Assessment ($\geq$26) participated (Nasreddine et al., 2005). The procedures were approved by the University's Human Research Ethics Committee and all subjects gave informed written consent before participating.

2.2. Behavioral methods

Manual dexterity was assessed with the Purdue Pegboard test and a task that required control of pinch force to match the amplitude of a target which appeared as a level change on a visual trace that moved from left to right across a computer screen with constant velocity. Administration of the Purdue Pegboard task followed the standardized testing procedure. The peg-moving subtest required subjects to retrieve small pegs from a well with one hand and to insert them, one at a time, into a vertical array of holes in the pegboard beginning at the top hole and working down. The assembly subtest required subjects to retrieve four items in turn with alternate hands (a peg, a washer, a collar, and a second washer) and to assemble them by inserting the peg in a hole, and by placing the remaining three items (the washer, the collar, and the second washer) on the peg in turn. Subjects were instructed to complete each test as quickly as possible. The measures taken were the number of pegs moved and placed by each hand in a 30-s period and the number of four-item objects assembled with both hands in a 60-s period. For the force-matching task, subjects sat in front of a computer screen with their dominant right arm supported comfortably while gripping a vertical rod fitted with two force transducers on opposed flat surfaces with a pinch grip of their thumb and index finger. On each trial, subjects controlled their pinch force to match a visual trace that moved across the screen with successive points plotted at 100 Hz. Each trace consisted of three segments, an initial 1-s segment in which the trace was steady at a baseline level, a 5-s target segment in which the trace either increased linearly to the target level (the ramp target) or jumped immediately to the target level (the square-wave target), and a final 1-s segment in which the trace returned abruptly to the baseline level. A second trace that showed the instantaneous pinch force (sampled at 100 Hz) was visible throughout the trial in the same coordinate space as the target trace. The target force level for both the ramp and square-wave targets was set at 40% of each subject's maximum pinch force which was determined immediately before testing began. Five trials were done for each target type with a 10-s inter-trial interval. Illustrative traces are shown in Fig. 1. Accuracy was quantified as the root-mean-square (RMS) error during the 5-s ramp and 5-s square-wave target segments of each trace. Precision was quantified for the ramp targets as the mean absolute residual error around the best-fitting straight line of the forces produced during the 5-s target segment. Because the forces applied during square-wave trials typically overshot the target before stabilizing, precision in these trials was quantified as the mean absolute residual error around best fitting straight line of the forces during the last 2 s of each 5-s target segment.

2.3. Electrophysiological methods

Subjects were seated in a height-adjustable chair with their right forearms supported comfortably on a cushion on a table in front of them. The importance of keeping the arm relaxed throughout the brief testing session was emphasized. Electromyographic (EMG) activity was recorded from the relaxed first dorsal interosseus (FDI) muscle of the right hand using surface Ag–AgCl electrodes in a standard belly-tendon configuration with a ground electrode placed laterally over the wrist. The EMG signal was amplified (1000×), band pass filtered at 10–1000 Hz, and digitized with 14-bit resolution at 4000 Hz.

TMS pulses were delivered by a MagStim 200^2 BiStim system through a figure-of-eight coil with a 9-cm diameter. The coil handle was oriented at 45° to the mid-sagittal line to induce current in a posterior to anterior direction, approximately perpendicular to the central sulcus. TMS pulses were delivered over the left hemisphere at the motor 'hot spot' for the right FDI muscle, defined as the scalp site at which the mean amplitude of the motor-evoked potentials (MEP) evoked by five successive single pulses was largest. SICI was measured with a conditioning-test pulse procedure with an inter-stimulus interval (ISI) of 2 ms. The intensity of the test TMS pulse was set for each subject using a computer-controlled adaptive procedure to elicit an MEP amplitude of about 1 mV in the relaxed FDI muscle (Sinclair et al., 2006). The intensity of the conditioning pulse was set at 70% of the test pulse intensity. The mean conditioning and test TMS intensities (expressed as percentages of stimulator output) were 43.3% and 61.9% respectively for the young group and 45.5% and 65.0% respectively for the old group; test stimulus intensity was not significantly different between the two age groups (Mann–Whitney $U = 123.5$, $p = .88$). Twelve single pulses and 12 paired pulses were delivered in random order, with the interval between successive pulses selected randomly from the set 6, 8, 10, and 12 s. The stimulation phase was completed in less than 4 min. MEPs were scored as both peak-to-peak amplitude and total area; because these measures were very highly correlated in all subjects (mean $r = .98$, calculated using Fisher's r-to-z transformation) only the former measure is reported here. SICI was quantified as the ratio of the median MEP amplitude from the paired-pulse trials to the median MEP amplitude from the test-pulse trials; ratios less than one indicate the presence of SICI. The ratios were log transformed prior to statistical analysis, and back transformed means and standard errors are reported.