Proximal receptors and the mechanical stimulation of the fingers: a somatosensory evoked potential study

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Abstract

Objective: To characterize scalp responses to mechanical stimulation of the fingers and evaluate the contribution of different receptors.

Design and methods: Somatosensory evoked responses to mechanical stimulation of the right third finger were recorded from a P3-P4 montage (n = 15) and from a F3-P4 montage (n = 9) as well as after electrical stimulation (n = 9). Responses after mechanical stimulation of the distal region of the finger, with the hand at different positions, were also recorded (n = 8). Complementary experiments in a small number of individuals included EMG and accelerometer recordings as well as anaesthesia of the finger.

Results: Scalp responses characterized by an initial sequence of waves, here called NI-PI-NII, were recorded from the P3-P4 montage. Mean peak latencies were 20, 23 and 26 ms, respectively; electrical stimulation of the same region evoked an initial negativity (mean peak latency 23 ms). EMG recordings suggested the involvement of different receptors in response to electrical and mechanical stimulation. Accelerometer recordings showed the spread of a sizable mechanical wave at the forearm. Anaesthesia did not change the responses to mechanical stimulation.

Conclusions: Relatively small mechanical stimuli applied at distal phalanxes may activate proximal receptors which generate scalp recorded responses that may completely occlude the contribution of the distal receptors.

Key-words: Evoked potentials - Somatosensory - Mechanoreceptors - Muscle spindle - Mechanical stimulation.

Introduction

Research in evoked potentials elicited by natural forms of stimulation of the human somatosensory system may improve our understanding of specific mechanoreceptor pathways and provide a basis for a more refined diagnosis of peripheral and central neuropathies. Nevertheless, the interpretation of the results of such experiments has been quite difficult due to the activation of different types of mechanoreceptors. Unfortunately, the selective activation of specific receptors is a much more difficult task than may be expected.

Experiments directed at the stimulation of mechanical skin receptors have shown that short latency potential fields can be recorded at the scalp occurring a few milliseconds later than the ones obtained after electrical stimulation of the same region (10, 18, 24, 30, 34, 16, 23, 37, 19, 20, 32, 35).

Studies of scalp potential fields elicited by articular movements have also been done and it has been suggested that the activation of muscle (36, 33, 38, 39, 2, 17, 1, 7, 8, 9, 25, 40, 29) and articular receptors (11) may also generate short latency scalp potentials.

One complexity related with these observations is that a mechanical stimulus applied to the skin can also produce articular movements and, imposed

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movements also involve the activation of cutaneous receptors.

In order to increase the selectivity of the mechanical stimulation, a stimulus represented by an "air puff" was developed (37, 19). However, it has recently been shown that, as indeed expected, increasing the intensity of such a stimulus ends up stimulating others than the intended receptors (12).

During exploratory experiments using a system to generate and record mechanical SEPs, we obtained scalp responses with *shorter* latencies than the ones recorded in response to electrical stimulation of the same anatomical region. Considerations about recording sites, conduction velocities and variations in the stimulus sites suggested that the responses were cortically-generated and elicited by the coherent activation of distal and proximal receptors (27).

In regard to the interpretation of these experiments it seemed that a further characterization of these mechanical evoked SEPs would offer an opportunity to evaluate the contribution of proximal and distal receptors to the responses generated by a natural stimulation.

Material and methods

Seventeen normal subjects (8 men and 9 women), with ages ranging from 19 to 47 years (median 32 years), were examined after giving an informed consent. Procedures were approved by a local ethics committee. On the main and complementary experimental paradigms the number of subjects varied from 3 to 15, with some of them participating in more than one experimental paradigm. The specific number of subjects examined in each experimental paradigm will be mentioned in the corresponding description of the results.

Somatosensory evoked potentials (SEPs) were recorded after mechanical and electrical stimulation.

Procedures

Subjects sat relaxed in a comfortable armchair with the forearms lying pronated on the armrests. The fingers rested naturally, with the phalanxes

partially flexed around the armrests; on the right side, the third finger was kept straight with the pad of the distal phalanx resting on the mechanical stimulus probe (position A) (the pre-indentation of the probe on the finger's pad was not measured).

