Mechanically and electrically evoked somatosensory potentials in humans: effects of stimulus presentation rate.
MECHANICALLY AND ELECTRICALLY EVOKED SOMATOSENSORY POTENTIALS IN HUMANS: EFFECTS OF STIMULUS PRESENTATION RATE

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Procedures for recording mechanically evoked potentials from various levels of the somatosensory pathway have recently been described (Pratt et al. 1979a). The mechanically evoked potentials have been compared with electrically evoked potentials (Pratt et al. 1979b), and the clinical utility of a combination of electrical and mechanical stimuli at a stimulation rate of 4/sec has been studied (Starr and Pratt in preparation). These studies required 1000 stimulus trials to define the evoked potentials. The duration of the recording session may be substantially shortened if the rate of stimulation were increased without appreciable loss in the definition of the potentials. Thus, the purpose of this study was to examine, in the same subjects, the potentials evoked at several levels of the somatosensory pathway by both mechanical cutaneous stimulation and electrical stimulation of nerves at different stimulus rates. Furthermore, changes in the evoked potentials from various levels of a pathway as a function of stimulus rate may contribute to the understanding of their generation. For instance, postsynaptic components will be affected at lower rates of stimulation than peripheral nerve components and components that are generated in a polysynaptic pathway will be increasingly sensitive to rapid stimulus rate.

Methods

Subjects were 7 adults 21—37 years old, without neurological disease. They rested on a bed in a sound-attenuating chamber, with their left hand supported on a warmed plastic mold. Digital skin temperature was monitored continuously and maintained between 33°C and 36°C. The evoked potentials from each subject were collected in a single session in response to: (1) electrical stimulation of digital nerves, (2) electrical stimulation of the median nerve at the wrist, and (3) mechanical stimulation of the fingernail. Stimuli were delivered at rates of 2, 4, 8, 16 and 32/sec. Three of the subjects were stimulated starting with the highest rate, and the remaining four starting with the lowest rate. Each recording session lasted 4—5 h during which subjects usually fell asleep.

The electrical stimuli were 0.2 msec duration square pulses of constant current, delivered to the digital nerves through ring electrodes around the middle and proximal phalanges of the index finger, or to the median nerve through silver cup electrodes, placed at the wrist 3—4 cm apart, over and parallel to the nerve. The proximal electrode of each pair was the cathode. The current was adjusted to a level just below that producing either discomfort or a muscle twitch (in median nerve

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stimulation), whichever was lower.

The mechanical stimulus was generated by activating a moving coil vibrator with a 5 msec duration electric pulse. This pulse was shorter than the 50 msec duration pulse used in our previous studies (Pratt et al. 1979a, b), since the latter could only be used up to 16/sec. In order to verify the relevance of the findings using the shorter duration pulse to the findings in our previous studies which used the 50 msec pulse, and in order to evaluate the contribution of ‘off’ responding cutaneous fiber input, the potentials evoked by the two pulse durations were compared at rates of 2--16/sec. The sound produced by the movement of the vibrator was masked by white noise from a speaker near the subject. Further details of the mechanical stimulus have been provided elsewhere (Pratt et al. 1979a). The wave form of the force applied by the vibrator was monitored simultaneously with mechanical stimulation using a strain gauge.

Digital nerve potentials to electrical stimulation at the wrist were recorded from the ring electrodes on the digit. The other recording electrodes were 9 mm diameter silver cups attached to the skin, with resistance less than 3 kΩ. Recordings were obtained from appropriately placed surface electrodes over the peripheral nerve at the wrist, near the axilla, and over the brachial plexus (Erb’s point). The potentials recorded from an electrode placed over the second cervical vertebra (CII) referenced to the middle of the forehead (Fpz) included spinal cord activity. Cortical activity was recorded from a scalp electrode at C4 (according to the 10-20 system) referenced to Fpz. When the electrode at C4 was referenced to the contralateral Erb’s point electrode, components reflecting activity from peripheral nerve, spinal cord, subcortical somatosensory pathway and cortex could be simultaneously detected. The electrode configurations used for each stimulus modality are included in Fig. 2.

The potentials were amplified with a gain of 200,000 using a bandpass of 30—3000 c/sec (3 dB down points, 6 dB/octave slope). The potentials evoked over a 51 msec period in response to 1000 stimuli were averaged by a 4-channel averager using a dwell time of 200 μsec and 256 addresses per channel. The averaged potentials were plotted, with positivity at grid 1 of the differential configuration as an upward deflection, and stored on magnetic tape for further analysis. A duplicate of each average was made to assess reproducibility. Latencies and amplitudes of various components of the potentials recorded were determined from the computer CRT screen with a cursor. Latencies were measured from the onset of the electrical pulse delivered to the peripheral nerves or to the mechanical vibrator. Amplitudes were measured between positive and negative peaks. Amplitudes of components with latency longer than 35 msec were not analyzed due to their large variability.

