REVIEW ARTICLE

The World of Touch – From Evoked Potentials to Conscious Perception

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ABSTRACT: Microelectrode recordings have enabled several maps of the body surface to be recognized in the mammalian somatosensory cortex. The maps appear to represent increasingly complex levels of analysis of the sensory message. At present the prevailing opinion is that the different components of the ERPs (event related potentials) represent sequential steps in such an analysis, and such an interpretation is supported by the enhancement of the ERPs when attention is paid to a somatic stimulus. However, there are a number of critical observations which are inconsistent with this view and suggest that the ERP enhancement may be an epiphenomenon. An alternative explanation for the ERPs is that they reflect discharges from the non-specific thalamic nuclei, and are essentially similar to the long latency responses which can be recorded from the cortex during sleep or anaesthesia. Lastly, a hypothesis is proposed for the neuronal events in the somatosensory cortex which culminate in a conscious perception. In this "RULER" model, the deep pyramidal neurones read out the sensory information which has been retained in the apical dendrites of more superficial cells, and do so at the end of successive "time-chunks".

RÉSUMÉ: Le monde du toucher – Des potentiels évoqués à la perception consciente. Les enregistrements par microélectrodes ont permis d'établir plusieurs cartes de la surface du corps dans le cortex somesthésique de mammifères. Ces cartes semblent représenter des niveaux de plus en plus complexes d'analyse des messages sensitifs. Actuellement, l'opinion courante est que les différentes composantes des potentiels liés aux événements (PRÉs) représentent des étapes séquentielles dans cette analyse et cette interprétation est supportée par le rehaussement des PRÉs quand on considère le stimulus somatique. Cependant, il existe un certain nombre d'observations critiques qui sont incompatibles avec cette interprétation et qui suggèrent que le rehaussement des PRÉs pourrait être un épiphénomène. Une autre explication des PRÉs est qu'ils reflètent des décharges de noyaux thalamiques non spécifiques et sont essentiellement semblables aux réponses à longue latence qui peuvent être enregistrées dans le cortex pendant le sommeil ou l'anesthésie. Finalement, nous proposons une hypothèse expliquant les événements neuronaux dans le cortex somesthésique dont le point culminant est la perception consciente. Dans le modèle "RULER", les neurones pyramidaux profonds lisent l'information sensitive qui a été retenue dans les dendrites apicaux de cellules plus superficielles et le font à la fin de "portions de temps" successives.

Can. J. Neurol. Sci. 1999; 26: 7-17

It is now just over 50 years since Dawson[1] made the first systematic recordings of evoked potentials from the human somatosensory cortex using surface electrodes applied to the overlying scalp. He did so initially by photographic superimposition of faint traces and then by electronic averaging, having designed all parts of the first mechano-electric averaging machine himself (Figure 1).[2,3] Nowadays response averaging is taken for granted and, indeed, compared with functional MRI, PET and magnetic EEG, it seems almost an old-fashioned technology. Yet SSEPs (somatosensory evoked potentials) remain of considerable value in the clinical neurophysiology laboratory and are widely used in the study of brainstem disorders, multiple sclerosis, perceptual problems, and brain failure.[4] Furthermore, evoked potentials are electrical events, made up of the impulses and postsynaptic potentials with which the nervous system conducts all its business; as such they have a validity not shared by measurements of glucose uptake or of changes in blood flow. The purpose of this presentation is to look at the cortical SSEPs again, in the light of contemporary knowledge of the somatosensory cortex, and to see if they bring us any closer to understanding the neuronal steps which culminate in the perception of a tactile or electrical stimulus applied to the body surface. As part of this analysis, a hypothesis is put forward, as to how the different layers of neurons in the somatosensory cortex may interact.

Cortical somatosensory evoked potentials (SSEPs)

Early components

The cortical SSEP, as recorded with an active scalp electrode at C3 or C4, in the 10-20 electrode system, and a reference electrode attached to the ear lobe or mastoid process, can be considered to have early and late components. Thus, when electrical stimuli are applied to the contralateral median nerve at the wrist,

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RECEIVED AUGUST 7, 1998. ACCEPTED IN FINAL FORM OCTOBER 29, 1998. Presented as the Canadian Society of Clinical Neurophysiology Guest Lecture at the 33rd Meeting of the Canadian Congress of Neurological Sciences, Montreal, June 16-20, 1998.

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Figure 1:* A.** *Photograph of the mechano-electrical averaging device designed by Dawson.*[3] *With reduction gears, the motor rotated the spindle carrying the distributors at 10 Hz; the distributors passed the electrical activity from the cortex to a series of 62 capacitors every 10th revolution, following a stimulus. After the procedure had been repeated the requisite number of times, the charge stored on each of the capacitors during successive 100 ms epochs was read out, giving the averaged response. An example, following ulnar nerve stimulation, is shown for the contralateral and ipsilateral somatosensory areas in* ***C *(upper and lower traces respectively).* ***B*** *(upper) shows an earlier method of recording evoked potentials, in which photographic superimpositions of faint traces were made, following median nerve stimulation at the wrist. The centripetal impulse volley is recorded from the median nerve at the elbow (lower trace). From Dawson*[2,3] *with permission.*

there is a small negative wave with a peak latency around 20 ms, the N_{20} wave (Figure 2A). With this recording configuration a smaller, increasingly positive, wave is also seen, prior to the onset of the N_{20} wave. It is usually stated that the N_{20} wave reflects the depolarization of pyramidal cells in the postcentral gyrus, in which case the antecedent positivity would be caused by approaching action potentials in thalamocortical fibres. However, this opinion is not universally held, as some authors interpret the N_{20} as activity in the thalamus or in thalamocortical afferents (e.g., refs. 5,6). Fortunately, the issue can be resolved in two ways. One experiment aimed at resolving this issue has been to record scalp responses from patients with unilateral hemispherectomies, and, on the affected sides, N_{20} is absent although earlier potentials are present.[7] However as Chiappa and Hill[6] correctly point out, the anatomical situation is complicated by the retrograde changes in thalamic neurones, which would be expected to follow surgical ablation of the cortex. A more decisive approach is to measure latencies of single thalamic neurons to median nerve stimulation and this has been possible in stereotactic operations for Parkinsonian tremor or for intractable pain. In an early study we found the latencies to range from 13 to 19 ms and to be associated with negative-going field potentials, presumably EPSPs (excitatory postsynaptic potentials), with similar short delays (Figure 2C,D; ref. 8); these values would certainly be consistent with N_{20} being a postsynaptic cortical response.

