

## SUBJECTIVE REFERRAL OF THE TIMING FOR A CONSCIOUS SENSORY EXPERIENCE

A FUNCTIONAL ROLE FOR THE SOMATOSENSORY SPECIFIC PROJECTION SYSTEM IN MAN

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### INTRODUCTION

PREVIOUS studies had indicated that there is a substantial delay, up to about 0.5 s, before activity at cerebral levels achieves 'neuronal adequacy' for eliciting a conscious somatosensory experience (Libet, Alberts, Wright, Delattre, Levin and Einstein, 1964; Libel, 1966). The delay appeared necessary not only with stimulation of medial lemniscus, ventrobasal thalamus, or postcentral cortex, but even when the stimulus was a single electrical pulse at the skin (Libet, Alberts, Fright, and Einstein, 1967, 1972; Libel, 1973). The present investigation began with an experimental test of whether there is in fact also a subjective delay in the conscious experience for a peripheral sensory stimulus. That is, is there a delay in the subjective timing of the experience that would correspond to the presumed delay in achieving the neuronal state that 'produces' the experience? The results of that test led to a modified hypothesis; this postulates (a) the existence of a subjective referral of the timing for a sensory experience, and (b) a role for the specific (lemniscal) projection system in mediating such a subjective referral of timing. Experimental tests of the new proposal were carried out and are reported here.

The timing of a subjective experience must be distinguished from that of behavioral response (such as in reaction time), which might be made before conscious awareness develops; or even from minimum time intervals that are perceptually discriminable, since the question of *when* the subject becomes introspectively *aware* of the stimuli or of the discrimination is not answered by such measurements. There seemed to be no method by which one could determine the absolute timing of a subjective experience. Instead, we adopted a procedure in which the subject reported the subjective timing order of two sensory experiences. The validity of this procedure depended on the availability of a 'reference' sensation, with known constraints on its subjective timing, to which the timing for the peripherally-induced sensation could be meaningfully related. The reference sensation employed was that elicited by a stimulus applied directly to postcentral, somatosensory (SI) cortex. This cortical stimulus could be set experimentally so as to require a minimum train duration of up to about 0.5 s before it could elicit any conscious sensory experience (Libet *et al.*, 1964; Libet, 1966). Consequently, it could be assumed that the cortically-induced subjective experience could not 'arise' before the end of the experimentally fixed minimum train duration. (Preliminary reports of some of these findings have been made before the Society for Neuroscience in Toronto, Canada, November 7-11, 1976—see summary in *Brain Information Service Conference Report No. 45, 1977, UCLA, Los Angeles, Ca. 90024, pp. 103-121*; and in a symposium on *Cerebral Correlates of Conscious Experience, see Libet, 1978*).

### METHODS AND PROCEDURES

#### *Subjects*

Subjects were drawn from among two groups of patients in whom a stereotactic neurosurgical procedure was to be carried out, one with dyskinesias (chiefly parkinsonism or hereditary familial tremor) and another with chronic intractable pain. Only those patients were selected for the present studies whose physical and mental condition permitted them to give their fully informed consent, as well as the necessary degree of attention and responsiveness to somatosensory stimuli. Upon any indication of fatigue or loss of interest, or of a preference not to continue, the study session was terminated. All the investigational procedures have been reviewed (in relation to any possible risk factors and to the conditions of informed consent) and approved by an independent Committee on Protection of Human Subjects in Mount Zion Hospital (in accordance with guidelines set out by the National Institutes of Health, US Public Health Service). We note here our deep gratitude to the patients whose co-operation and interested participation made this type of investigation possible.

### *Stimulation and Recording Electrodes*

The procedures employed were similar to those employed previously (Libet *et al.*, 1964, 1967, 1972). The subdural electrode assembly (Delgado, 1955) contained five or seven separate wires enclosed in a flat, flexible plastic carrier. Each wire has one uninsulated region about 1 mm long, and the exposed contacts for the separate wires are spaced 3 to 10 mm apart. (These assemblies are similar to those which have been used routinely for subdural explorations of cortical epileptogenic areas in certain epileptic patients).