All latency and amplitude data were calculated relative to the 2/sec stimulus rate. The mechanical stimulus was found to change in physical properties (displacement, force, acceleration) with changes in stimulus rate, probably due to the resonant frequency of the vibrator and its coupling to the fingernail. Fig. 1A includes data on both the changes of peak magnitude and latency of the force applied by the vibrator and the amplitude and latency of the compound action potential evoked by the mechanical stimulus and recorded at the wrist. The changes in both latency and amplitude of the neural activity cannot be fully accounted for by the respective changes in peak force. This may be due to changes in receptor activity from increasing stimulus rate or to the force applied not being the only effective parameter of the mechanical stimulus. This ambiguity made it necessary to use the latency or amplitude of the compound action potential recorded at the wrist as a measure of the peripheral sensory input. The latency difference between the mechanically evoked potentials, recorded at the wrist at a given rate and then at 2/sec, was subtracted from the latency difference for me-
Mechanically evoked components recorded at the two stimulus rates (Fig. 1B). The resultant latency change then reflects the effects of stimulus rate independent of changes in the mechanical stimulus itself. Similarly, the amplitude ratio of the compound action potential at the wrist evoked at one rate relative to the 2/sec rate was divided into the amplitude ratio of a mechanically evoked component at the two rates (Fig. 1B). The ratio thus obtained reflected only the neural changes (central to the wrist) related to rate. These calculations prevent an evaluation of the effect of the mechanical stimulus rate on the peripheral nerve distal to the wrist and on the receptors.

The significance of the effects of rate on latency and amplitude of each of the components studied was tested using a single factor analysis of variance ($P < 0.05$ was considered significant).

Results

The potentials evoked by mechanical stimuli generated by 5 and 50 msec duration pulses and the effects of rate on them were the same. The results described below regarding mechanically evoked components relate to those evoked by the 5 msec pulse duration. The recordings obtained at a stimulus rate of 4/sec, from a subject with potentials of average latency and amplitude, are presented in Fig. 2. Components have been labeled according to their polarity (P or N) at grid 1 of the differential amplifier and their average latency in msec. Hereafter the components will be referred to according to these labels regardless of their actual latency at a given rate. In addition, the label may include the electrode configuration used to record the component and the stimulus that evoked it (EW for electrical stimulation of the nerve at the wrist, ED for electrical stimulation of the digital nerve and MD for mechanical stimulation of the fingernail).

Some of the components labeled in Fig. 2 were not analyzed statistically. P22 (C4-Erb's point, EW) could not be identified consistently when the rate of stimulation was 32/sec. P28 (CII-Fpz, EW) and P27 (C4-Erb's point, EW), recorded from some of the subjects at stimulus rates of 2 and 4/sec, disappeared at higher rates of stimulation. This dis-
Fig. 2. Recordings obtained from a subject with potentials of average latencies and amplitudes, using a stimulus rate of 4/sec. The components are labeled according to their polarity (positivity at grid 1 or negativity at grid 2 of the differential amplifiers labeled P) and average latency (in msec).
appearance may be related to the paradoxical shortening of latency observed for N34 (C2-Fpz, EW) (see Discussion). Due to the small number of subjects and the small number of rates in which they were recordable, P22 (C4-Erb's point, EW), P28 (C2-Fpz, EW) as well as P27 (C4-Erb's point, EW) were excluded from the statistical analysis.

The significance of the effects of stimulus rates between 2 and 32/sec on the latency of all the components studied are summarized in Table I. The latency changes of the components that showed significant effects are also listed in that table.

In general, the latency/rate functions cluster in 4 groups best identified at a rate of 32/sec: (1) with latency increase of around 0.2 msec, (2) with latency increase of 0.6–1.0 msec, (3) with latency increase of 1.4–1.6 msec, and (4) with a latency decrease of