In passing, it should be noted that SSEPs recorded with subdural electrodes are not only very much larger than those derived from scalp electrodes, but also show sharp spatial discriminations. Thus, the electrode most favourably positioned over the somatosensory receiving area in the postcentral gyrus records a large initially positive potential, whereas neighbouring areas show smaller initially negative waves.[9]

The N_{20} wave, recorded with scalp electrodes, is followed by a positive wave which is normally larger and more prolonged (Figure 2A). The peak latency of the positive wave differs between subjects and also depends on the form of the wave, as well as whether the wrist or fingers are the site of median nerve stimulation. With stimulation at the wrist, the positive wave occurs earlier, with a peak latency of approximately 22 ms, and is usually

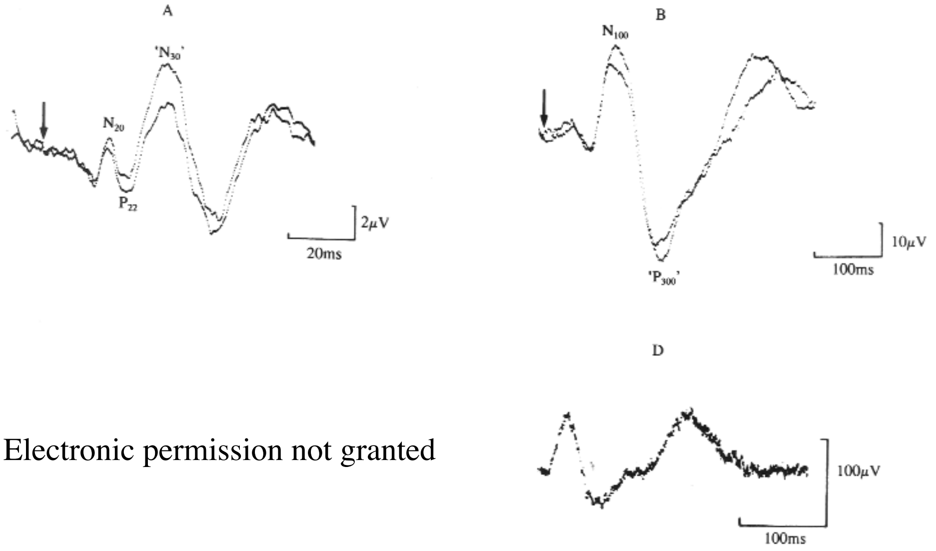

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Figure 2: ***A.*** *Averaged responses, showing identified waves, recorded from C3, with respect to the mastoid. Two series of 20 stimuli were delivered to the right median nerve, with irregular stimulus intervals of more than 1 s.* ***B.*** *Responses evoked at vertex (C2) with respect to mastoid, following similar stimulus sequences, and displayed on a slower sweep. In A and B the times of stimulation are shown by arrows.* ***C.*** *Four superimposed traces of a cell in the ventral posterolateral (VPL) nucleus of the human thalamus, responding to contralateral wrist stimulation. The shortest latency is 13 ms. From McComas with permission.[45]* ***D.*** *Field potentials recorded in human VPL following wrist stimulation.*

succeeded by a relatively large negative wave (peak latency, approximately 30 ms). The sequence of waves, particularly after stimulation at the wrist, often has a "W" shape (Figure 2A), as was first pointed out by Giblin.[5] The early components are quite markedly affected by exploratory activity, but not in the manner which might have been predicted. Thus the potentials evoked by passive movement of a finger are larger than those recorded when the same movement is produced by a voluntary contraction.[10] This last finding is consistent with the results of single unit studies in the monkey cortex[11] and suggests that incoming neural activity is "gated" at some point in the somatosensory pathway. It is interesting that Dawson, the inventor of averaging, was one of the first to explore gating at the level of the dorsal column nuclei.[12]

Late components

Waves with peak latencies greater than 40 ms are also termed event-related potentials (ERPs). Of these the most studied is the P_{300}, but there is usually a substantial negative wave which precedes it and which has a peak latency of 70-100 ms (Figure 2B). It is important to note that the latencies and configurations of both potentials are very approximate, considerable variation occurring not only between subjects but also between successive trials in the same subject. This variability becomes important in discussions of the relevance of these waves to cognitive proces-sing (see below). Another major difference from the early somatosensory responses is that the late ones are widely distributed and can be recorded from the frontal, temporal and parietal areas of both hemispheres following unilateral stimulation (e.g., ref. 13).