In some subjects recordings were also made with the right elbow resting on the armrest with the forearm and hand fixed to a vertical support by Velcro straps. All the fingers were kept straight up except the third, which was flexed (90°) between the proximal and middle phalanx (position B). In the same series of experiments all the fingers were fixed at the proximal phalanx and the other phalanxes were flexed, except for the third finger which was kept with the distal phalanx straight (position C) (the same positions described by Gandevia et al. 14, 15). Mechanical stimulation was always applied to the pad of the right third finger distal phalanx.

Stimulus

The mechanical stimulus consisted of an upward movement of an approximately conical epoxy prong, having 1 mm² flat square surface, driven by a moving coil (Bruel-Kjaer type 4810). The amplitude of the stimulus was 0.50 mm at the peak with a rise time of 4.0 ms and a total duration of 10.0 ms. Electrical stimuli consisted of rectangular pulses, 0.2 ms in duration and with an intensity equivalent to three times the sensory threshold. Stimulus frequency was 7/s.

The electrical stimulus was applied through ring electrodes with the cathode placed proximally at the level of the distal interphalangeal joint.

In some subjects the amplitude of the mechanical stimulus was changed to lower and higher values than that previously described.

Recordings

Recording electrodes were applied to P3, P4, F3 and FZ, standard positions of the 10-20 system, after skin preparation that resulted in impedances of less than 5 kOhms. Somatosensory evoked responses were recorded in the P3-P4 montage and, in some subjects, potential differences were

also measured on the F3-P4 montage, FZ being connected to ground.

Signals were amplified, bandpass filtered (5-3,000 Hz) and averaged on a Nihon-Kohden equipment (model MEB 4200), with an acquisition window of 100 ms and a sampling rate of 10,000 samples/s. From 1,000 to 8,000 responses were averaged and replicated two to four times to assure replicability.

In some subjects recordings were obtained from the forearm flexor muscles while the subject exerted a small to moderate downward force on the epoxy prong with the third right finger. The ongoing EMG was recorded with surface electrodes placed 4 cm apart, amplified and filtered (5-3,000 Hz) and averaged while a mechanical or electrical stimulus was applied at the pad of the distal phalanx of the third finger.

In some other subjects recordings were obtained during the mechanical stimulation, in all hand positions described above, from an accelerometer (model ADXLO5 by Analog Devices) attached to the anterior surface of the mid-forearm.

Anaesthesia

In one subject a tourniquet was applied at the middle of the second phalanx and electrical responses were recorded after stimulation of the distal phalanx; when the electrical responses disappeared, responses to mechanical stimulation were obtained in positions A, B and C; in these subject the observations were repeated in different days. In another subject the same observations were repeated after the injection of a 2% solution of lidocaine around the digital nerves of the third finger at the level of the middle phalanx.

No auditory masking was used since no evoked responses were detected when the finger was not touching the vibrating probe in pilot observations.

Results

Somatosensory evoked responses to mechanical stimuli were recorded from 15 individuals. Responses with morphology and latencies (described below) suggesting the stimulation of prox-

imal receptors were found in 13 of these individuals, in the other 2 the responses had the characteristics of the responses related to distal mechanoreceptors as described by others (10, 18, 24, 30, 34, 16, 23, 37, 19, 20, 32, 35).

In these 13 individuals, the mechanically evoked responses at the P3-P4 montage were characterized by a sequence of negative-positive waves which, to avoid confusion with previously described components, will be described as NI, PI and NII. Discussions will be restricted to these 3 initial deflections (Figure 1).

The latencies of these peaks (mean \pm SD) were 20.6 \pm 1.0 ms, 23.8 \pm 1.3 ms and 26.8 \pm 1.6 ms for NI, PI and NII, respectively.

In 9 of these 13 individuals, recordings were also obtained from the F3-P4 montage and they disclosed the occurrence of peaks with similar latencies but opposite polarities (Figure 1), suggesting that these responses share similar potential fields with those generated by electrical stimulation of upper limb nerves.

