Measuring the latency and latency distribution in the peripheral and central nervous systems using neurophysiological technique

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Synopsis

Measuring latencies and latency distributions among different cortical areas would open a new window on brain network function. While recently, neuroimaging based methods to do this have been proposed, neurophysiological techniques can provide 'ground truth' data with which to determine how long it takes for neural impulses to travel along nerve fibers within living humans. Hopf's collision technique with two electrical stimulations on the nerve bundle was used to measure latencies and latency distributions in peripheral nerves. Interhemispheric inhibition measured by transcranial magnetic stimulation was used to determine latency measurements along transcallosal fibers in the brain.

Introduction

Recent advances in neuroimaging technology have enabled non-invasive mapping of the mesoscale connectome of human brain •[1, 2]◘. However, it is currently not known how long it takes for neural impulses to travel along white matter pathways using tractography data alone. By using diffusion weighted imaging data •to measure the mean diameters and diameter distributions of nerve fibers it has been proposed that these time delays or latencies could be measured via magnetic resonance imaging in a living human brain •[3-6]◘. To test and validate this proposed pipeline, we used a variety of neurophysiological techniques to measure latencies and latency distributions both in the peripheral and central nervous systems.

Methods

Eight healthy subjects were tested. In the first experiment, Hopf's collision technique (Figure 1A) was used to measure the latency and latency distribution on the ulnar nerve in the peripheral nervous system •[7]◘. Compound muscle action potentials were recorded from the right abductor digiti minimi muscle. Electrical stimulation with supramaximal intensity was delivered at both proximal and distal sites. The interstimulus interval between the first distal stimulation and the second proximal stimulation was varied to produce collision between the distal stimulation generated antidromic action potentials and proximal stimulation generated orthodromic action potentials (Figure 1B).

In the second experiment, interhemispheric inhibition was monitored to measure the latency and latency distribution of transcallosal fibers in the central nervous system (Figure 2A). A paired-pulse transcranial magnetic stimulation technique •[8]◘ with the first conditioning stimulation applied to the right primary motor cortex and second test stimulation applied to the left motor cortex was used to measure interhemispheric inhibition from the right to left hemisphere •[9]◘. Motor evoked potentials were recorded from the right first dorsal interosseous muscle. Interhemispheric inhibition was represented as the ratio of motor evoked potential induced by paired-pulse stimulation to that induced by the second test stimulation alone.

The conduction velocity of the fibers on the ulnar nerve was calculated by dividing the distance between two stimulation sites by the interstimulus interval. The distribution of conduction velocities in the peripheral nerve fibers in the ulnar nerve bundle was calculated by dividing the muscle response produced by the second proximal stimulation after collision to the maximal action potential in the target muscle. The conduction velocities and their distribution in the corresponding transcallosal fibers in the central nervous system were calculated in a similar way by tracking the changes in interhemspheric inhibition as it related to the interstimulus interval.

Results

The Hopf's collision test showed that muscle response produced by the second stimulation at the proximal site was blocked by the antidromic action potentials generated by the first distal stimulation at short interstimulus intervals. The muscle response started to emerge at interstimulus interval of about 3 ms and increased gradually with the increment in the interval. The muscle response reached maximum at interstimulus interval of about 5 ms when neural impulses on all nerve fibers escaped from the collision (Figure 1). In the second experiment, time course of interhemispheric inhibition with 1 ms time scale in a wide range of interstimulus interval showed that inhibition started to emerge at about 8 ms interstimulus interval and increased gradually with increment in the interval (Figure 2C inset). Precise time course with 0.1 ms increment in the interstimulus interval showed that the maximal inhibition was reached at about 10 ms interval. Further increase in the interval decreased the degree of interhemispheric inhibition (Figure 2).

Discussion

A diffusion weighted neuroimaging pipeline •[3-6]◘ applied at different locations generates latencies and latency distributions matrices (also known as the latency connectome) in both the peripheral and central nervous systems. The established neurophysiological techniques showed great potential for measuring the latency and latency distribution with a temporal resolution at 0.1 ms time scale. Further studies with similar techniques but targeting other peripheral nerve fibers and cortical fibers connecting different brain areas will provide essential ground truth data for validating the latency and latency distribution measurements using

proposed neuroimaging approach. The combination of novel neuroimaging and neurophysiological techniques will also provide a window into both normal neural network function and dysfunction in disease, development, degeneration and trauma.

Conclusion

Neurophysiological techniques using noninvasive stimulation are powerful to identify the nerve fibers with different conduction velocities both in the peripheral and central nervous systems.

Acknowledgements

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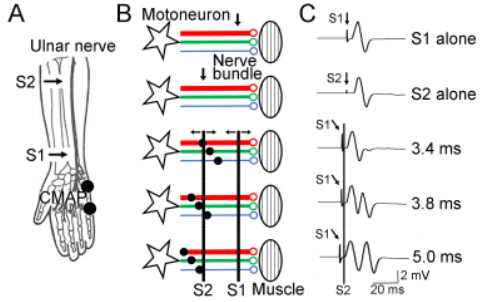
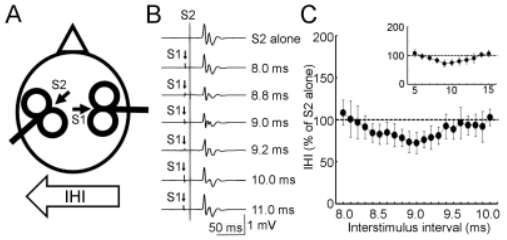
Figures



Peripheral nerve tested with Hopf's technique

(A) Experimental setup. The ulnar nerve was stimulated at distal (S1) and proximal sites (S2) with supramaximal intensity. (B) Mechanism and (C) Compound muscle action potential (CMAP) recordings under different experimental conditions. S1 alone generated both an orthodromic and antidromic currents. The antidromic current blocked S2 given after S1 at certain interstimulus interval and reduced the amplitude of the second component in the CMAP. Progressively increasing the interval allowed the antidromic current to pass the site of S2 on the nerve fibers and led to increase of CMAP.



Transcallosal fibers tested with interhemispheric inhibition.

(A) Experimental setup. Interhemispheric inhibition (IHI) from the right primary motor cortex (M1) to the left M1 was used to test the latency distribution of the transcallosal fibers. The first conditioning stimulus (S1) was given to the right M1. The second test stimulus (S2) was given to the left M1. (B) Example recording and (C) Group data analysis. S2 alone produced a test motor evoked potential (MEP) in the target muscle. S1 activated the local inhibitory interneurons in the left M1 through the transcallosal fibers and inhibited the test MEP.