The somatosensory receiving areas in the cerebral cortex

A detailed map of the representation of the body surface on the human cerebral cortex was made by Penfield and his colleagues, and was obtained by faradic stimulation of more than 100 brains exposed prior to neurosurgical interventions. These authors showed that the map was an inverted one which occupied the postcentral gyrus but which extended into the precentral (motor) region as well. The map was distorted in that the largest surfaces were devoted to the hand and tongue, with the lips, arm, jaw, face, thumb and leg having progressively smaller areas.[14] This distortion was portrayed in the well-known sensory homonculus which continues to be widely reproduced. Rather later, another representation of the body surface was identified by evoked potential techniques in the cat[15] and subsequently in the monkey, where it occupied part of the lateral sulcus.[16] This representation became known as the secondary (SII) somatosensory area, as opposed to the primary (SI) area occupying the postcentral gyrus. In contrast to the situation for SI, the body is represented erect in SII, with the head anterior.[17]

In 1959, Powell and Mountcastle[18] showed that SI comprised the Brodmann cytoarchitectonic areas 3, 1 and 2 and that there was a higher incidence of responses from deep tissues than from skin in area 2, while the opposite was true for area 3. Stimulation of a region of the body was considered to activate a corresponding rostrocaudal band in the postcentral gyrus, which included all 3 cytoarchitectonic areas. This concept was subsequently modified by Kaas et al.[19] who systematically explored the postcentral gyrus in monkeys with large numbers of microelectrode tracks. They were able to show that three of the cytoarchitectonic areas (3b, 1 and 2) each contained a complete map of the contralateral body surface with area 3a, the rostral subdivision of area 3, probably containing a fourth map; the representations in 3b and 1 were mirror images of each other (Figure 3). In the opinion of Kaas et al.,[19] only 3b should be equated with SI. Confirming Powell and

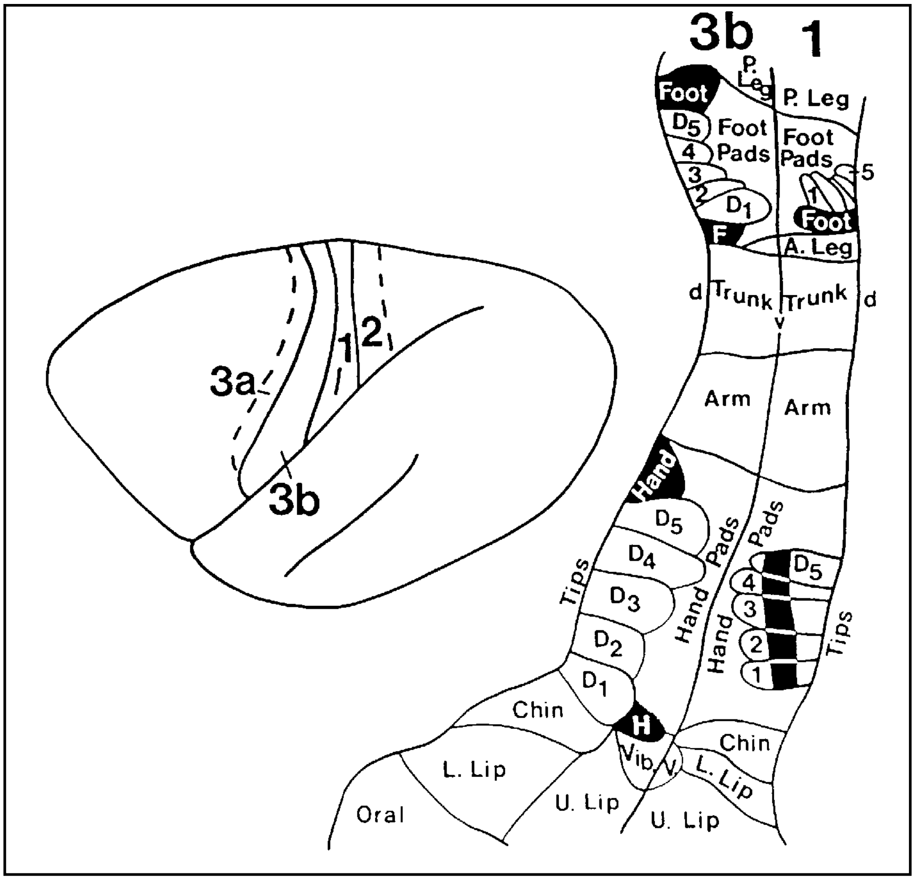

Figure 3: Left. Lateral view of main somatosensory cytoarchitectonic areas in the owl monkey brain. Right. Detailed representation of body surface in the areas 3b and 1. Note that the two maps for the fingers face away from each other. From Kaas[20] *with permission.*

Mountcastle,[18] Kaas and associates found that the great majority of cells in 3b and 1 responded to skin stimulation, whereas most 3a neurones were driven by muscle spindles; area 2 cells ultimately received inputs from joint or cutaneous afferents (cf. ref. 20).

More recent studies have enlarged the cortical somatosensory region to include parietal areas 5 and 7b, posterior to the postcentral gyrus, and have shown that there are also several small somatosensory areas behind SII (retroinsular, postauditory, insular granular and insular dysgranular areas). Taking into account the observation of Penfield and Boldrey,[14] that somatic sensations can be elicited from the human precentral gyrus, there could be as many as 11 somatosensory areas in all.

Somatosensory cartography in relation to early and late SSEPs

Although, in human subjects, it has been possible to study the responses of single cutaneous peripheral nerve fibres, and of single neurones in the thalamus, there have been no single unit recordings in the somatosensory cortex. However, with knowledge of the anatomical extents of the somatosensory receiving areas (see above), it is now possible to predict how the cortex will be activated by an electrical or mechanical stimulus in the periphery. First, a brief or sustained touch on the skin, insufficient to excite deep receptors, should induce activity in areas 3b and 1, and possibly in SII and the posterior insula as well; the same would be true for electrical stimulation of a finger tip. Suppose now, that, as routinely happens in the clinical neurophysiology laboratory, electrical stimuli are delivered to the median nerve at the wrist, of an intensity that induces a weak thumb twitch as well as sensations referable to the skin under the electrodes and to the thumb and fingers. Under these conditions there will be activation, not only of areas 3b and 1, but also of areas 3a and 2, since muscle and joint afferents will have been excited. We suggest that it is these latter areas, extending into sulci, which cause additional early components of the SSEP following the N_{20} wave, and are largely responsible for the W-configuration described by Giblin.[5] Because of the involvement of the four cytoarchitectonic areas, the activated region of the cortex will take the form of a rostrocaudal band across the postcentral gyrus. However, median nerve stimulation at the wrist will excite the cutaneous afferents of up to 4 digits, as well as those of the palm. The activated region of cortex will therefore be considerably more extensive in the mediolateral axis, than if a single finger tip had been stimulated. Since many more cortical neurones will develop postsynaptic potentials and impulses, the N_{20} and other SSEP waves would be expected to enlarge, and this is what is observed.