The suggestion that proximal receptors are responsible for the generation of these fields was mainly based on the shorter latency of the NI wave in relation to the standard N20 peak elicited by electrical stimulation of the same region. To confirm this, electrical responses to stimulation of the distal phalanx of the third finger were recorded in the same 9 subjects of the last experiment. In all cases the latency of the N20 peak $(23.7 \pm 1.3 \text{ ms})$

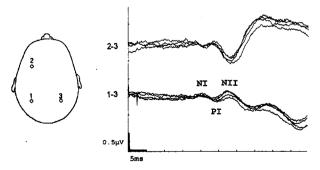


Fig. 1. – Evoked responses to mechanical stimulation of the distal phalanx of the right third finger. Upper curve recorded between F3-P4; lower curve between P3-P4. Note the apparent phase reversal between the frontal and parietal fields. NI-PI-NII peaks are marked.

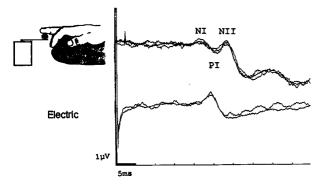


Fig. 2 – Evoked responses to mechanical and electrical stimulation of the distal phalanx of the right third finger. Upper curves obtained after mechanical stimulation; lower curves after electrical stimulation. Recordings between P3-P4.

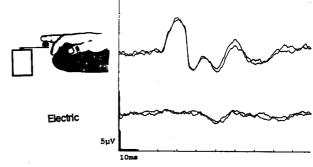


Fig. 3 – Averaged surface EMG signal from flexor muscles of the forearm, during a mild to moderate contraction. Upper curves obtained in response to mechanical stimulation of the distal phalanx of the third finger; lower curves during electrical stimulation of the same region.

was between the latencies of the NI and NII peaks in the same individuals (Figure 2).

To confirm the suggestion that the NI peak was related to activation of muscle spindles at the forearm (27), we recorded the effect of the mechanical and electrical stimuli on the ongoing EMG from the flexor muscles in the forearm. The results showed that when the distal phalanx was mechanically stimulated there was an excitatory period beginning at around 20 ms and peaking at around 30 ms, which dominated the modulation of the response. On the other hand when the distal phalanx was electrically stimulated, the response showed an excitatory period with peak occurring around 60 ms (Figure 3).

The earlier excitatory period after mechanical stimulation is compatible with the hypothesis of stimulation of muscle spindles located in the forearm, since its latency may be explained by stimulation of forearm located muscle spindles and monosynaptic influence from these receptors on motoneurons.

As muscle spindles in the forearm seemed to be responsible for the responses to mechanical stimulation applied to the third finger we decided to try to eliminate their contribution by holding the fingers in different positions. More specifically, a test was made with the third phalanx of the middle finger functionally disengaged from the flexor and extensor muscles located in the forearm. Therefore, somatosensory responses were recorded from 8 sub-

jects in the three different positions described in the Material and Methods section. Invariably when the forearm was fixed with the fingers kept straight except for the third (position B), the NI-PI peaks disappeared, remaining only the NII peak; on the other hand when the phalanxes of all fingers where flexed (position C), the NI-PI peaks reappeared (Figure 4, left), except in one individual.

These results showed that when forearm muscle spindles were functionally disengaged (position B) the first waves (NI,PI) disappeared, however, when the muscle spindles of the flexor muscles were reengaged (position C) the initial waves returned.

The findings up to this point suggested that the muscle spindles on the flexor side of the forearm were involved in the genesis of the NI wave and that the NII wave could be due to the mechanical stimulation of the distal finger mechanoreceptors.

The suggestion that the NII wave was due to distal finger mechanoreceptors was tested directly by anesthesia of the distal phalanx of the middle finger. As there was no N20 wave after electrical stimulation of the fingertip we would expect no NII wave for mechanical stimulation of the fingertip but that was not what was found. The NII wave did not disappear in any position tested (Figure 4, right). These results indicate that the NII wave is not due to distal finger mechanoreceptors stimulation.