| Component | P 2/sec | 4/sec | 8/sec | 16/sec | 32/sec |
|-----------|---------|-------|-------|--------|--------|
| N3 (digit, EW) | < 0.025 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 |
| N3 (wrist, ED) | < 0.25 | | | | |
| N7 (axilla, EW) | < 0.001 | 0.0 | 0.0 | 0.0 | 0.2 | 0.2 |
| N10 (axilla, ED) | < 0.025 | 0.0 | 0.0 | 0.0 | 0.2 | 0.2 |
| N14 (axilla, MD) | < 0.25 | | | | |
| P10 (C4-Erb's point, EW) | < 0.001 | 0.0 | 0.0 | 0.0 | 0.2 | 0.2 |
| N13 (CII-Fpz, EW) | < 0.001 | 0.0 | 0.0 | 0.2 | 0.4 | 0.6 |
| N16 (CII-Fpz, ED) | < 0.01 | 0.0 | 0.2 | 0.4 | 0.4 | 0.8 |
| N20 (CII-Fpz, MD) | < 0.001 | 0.0 | −0.2 | 0.6 | 0.8 | 1.0 |
| P13 (C4-Erb's point, EW) | < 0.25 | | | | |
| P14 (C4-Erb's point, EW) | < 0.001 | 0.0 | 0.0 | 0.2 | 0.2 | 0.6 |
| P17 (CII-Fpz, EW) | < 0.001 | 0.0 | 0.2 | 0.2 | 0.4 | 0.8 |
| P20 (CII-Fpz, ED) | < 0.001 | 0.0 | −0.2 | 0.2 | 0.4 | 1.0 |
| N18 (C4-Erb's point, EW) | < 0.01 | 0.0 | 0.2 | 0.2 | 0.4 | 0.8 |
| N22 (C4-Fpz, ED) | < 0.05 | 0.0 | 0.2 | 0.6 | 0.4 | 1.0 |
| P23 (CII-Fpz, MD) | < 0.001 | 0.0 | 0.2 | 1.2 | 1.4 | 1.4 |
| P22 (CII-Fpz, EW) | < 0.01 | 0.0 | 0.2 | 0.8 | 0.8 | 1.4 |
| P26 (C4-Fpz, ED) | < 0.1 | | | | |
| P26 (CII-Fpz, ED) | > 0.25 | | | | |
| P29 (CII-Fpz, MD) | < 0.001 | 0.0 | −0.4 | 0.6 | 1.0 | 1.6 |
| P31 (C4-Fpz, MD) | < 0.025 | 0.0 | −0.2 | 0.2 | 1.4 | 1.4 |
| N32 (C4-Erb's point, EW) | > 0.25 | | | | |
| N36 (CII-Fpz, ED) | < 0.25 | | | | |
| N37 (CII-Fpz, MD) | > 0.25 | | | | |
| N38 (C4-Fpz, MD) | > 0.25 | | | | |
| P40 (C4-Erb's point, EW) | > 0.25 | | | | |
| P43 (CII-Fpz, EW) | < 0.25 | | | | |
| P44 (C4-Fpz, ED) | < 0.05 | 0.0 | −0.4 | 0.0 | 1.2 | 1.6 |
| P44 (CII-Fpz, ED) | > 0.25 | | | | |
| P47 (C4-Fpz, MD) | > 0.25 | | | | |
| P47 (CII-Fpz, MD) | > 0.25 | | | | |
| N34 (CII-Fpz, EW) | < 0.025 | 0.0 | 0.0 | −1.4 | −3.0 | −2.8 |
| N36 (C4-Fpz, ED) | < 0.025 | 0.0 | 0.4 | −2.2 | −2.6 | −2.4 |
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TABLE II

Significance of the effects of increasing stimulus rate between 2 and 32/sec on the amplitudes of the components studied, as indicated by a one-way analysis of variance. Amplitude decreases (calculated using the procedures summarized in Fig. 1) of components that showed significant rate effects \((P < 0.05)\) are also listed.

| Component | \(P\) | 2/sec | 4/sec | 8/sec | 16/sec | 32/sec |
|-----------|------|-------|-------|-------|--------|--------|
| N3 (digit, EW) | <0.001 | 1.00  | 1.00  | 1.02  | 0.84   | 0.62   |
| N3 (wrist, ED) | >0.25 |       |       |       |        |        |
| N7 (axilla, EW) | <0.001 | 1.00  | 1.00  | 0.98  | 0.88   | 0.67   |
| N10 (axilla, ED) | <0.025 | 1.00  | 1.03  | 0.98  | 1.02   | 0.89   |
| P10 (C4-Erb's point, EW) | <0.001 | 1.00  | 1.01  | 1.00  | 0.93   | 0.67   |
| N14 (axilla, MD) | >0.25 |       |       |       |        |        |
| N13 (CII-Fpz, EW) | <0.001 | 1.00  | 0.93  | 0.76  | 0.59   | 0.39   |
| N16 (CII-Fpz, ED) | <0.001 | 1.00  | 0.98  | 0.93  | 0.75   | 0.63   |
| N20 (CII-Fpz, MD) | >0.25 |       |       |       |        |        |
| P14 (C4-Erb's point, EW) | <0.05 | 1.00  | 1.06  | 0.87  | 0.88   | 0.83   |
| P17 (CII-Fpz, EW) | <0.05 | 1.00  | 0.89  | 0.95  | 0.72   | 0.64   |
| P20 (CII-Fpz, ED) | <0.05 | 1.00  | 1.06  | 0.94  | 0.92   | 0.58   |
| P22 (CII-Fpz, EW) | <0.01 | 1.00  | 0.81  | 0.78  | 0.72   | 0.74   |
| P26 (C4-Fpz, ED) | <0.01 | 1.00  | 0.78  | 0.70  | 0.68   | 0.56   |
| P26 (CII-Fpz, ED) | <0.25 |       |       |       |        |        |
| P29 (CII-Fpz, MD) | <0.1 |       |       |       |        |        |
| P31 (C4-Fpz, MD) | <0.001 | 1.00  | 0.83  | 0.77  | 0.43   | 0.17   |