Relationship of late SSEP components to multiple somatosensory areas

It seems natural to relate the later components of the SSEPs, the ERPs, to cognitive events taking place in the multiple somatosensory areas in the cortex discovered by neurophysiological

Figure 4:* *A. *Grand average of responses of contralateral cortical somatosensory areas in 9 subjects to stimulation of the thumb during inattention (reading; top trace) or during attention to stimuli (bottom trace).* ***B.*** *Subtraction of unattended from attended responses, so as to yield "cognitive" components (labelled).* ***C.*** *Detail of the earliest components of the unattended and attended responses, showing that waves as early as 30 ms, post-stimulus, are enlarged during attention. From Desmedt and Tomberg[23] with permission.*

and anatomical techniques (see above). That the ERPs reflect cognitive events is suggested by the enlargement of the various waves when attention is drawn to the stimulus (Figure 4; refs. 21-24). The physiological significance of the multiple cortical areas is that they provide a means for interpreting incoming messages from the contralateral body in an hierarchical manner. As shown in Figure 5 (A, B), following stimulation of the skin, area 3b would be activated first, with progressively more subtle analyses being performed in sequence by areas 1 and 2[20] and then by areas 5 and 7b.[25] In a lateral direction, areas 3b, 1 and 2 would project to SII, the second somatosensory area, which also receives a thalamic input, and thence to the region around the insula (areas Ri, PA, Ig and Id in Figure 5B).[26]

The prolongation and dissemination of electrical activity through a cortical hierarchy at once provides a convenient explanation for the long-lasting components of the SSEPs. Thus, Hillyard[27] has written that "separate ERP components demarcate processes of stimulus selection, evaluation, and classification, thus providing a window into the timing of complex mental operations." Similarly, Tomberg and Desmedt[28] state ". . . sensory stimuli evoke brain potentials with enlarged components at characteristic latencies and scalp locations. Such distinct cognition-related electrogeneses help in documenting the sequential activity of brain neurones that underlie stages of perceptual processing". While accepting that the soma and apical dendrite of each cortical pyramidal cell constitutes an electrical dipole, and that variations in the polarization of these dipoles underlie most of the slow wave activity at the cortical surface, it is still difficult to interpret the slow waves in terms of postsynaptic potentials. As Creutzfeldt[29] has shown, a surface negativity may reflect not only excitatory depolarization of apical dendritic membrane in superficial layers of cortex but also an inhibitory hyperpolarization of the deeper lying soma. Despite this uncertainty, the P_{300} component of the ERP has been identified by Desmedt as an inhibitory "post-decision closure" whereby currently activated brain circuits are cleared for the next perceptual task.[30] Indeed, so attractive is the identification of the late SSEPs with perceptual processing that the waves are often referred to as cognitive potentials. Moreover, such an identification of long latency waves is consistent with the brain stimulation experiments of Libet et al.,[31] who found that weak ("liminal") repetitive stimulation of the exposed human somatosensory cortex had to be maintained for approximately 0.5 s before a conscious perception ensued.

Arguments against equating ERPs with cognitive events

As documented above, there are seductive arguments for regarding the ERPs as the electrical signs of those neural processes in the human cerebral cortex which ultimately enable the qualities of a stimulus to be appreciated at a conscious level. On the other hand, there are a number of reasons to question the linkage between ERPs and cognition, and these are listed below:

(i) The ERPs are surprisingly large in comparison with the early cortical SSEPs. With the temporal and spatial dispersion of the putative cognitive processing, the corresponding potentials would be expected to be smaller in amplitude.

(ii) The ERPs are also large in relation to the cognitive challenge of the stimulus. For example, a tap on the skin, or a single electrical pulse to a peripheral nerve, allows the brain to discriminate only the location, intensity and brevity of the stimulus. These are all qualities for which the receptive properties of the cells in areas 3b and 1 are best equipped to distinguish. Only when the stimulus becomes more complex would other areas be expected to come into play, as when a stimulus is passed across the skin and activates motion-sensitive neurones in area 2.[32] Likewise, when discriminations are made by "active touch", as in running the fingers over a surface or in feeling the shape of an object with the hand, it would be expected that cortical areas beyond 3b and 1 would be involved, even though gating mechanisms may be operating (see above). However, these are not the circumstances in which ERPs are studied. Other examples of ERPs which seem extravagantly large in relation to cognitive elements in the stimulus are those which follow brief pulses to the oesophagus.[33]

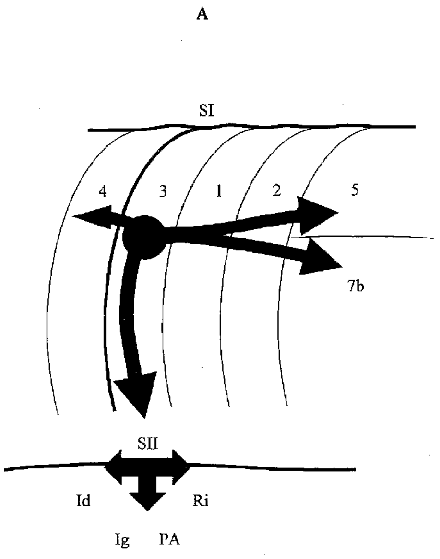

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Figure 5: ***A.*** *Hypothetical spread of neural information from area 3b to other regions of the primary and secondary somatosensory areas (Ri, retroinsular; PA, postauditory; Ig, insular granular; Id, insular dysgranular).* ***B.*** *Hierarchical scheme for the processing of somatosensory information in different cortical areas. From Felleman and Van Essen*[25] *with permission.*

(iii) The distribution of the ERPs, including the frontal areas, is much wider than the areas of cortex which have been found, in animals, to have single unit responses to somatic stimulation, or, in man, to yield cutaneous sensations when stimulated electrically.