In view of the small amplitude of the mechanical stimulus, suggesting that muscle stretch was improbable as the mechanism of spindle activation,

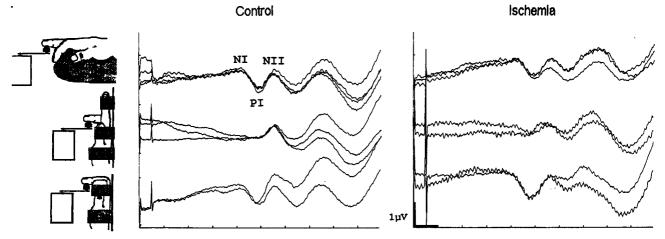


Fig. 4 – Evoked responses to mechanical stimulation of the distal phalanx of the right third finger. Recordings between P3-P4. Drawings on the left show the approximate positions of the hand and fingers (positions A, B and C as described in Methods) for the mechanical stimulation. Curves on the left are controls and on the right are after ischemic anaesthesia of the distal phalanx.

and also considering the apparently different resistance imposed by the finger to the mechanical stimulus in the different positions, it was decided to measure the amplitude of the propagated component of the mechanical wave at the level of the forearm.

In the three subjects that we measured the amplitude of the propagated wave at midforearm it was found that a sizable wave was detected at that region in all the positions tested (A, B, C), however in position B there was a clear reduction in the amplitude of the recorded wave (Figure 5).

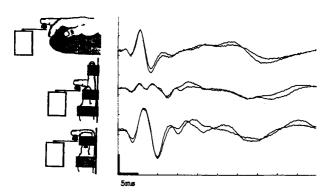


Fig. 5 – Responses obtained from an accelerometer placed on the mid-forearm during stimulation of the distal phalanx of the third finger in the three different finger positions. Calibration 0.25 m.s⁻²/vertical division.

Although the mechanical waves were complex in shape, the velocities of propagation, estimated from the time to the first deflection detected by the accelerometer and from the distance of the point of application of the stimulus to the point of attachment of the accelerometer, gave a mean value of 147 m/s and a standard deviation of 24.3 m/s.

As the last observation suggested that reduction of the propagated waves could be responsible for the disappearance of the NI-PI sequence in position B, in another three subjects the amplitude of the mechanical stimulus was changed while the hands were kept in position A. Increasing the amplitude of the stimulus did not change the responses significantly, whereas a reduction of the amplitude was associated with the disappearance of the NI-PI peaks (Figure 6).

Discussion

We obtained scalp responses to mechanical stimulation of the third finger with *shorter* latencies than the ones recorded after electrical stimulation of the same anatomical region. Even though we confirmed the initially appealing suggestion that this was due to the activation of more proximal mechanoreceptors (than those at the finger pad) two interesting aspects deserve special analysis:

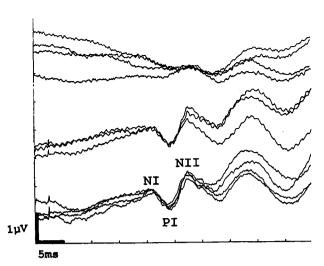


Fig. 6 – Evoked responses to mechanical stimulation of the distal phalanx of the right third finger. Responses recorded between P3-P4. The upper group of curves was obtained with reduced amplitude of the mechanical stimulator, the middle group of curves with the same intensity used in most experiments and the lower group with a larger amplitude. Note that the peak latency of the first negativity on the upper group of curves is similar to the peak latency of the second negative peak on the curves obtained with larger amplitudes.

i) the mechanism of activation of the receptors with the consequent effect on the scalp responses and ii) the observation that, at low levels of stimulation, responses with latencies *longer* than the ones caused by electrical stimulation of the fingertip could also be caused by more proximal receptors.

Response characteristics

The scalp responses studied here occurred frequently, they were observed in 87% (13/15) of the subjects.