2.4–2.8 msec. The largest effects were seen with the longest latency components. In each cluster, EW evoked components show the lowest values, ED intermediate and MD evoked components show the highest values. The significance of the clusters will be addressed in the Discussion.

The significance of effects of stimulus rates between 2 and 32/sec on the amplitude of the components studied are summarized in Table II. The amplitude changes of components that showed significant effects are also listed in that table. In general, fewer components showed significant amplitude changes than latency changes, and no clear clustering of functions could be detected.

The amplitude of N16 (CII-Fpz, ED), P17 (CII-Fpz, EW) and P20 (CII-Fpz, ED) decreased by approximately 40% when stimulus rate increased to 32/sec. The amplitude of N13 (CII-Fpz, EW) decreased by approximately 60% as stimulus rate increased from 2 to 32/sec. Because the peripheral nerve potentials evoked by EW decreased by 35% and those evoked by ED by only 10%, these data show these potentials, evoked by ED, to have an amplitude decrease (after changes in the input from peripheral nerve have been corrected for) which is as high as the decrease in the EW upper neck negativity. The exclusion of peripheral nerve related effects from the amplitude changes calculated for MD evoked components (using the procedure summarized in Fig. 1B), and the relatively large variability in the amplitude of this component probably account for the non-significant amplitude decrease at the upper neck level. P23 (CII-Fpz, MD) was not examined for the effects of rate on its amplitude because of its tendency to blend with P29 (CII-Fpz, MD) resulting in a very variable amplitude. P13 (C4-Erb's point, EW) was not analyzed because of possible overlap with P14 following it.

Discussion

The similarity in the wave form of the potentials evoked by mechanical stimuli generated by 50 and 5 msec duration pulses supports the suggestion that the mechanically evoked potentials are initiated primarily by
the fast adapting ‘on’ cutaneous nerves.

In general, the results of this study indicate that a stimulus rate of 4/sec enables recording the maximal number of components with a minimal duration of the recording session. At higher rates of stimulation P28 (CII-Fpz, EW) and P27 (C4-Erb’s point, EW) could not be recorded. A stimulus rate of 8/sec could be adopted, without considerable attenuation of peripheral nerve or upper neck components. However, if the maximal amplitude of later components is of interest, a stimulus rate of 2/sec, and most probably an even lower rate, should be used.

The clusters of latency/rate functions coincide with suggested generators of the components at peripheral nerve, subcortical and cortical levels. The fourth cluster which showed a paradoxical shortening of latency of certain negative components at high stimulus rates also consists of presumably cortically generated potentials. The decrease in latency may be the result of the loss of partially superimposed positive components immediately preceding the negative components (e.g., P28 (CII-Fpz, EW) which precedes N34 (CII-Fpz, EW) at the lower rates), causing these negativities to be unmasked and appear earlier.

The small number of components that showed significant amplitude effects and the lack of clustering of functions probably result from the greater variability of amplitude measures and from the partial superimposition of the activity of a few generators contributing to some of the recorded wave forms.

The amplitude decrease observed in the peripheral nerve potentials at rates above 8/sec is consistent with a previous report (Shagass and Schwartz 1964) on subnormal amplitude of an elbow recorded potential at rates of 10–70/sec. The rates of stimulation used here were much slower than those described for the relative refractory period or supernormality following a single stimulus (Uttal 1959; Gilliatt and Willison 1963; Shagass and Schwartz 1964; Betts et al. 1976). The amplitude decrease with increasing rate may, however, be explained by a subnormal-
and P29 following P17 and P23, respectively). The larger increase in the latency of the succeeding components (P22 and P29) results in further exposure of the preceding and partly superimposed components (P17 and P23) which then appear to peak at a later point in time.