(iv) Similarly, the durations of the ERPs, e.g., to 0.5 s, are far larger than the latencies of any single cortical units discharging in response to peripheral stimulation.

(v) If the slow waves were associated with cognitive events then there should be a close association between their maxima and minima and the presence or absence of impulse activity. However, if the results of experiments on anaesthetized animals are any guide, such an association is often absent (e.g., Figures 5 and 6 in ref. 34).

(vi) Well developed ERPs can be recorded during sleep and

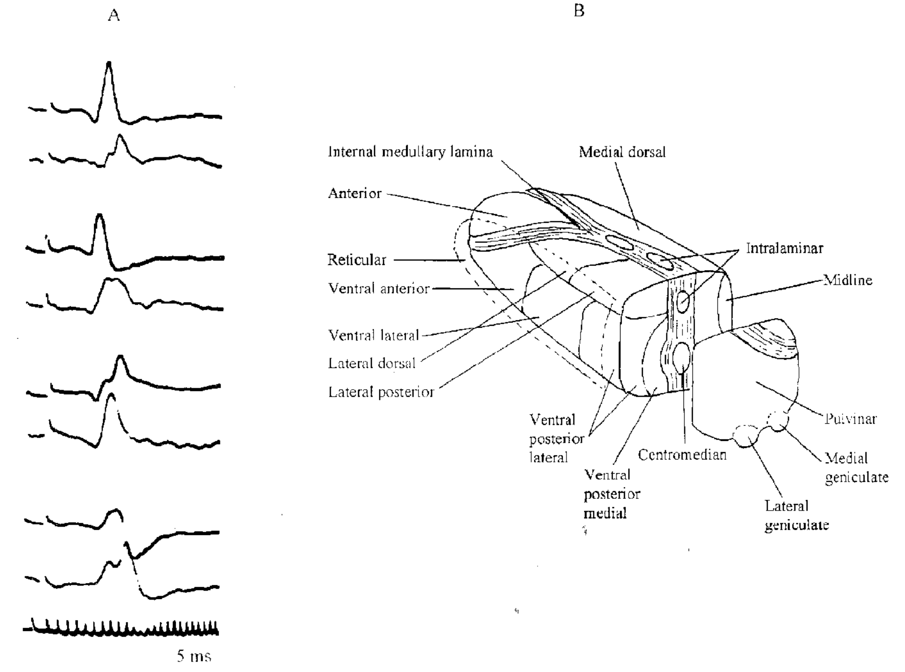

Figure 6: ***A****. Cortical slow wave responses evoked by single stimuli to the non-specific nucleus reuniens of the cat thalamus; top and bottom traces in each pair are from cell populations in the region of the lateral gyrus. Note the long latencies and the variable wave forms and amplitudes of the responses. From Jasper and Ajmone-Marsan*[38] *with permission.* ***B****. Human thalamus, with transverse cut, showing some of the main nuclei, including the intralaminar ones.*

anaesthesia, in the absence of cognition. Indeed, the largest ERP of all, the K-complex, is a feature of the sleep state.[35] Hypnotic suggestion has also been found without effect on the amplitudes of SSEPs following tactile stimulation.[36]

(vii) Although no attempts have been made to link specific aspects of cognitive processing to individual components of the ERPs (other than the P_{300} representing "post-decision closure"[30]), one might nevertheless expect the ERPs, if they truly signified cognition, to show some constancy between the amplitude and configuration of the response, on the one hand, and the perception of the stimulus, on the other. If, however, instead of using averaging, single traces are examined, it can be seen that identical stimuli, yielding identical perceptions, are associated with widely varying ERPs. This variability between trials is true not only for relatively large waves such as N_{100} and P_{300}, but also for the earlier, smaller, P_{40}.[28]

(viii) As a corollary of the above, if the ERP is approximately halved, by giving a conditioning stimulus 500 ms before the test one, the second stimulus is nevertheless felt to be the same as the first in intensity (as well as in location and quality).

What, then, are the ERPs?

The question is whether there is a neural system, other than the sequence of cortical areas described earlier, which could cause widespread activation of the cortex following a peripheral stimulus. Moreover the activation should be labile and have a longer latency than the earliest components in the evoked response. In fact, such a system was described in 1942 by Morison and Dempsey[37] who showed that electrical stimulation of the medial thalamus in anaesthetized cats evoked diffuse responses in the cortex and that the potentials waxed and waned as the stimuli were repeated ("recruiting responses"). When the same thalamic regions were subjected to single shocks, Jasper and Ajmone-Marsan[38] demonstrated that the cortical potentials were not only widely distributed but were variable from trial to trial, and had long latencies (Figure 6A).

Several thalamic nuclei are capable of generating this type of activity in the cortex and are found medially within the lamina; of these intralaminar nuclei (Figure 6B), the centrolateral and paracentral are especially important, together with the ventral medial nucleus.[39] These non-specific nuclei do not receive inputs from the "specific" thalamic nuclei, which are the nuclei projecting to the primary sensory receiving areas. Rather, the non-specific nuclei are excited by spinothalamic and spinoreticular fibres, as well as by cells in the midbrain reticular formation.[40] The reticular neurones, in turn, receive inputs from many sources, including collaterals from the medial lemniscus and spinothalamic tracts,[41,42] as well as auditory and visual pathways. The cells in the non-specific thalamic nuclei tend to have large receptive fields and some can be excited from the entire body surface.[43]

A further feature which would tend to identify the non-specific thalamic system with the ERPs is the relationship of both to spontaneous EEG activity. Thus, with the eyes closed, the later parts of the ERPs will often continue into an α-spindle. However, as already noted, the non-specific thalamic nuclei, when stimulated repetitively, produce recruiting responses at the cortical surface which strongly resemble α-spindles. It is also relevant that, when the cortex is destroyed, brief stimuli to the contralateral body surface evoke fluctuating discharges in thalamocortical afferents, an observation which also shows that long-lasting responses in the cortex can have a thalamic origin.[44]

Figure 7 summarizes the preceding discussion by contrasting the ERP mechanism involving the non-specific thalamic nuclei with that based on hierarchical processing in multiple cortical areas. Although both schemes may co-exist, we suggest that the former is the more important of the two.