Using the ipsilateral parietal scalp as a reference, an exploring electrode on the contralateral parietal scalp disclosed the peaks NI, PI and NII. The sequence of waves (NI-PI-NII) recorded in the parietal-parietal montage, between approximately 19 and 30 ms, gave to the recorded response a unique morphology, while responses to electrical stimulation of the distal phalanx showed, at this same time base, an initial negative peak (N23) followed by a positivity (P30).

Receptors involved

Electrical stimulation of the distal phalanx evoked an initial cortical response (N23), peaking about 3 ms after the NI peak and 3 ms before the NII peak. Blocking conduction of the digital nerves was associated with disappearance of the responses after electrical stimulation and persistence of the responses after mechanical stimulation. These observations leave little doubt that these NI-PI-NII waves relate to the stimulation of proximal receptors.

What receptors are then involved?

Articular receptors are unlikely to be involved, since no overt movement was produced, and it was shown that they tend to fire in response to large movements (6). Among the other possible involved receptors, Pacinian corpuscles and muscle spindles are potential candidates. Both receptors are very sensitive to the passage of fast mechanical waves and their impulses are conducted by fast fibers at the peripheral nervous system. The EMG recordings suggest that muscle spindles of forearm muscles were indeed stimulated.

Mechanism of receptor activation

Changing from position A to B, eliminated the possibility of stretch as the mechanism of activation of muscle spindles; a situation reversed for the flexor muscles, but not for extensor muscles, in position C; accordingly the scalp potential changed with these maneuvers as if stretch of the flexor muscles was the mechanism of spindles activation. However, the possibility that other mechanisms of activation of the receptors could be involved was tested by the measurement of the propagated mechanical wave at the forearm in the three positions. These measurements indicated that in position B there was an accentuated reduction of the amplitude of the propagated wave. This observation could also explain our results. In favor of this last explanation is the observation of similar changes in the evoked responses after reduction in the stimulus intensity.

As the mechanical stimulus on the distal phalanx would probably be too small to cause enough stretch of the flexor muscles, propagation of the mechanical wave through the forearm, therefore, seems to be responsible for the activation of proximal receptors.

A sizable mechanical wave propagated through the forearm as documented by the accelerometer measurements. The corresponding propagation velocity was estimated at around 147 m/s, which is in accordance with the data of Burke et al. (5) but does not agree with what was found or assumed by others of 40-80 m/s (13, 7).

If we assume that the conduction velocity of the fastest peripheral fibers in the upper limbs are of the order of 67-83 m/s (26), it is clear that the propagation velocities of the mechanical waves found by different researchers fall in two different cases: one with similar velocities as those of peripheral nerve fibers and the other with velocities about two times higher. If the propagation velocity of the mechanical waves and of the peripheral nerve fiber action potentials were similar then the cortical responses would be expected to occur with latencies related to the activation of the finger mechanoreceptors, since at the cortical level we would expect only some partial occlusive interaction (4, 16, 3, 31, 22, 21, 28); however if the mechanical wave propagated with a faster velocity, it could be expected that the response of the proximal receptors would completely occlude the responses related to the distal receptors (4). Our results are in accordance with the latter case since we found a complete occlusion of the response related to the activation of the mechanoreceptors located at the distal phalanx of the middle finger.

Contribution of different receptors to the response

Lowering stimulus amplitude, changed the morphology of the mechanical evoked response. Instead of the initial sequence of negative-positive-negative waves, the response changed to an initial negative wave, with the peak latency similar to that of the NII wave. Therefore it looks as if the NI-PI waves disappeared and the NII wave remained.

The simplest explanation would be that these responses are now directly related to stimulation of distal mechanoreceptors. The observations in position B suggest, however, that this may not

always be the case; similar morphological changes (accompanied by reduction in the amplitude of the propagated mechanical wave) which persisted after anaesthesia of the distal finger were observed when recording responses in this position. These observations suggest that proximal receptors were still responsible for the recorded responses. In relation to the change of the response morphology (disappearance of the NI-PI peaks with preservation of a negative peak similar to NII), our data cannot determine if it was due to a different set of proximal receptors activated at the low stimulus levels or to a less favorable signal to noise ratio at these levels of stimulation.

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