P14 (C4-Erb's point, EW) was found to have a larger latency increase than P10 (C4-Erb's point, EW) and a smaller increase than P22 (CII-Fpz, EW), when rate of stimulation increased. This would suggest a postsynaptic but subcortical generator for P14. Depth recordings from humans during stereotaxic surgery detected thalamic activity at comparable latencies (Goto et al. 1968; Larson and Sances 1968; Narabayashi 1968; Matthews et al. 1970; Haider et al. 1972; Fukushima et al. 1976; Sances et al. 1978).

The longer latency potentials were the most affected components with regard to both latency and amplitude. A comparable larger reduction of the amplitude of cortical components, relative to subcortical components, with increasing stimulus rate has been described for the simian somatosensory evoked potentials (Arezzo et al. 1979). This is consistent with the larger number of synapses leading to their generators. The disappearance of P28 (CII-Fpz, EW) at the higher stimulus rates indicates that this component is more sensitive to rate than the respective P22. This could be the result of a longer chain of synapses leading to its generator, which is probably of a secondary cortical nature. A similar suggestion, based on recovery functions (Allison 1962) and on scalp distribution (Allison et al. 1980), has already been proposed.

The comparable effects of rate on the latency of P29 (CII-Fpz, MD) and P31 (C4-Fpz, MD) are consistent with its generation by the same generator. However, the inconsistent amplitude changes of the CII-Fpz recorded component, which contrast with the sharp changes of the C4-Fpz recorded component with rates, suggest a more complex generator, probably as a result of partial overlap of P29 (CII-Fpz, MD) with P23 preceding it.

The complex generators of many of the components indicated in this study stress the need for detailed mapping studies to determine the sources of the potentials recorded, and the need for multi-channel recordings in their clinical applications for the determination of sites and extents of lesions.

In conclusion, we suggest that in normal adult subjects a stimulus rate of 8/sec may be used without significant sacrifice in the ability to define the early components of the somatosensory evoked potentials. We conclude that the upper neck recorded negativity is generated postsynaptically, most likely in the upper cervical cord or lower medulla, and that the later components are generated by structures in a polysynaptic chain or parallel chains. The number of synapses leading to a generator seems to be larger for later components compared to earlier ones. Only careful mapping studies and correlations with well localized lesions and depth recordings can verify the generators of the somatosensory evoked potentials.

Summary

Somatosensory evoked potentials were recorded in response to: (1) electrical stimulation of the median nerve at the wrist; (2) electrical stimulation of the index finger; (3) mechanical stimulation of the index fingernail. Stimuli were presented at rates of 2, 4, 8, 16 and 32/sec, and the effects of presentation rate on components of the evoked potentials were evaluated. The effect of varying the duration of the mechanical stimulus was also observed. The findings suggest that stimulus rates of up to 8/sec can be used without significant loss in detectability of most of the components. The potentials recorded in response to a short duration mechanical stimulus were essentially identical to those evoked by the long duration stimulus. The findings of this study are consistent with a peripheral nerve generator for the Erb's point recorded component, a postsynaptic generator for the
upper neck recorded component, and in general with a larger number of synapses leading to the generators of the later components than to earlier ones.

Résumé

Potentiels somatosensoriels évoqués de façon mécanique et électrique chez l’homme: effets de la vitesse de présentation du stimulus

Les potentiels évoqués somatosensoriels ont été enregistrés en réponse à: (1) la stimulation électrique du nerf médian du poignet; (2) la stimulation électrique de l’index; (3) la stimulation mécanique de l’ongle de l’index. Les stimuli sont présentés à un rythme de 2, 4, 8, 16 and 32/sec, et les effets de la vitesse de présentation sur les composantes des potentiels évoqués ont été mesurés. Les conséquences de la variation de durée du stimulus mécanique ont été également observées. Les données suggèrent que les vitesses de stimulation supérieures à 8/sec peuvent être utilisées sans perte significative de la détectabilité de la plupart des composantes. Les potentiels enregistrés en réponse à un stimulus mécanique de brèves durées sont essentiellement identiques à ceux évoqués par les stimuli de longue durée. Les données de cette étude concordent avec l’hypothèse d’un générateur nerveux périphérique pour la composante enregistrée au point d’Erb, d’un générateur post-synaptique pour la composante enregistrée à la partie supérieure du cou, et en général avec un nombre de synapses plus grand pour les générateurs des composantes tardives que pour les composantes précoces.

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