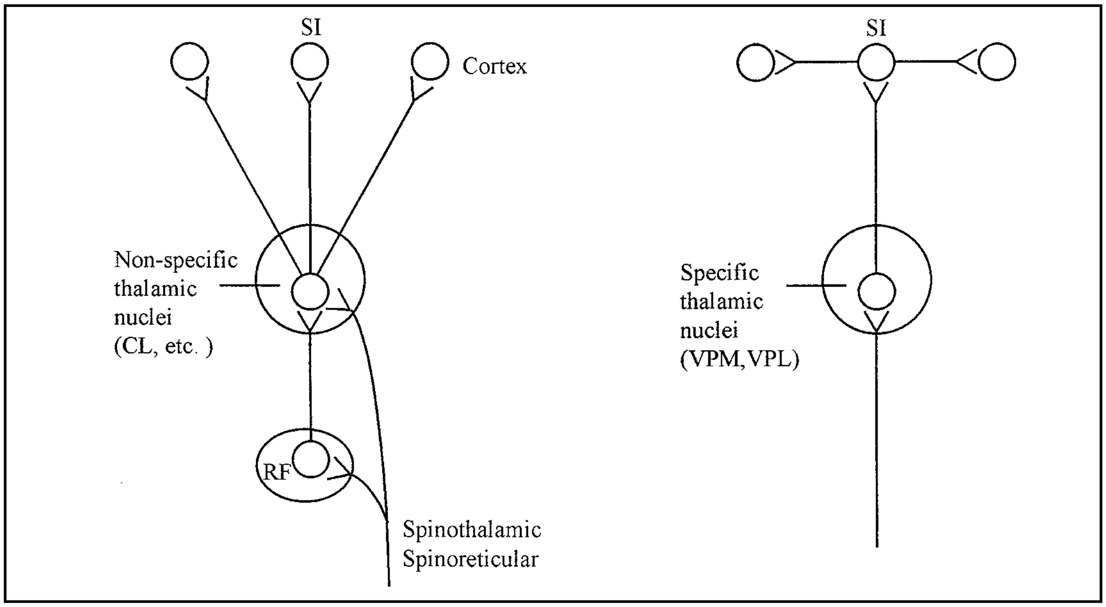

Figure 7: *Two different views of the spread of somatosensory activity in the cortex. In the scheme on the left, activity is widely distributed through the non-specific thalamic nuclei, such as the centrolateral nucleus (CL), which receive inputs from the spinothalamic and spinoreticular tracts either directly or via the midbrain reticular formation (RF). In the scheme on the right, activity spreads out from the primary somatosensory area (SI), which receives inputs from the specific thalamic nuclei VPM (ventral posteromedial) and VPL (ventral posterolateral).*

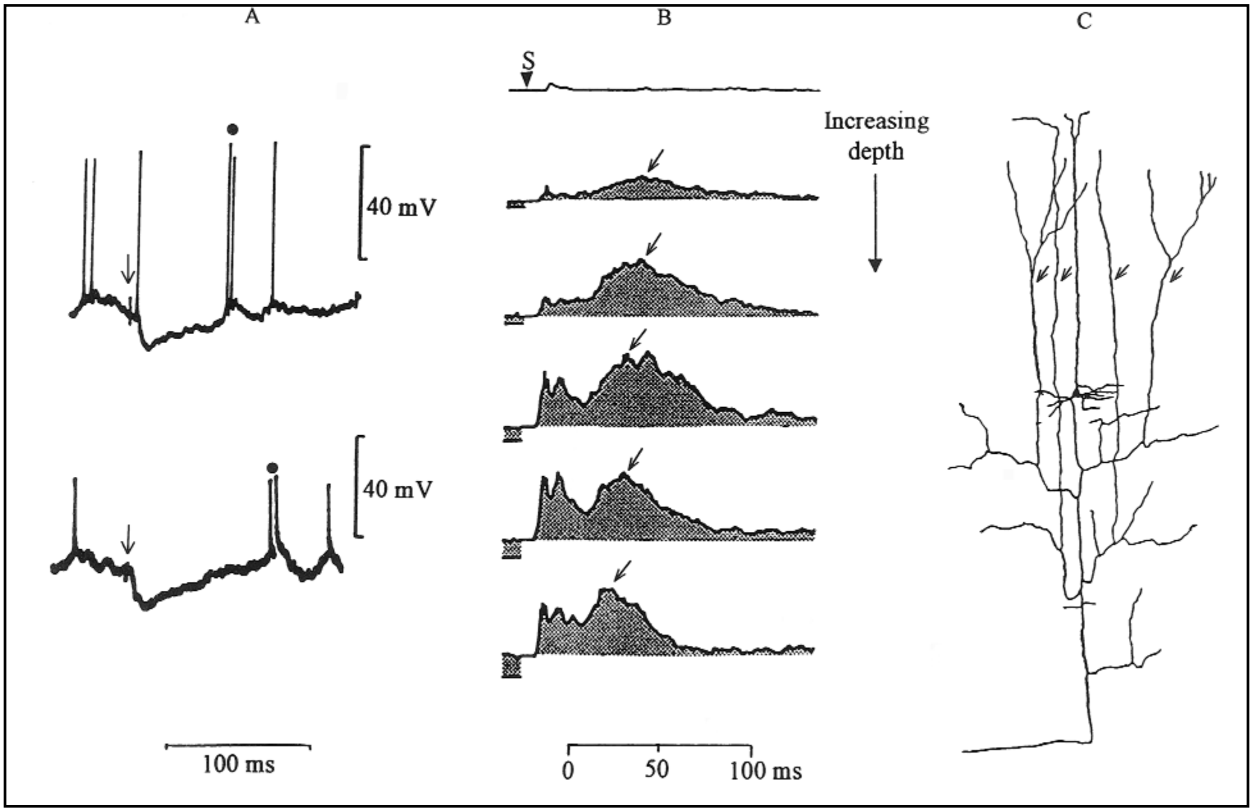

Figure 8: ***A****. Intracellular recordings from cat somatosensory cortex, showing early and late responses to stimulation of the contralateral face (arrows). In the top trace the cell fires a single impulse initially, followed by 2 impulses (dot) at the end of the IPSP. In the lower trace there is no initial discharge but 2 impulses (dot) after the IPSP. From Hellweg et al.*[50] *with permission.* ***B.*** *Averaged impulse activity at different depths of monkey somatosensory cortex, following electrical stimulation of the contralateral hand. In each trace the late activity (arrowed) is greater than the early activity, especially in the 2 most superficial recordings. From Kulics and Cauller*[52] *with permission.* ***C.*** *Camera lucida drawing of the cell body and processes of a pyramidal neurone in layer V of the mouse cortex. The arrows identify recurrent axonal branches. From Lorente de Nó*[53] *with permission.*

The RULER hypothesis

If, as I suggest, the ERPs are due to non-specific thalamic inputs, have they anything to do with cognition? In a new hypothesis of somatosensory cortical function, Dr. Cupido and I suggest that they may, but only in a grossly supportive manner. We have termed this hypothesis the RULER model, the title being an acronym for *R*ecurrent *U*pper *L*ayers *E*xcitatory *R*ead-out. This hypothesis, briefly mentioned elsewhere,[45] is built on four pieces of information – (i) the time-chunk phenomenon, (ii) intracellular recordings from cortical neurones, (iii) the discharge latencies of somatosensory cortical neurones, and (iv) the cortical architecture. Each of these aspects will now be considered.

The time-chunk phenomenon

Although the stream of conscious experience appears smooth and continuous, several lines of evidence indicate that the brain assesses the world in a series of summaries, each summary covering the preceding 50-80 ms. Each 50-80 ms epoch constitutes a "time-chunk".[46] In the case of the somatosensory system, some of the best evidence for time-chunking comes from backward masking experiments, in which a strong stimulus to the skin can obliterate perception of a weaker stimulus delivered up to 80 ms earlier (e.g., ref. 47). Again, two stimuli of similar intensities are not felt as completely distinct unless they are separated by at least 50 ms (McComas & Cupido, unpublished observations). Other evidence of time chunking is the inability to determine the order of presentation of different types of stimuli given within a short time of each other.[48] In the visual system the presence of time chunking is suggested by the flicker-fusion phenomenon and the wagon wheel illusion.[49] The implication from these different types of observation is that conscious perception must include a neural mechanism for storing up to 80 ms of activity.

Intracellular recordings

Intracellular recordings from somatosensory cortical neurones show that the cells respond to a single peripheral stimulus with a EPSP (excitatory postsynaptic potential), followed by an IPSP (inhibitory postsynaptic potential), and then another EPSP. It is significant for the RULER hypothesis that the second EPSP is usually larger than the first, and may then be sufficient to initiate action potentials when the first is ineffective (Figure 8A).[50]

Long-latencies of responding cells

From microelectrode studies it is evident that the more superficial cells in the mammalian somatosensory cortex discharge to peripheral stimuli with latencies which are longer than those of deeper cells. This aspect, first described by Amassian,[51] is well seen in Figure 8B, taken from the work of Kulics and Cauller.[52] In this figure the impulse activities of multiple cells at different depths of the monkey somatosensory cortex have been

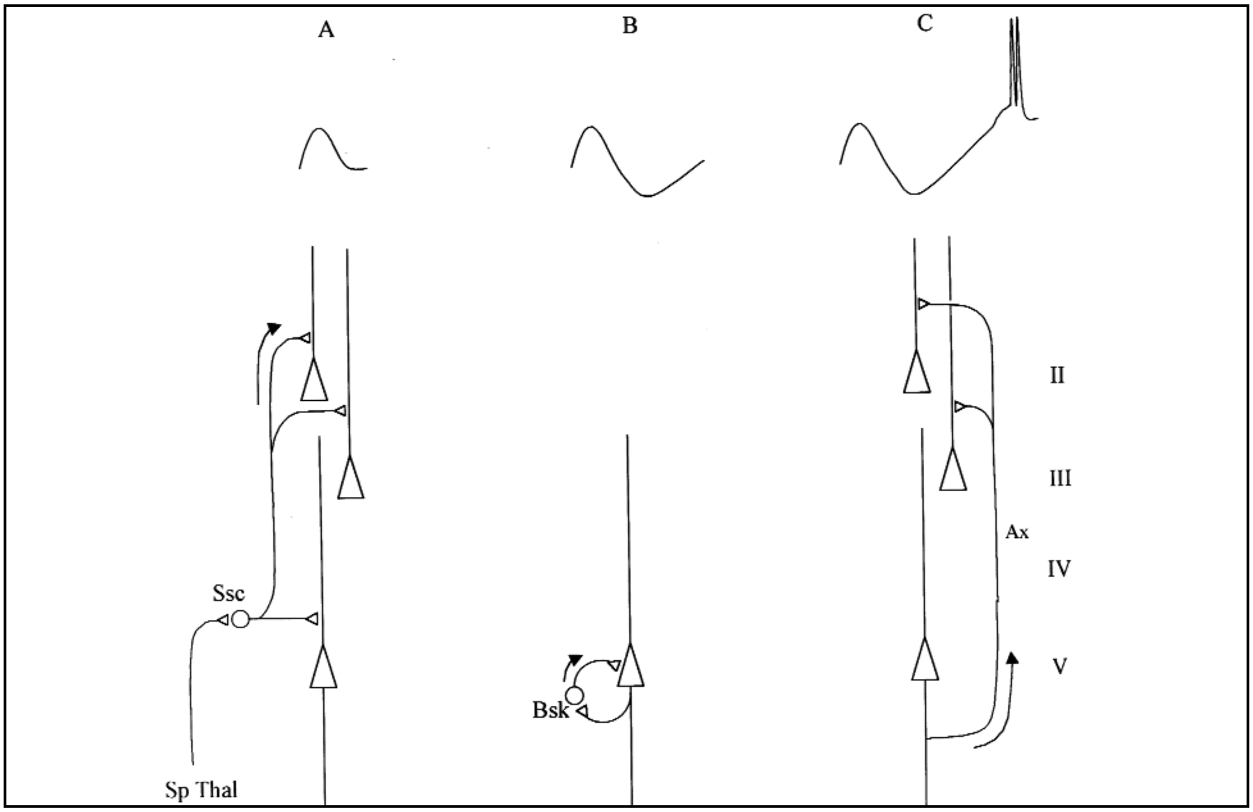

Figure 9: *Elements of the RULER model. In **A**, an impulse from a specific thalamic nucleus (Sp Thal) is transferred by a spiny stellate cell (Ssc) to the apical dendrites of pyramidal cells in layers II, III and V, evoking EPSPs in the superficial cells (top). In **B**, a basket cell (Bsk) is activated by a recurrent impulse in one of the layer V cells, causing widespread IPSP in this and other deep pyramids (top). At the conclusion of the IPSP (**C**) there is rebound excitations in all the deep pyramids within the local region of cortex. The axon collaterals (Ax) bring the superficial cells to the firing level, depending on the amount of residual EPSP retained in the dendritic tree.*

averaged. In the two most superficial recordings nearly all the evoked activity is late (peaking at the arrows), and even in the deeper levels the late activity dominates. Late neuronal activity was also noted in the cat somatosensory cortex by Li et al.,[34] particularly for low-intensity stimuli, though the relationship to depth was not stated.

Cortical architecture

It is well known that cortical neurones are arranged in columns and that the majority of axons, as well as the apical dendrites of the pyramidal cells, are also arranged vertically. Indeed, it was Lorente de Nó[53] who speculated that the most immediate connections must be between cells lying above or below each other. Two aspects of the columnar architecture are of particular importance for the RULER a hypothesis. First, considerably more pyramidal cells are found in the superficial layers (layers II and III) than in the deeper layers (V and VI).[54] Second, the pyramidal neurones in layers V and VI have prominent recurrent axons, which run to the upper layers (Figure 8C).[53]

In the RULER model, we propose that incoming information from the specific thalamic nuclei is stored as EPSPs in the apical dendrites of pyramidal cells in layers II and III (Figure 9); the longer the dendrite, the longer the EPSP will persist. Within 80 ms or so of its arrival, the stored information is read out by a recurrent discharge from the deep pyramids in layers V and VI. This recurrent discharge occurs during the rebound excitation at the end of an evoked IPSP. By analogy with the hippocampus[55] it is likely that basket cells in the deeper cortical layers are the GABA-releasing interneurones responsible for the IPSP. In addition to serving as integrators of incoming somatosensory information, the superficial cells, being more numerous than the deep ones, will act as biological amplifiers. The strength of their response will depend, to a large extent, on the background depolarization of the dendrites, and this will increase during general alertness and especially during attention, as reflected in the contingent negative variation.[56,57] The delayed (ERP-inducing) discharge from the non-specific thalamic nuclei would also be expected to add to the dendritic depolarization, and thereby to influence the strength of the superficial somatosensory readout. A cardinal feature of the RULER hypothesis is that if the superficial cells discharge, this, of itself, results in a conscious perception.

Lastly, is the RULER model compatible with the enhancement of the ERPs during attention? We suggest that the enhancement is a consequence of the depolarization of the apical dendrites which occurs during the attentive negativity of the cortical surface (see above); as such, the enlargement of the ERPs would be an epiphenomenon. A similar explanation could be used for the curious observation of Libet et al.,[31] that repetitive stimulation of the human somatosensory cortex must be continued for 500 ms or so if it is to be perceived. Thus, under the conditions of Libet's experiment, such prolonged stimulation might be needed to depolarize the apical dendrites to a critical level; indeed, a build-up of negativity at the cortical surface has been reported by Goldring et al.[58]

CONCLUSIONS

Animal experiments have been extraordinarily useful in demonstrating the complex organization of the somatosensory areas of the mammalian cortex. Indeed, there is a compelling case for a functional hierarchy of areas, with each area conducting a more elaborate analysis of the sensory message than the preceding one. However, it seems premature to regard the ERPs, recorded from the scalp or cortical surface, as electrical markers for cognitive processing, even though such activity must be taking place within the cortex. It must be emphasized that tactile or electrical stimulation of the body surface will produce activity in the midbrain reticular formation and non-specific thalamic nuclei, and that both regions project diffusely to the neocortex. Such discharges, which are still present in sleep and during anaesthesia, would provide an alternative, non-cognitive, explanation for the ERPs. At present, the most reliable approach to understanding cognition would seem to be the linking of single cell properties, as determined in animals, with psychological experiments in humans and with anatomical studies of cortical architecture. As an example of such an approach, a hypothesis is presented in which sensory information in apical dendrites is read out by a recurrent discharge from pyramidal cells in the deeper cortical layers.

ACKNOWLEDGEMENTS

I thank Dr. Cynthia Cupido and Ms. Rebecca Newberry BSc for help with experiments, and to Ms. Jane Butler MSc for secretarial and technical services. Financial assistance was received from the Natural Sciences and Engineering Research Council.

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