The carrier is inserted posteriorly via a frontal burr hole made for therapeutic purposes; the insertion is done slowly and gently so that, in the occasional case when any obstruction is encountered, it could be halted and withdrawn. Such insertions of these subdural electrode assemblies and the temporary periods of stimulation with them have, in our experience with hundreds of patients since 1957, never resulted in any detectable signs of damage. To determine whether a given contact was located on the pre- or postcentral gyrus the motor and sensory responses to subsequent stimulation were tested. The subcortical contacts, in the ventroposterolateral or ventroposteromedial nuclei of thalamus (n.VPL or n.VPM), and in the medial lemniscus (LM) at a point just a few mm below the thalamus, were part of electrode assemblies (0.5 mm diameter) that were inserted to reach therapeutic targets (Feinstein, Alberts and Levin, 1969). Each uninsulated contact had an exposure length of 0.5 mm at right angles to the long axis of the subcortical assembly. Obviously the precise structure in which a contact lay could not be identified histologically. However, physiological evidence for location in n.VPL (or VPM) or in I was considered to be confirmatory when stimulus trains of pulses with relatively low peak currents (0.1-0.2 mA) could produce a purely sensory response (usually a 'tingling', referred to a contralateral portion of the body), and when relatively small increases in stimulus strength gave large increases in the portion of the body to which the sensory response was referred. Production of any motor response by a cerebral stimulus had to be avoided, as the peripheral sensation generated by a muscular contraction could confuse the subjective timings for the test responses; fortunately, stimulus intensities must be raised far above the liminal sensory level at SI cortex of non-epileptic patients to produce any motor effects (Libet *et al.*, 1964), while in LM even very strongly supraliminal stimuli produce no motor responses (Libet *et al.*, 1967).

In each test trial two separate stimuli were presented in a temporally coupled fashion. The pair could consist of two peripheral stimuli (P<sub>1</sub>, P<sub>2</sub>); or, a 'Cerebral' stimulus replaced P<sub>2</sub>, producing the pair P<sub>1</sub>-Cerebral. Peripheral electrical stimuli (0.2-0.5 ms pulses) to the skin or median nerve were applied via two disc electrodes (Grass EEG type) separated by 1-2 cm. For a peripheral stimulus purely to skin the two electrodes were commonly applied to the back of the hand along a mediolateral axis; this usually results in the production of a sensation that is local and superficial in the skin, in contrast to one produced when stimulating a nerve bundle (Libet *et al.*, 1967). (In some experiments a visual flash constituted the P<sub>1</sub>-peripheral stimulus; for this, a brief (0.01 ms) flash was delivered from a Grass photic stimulator set at its lowest intensity and placed a meter or more away. The subject sat in a lighted room and usually did not gaze directly at the lamp. Under these conditions any visual after-image was minimized).

The 'Cerebral' stimulus could be applied either at the cortical (C) electrode, located subdurally postcentral or SI cortex, or via a subcortical contact in n.VPL/VPM or in LM. Cerebral stimuli consisted of brief trains of constant current pulses, each 0.2-0.5 ms and usually at 60 pps, applied via a contact (unifocally); a large metal armband (over saline-soaked gauze) served as the second electrode. Peak currents for liminal stimuli were usually in the range of 1-3 mA for SI cortex and 0.1-0.2 mA for LM. The total coulombs passed was kept to a value well below that regarded as the threshold producing irreversible tissue damage (Pudenz, Bullara, and Talalla, 1975; Bartlett, Doty, Lee, Negrao and Overman, 1977). This becomes especially important when purely unidirectional pulses are employed as for the cortical stimuli. Stimuli to LM were usually biphasic in nature; either the successive pulses alternated in polarity (*see* Results, Section III-C, 2) or each pulse was capacitatively coupled.

### *Instructions to Subject*

The subject was asked to report, within a few seconds after the delivery of each pair of temporally coupled P<sub>1</sub>-C stimuli, whether he subjectively experienced the peripherally-induced sensation (for first; or whether the cerebrally-induced sensation (for C) was first; or whether both appeared to him start 'together' (at the same time). The subject was asked to pay attention to the *onset* of the two sensations. In most experimental series, the sensation induced by a cerebral stimulus (sensation referred to area on the contralateral side, commonly in the hand or arm region) was subjectively timed with respect to a P<sub>1</sub> stimulus that was applied to a related area of the hand or limb on the side opposite to that of the referred cerebrally-induced sensation; this allowed the subject to report simply '-right first' or 'I first', or

`together'. With many subjects in the earlier part of the study, the P, was a brief, weak flash of light; in these cases the subject reported `flash first' or `hand first' (the latter being the cerebral: induced sensation) or `together'. For the control or `comparison' series of trials, in which the temporally coupled stimuli were both peripheral ones (P<sub>1</sub>-P<sub>2</sub>), the nature of the subject's task and reporting was a similar one; the P<sub>2</sub>-peripheral stimulus that replaced the experimental cerebral stimulus was placed on the skin generally within the referral area of the cerebrally-induced sensation.

#### *General Procedure in an Experiment*

The following features were common to most of the experiments in Section III of the `Results a Discussion'. (They also apply with some obvious modifications to Section I, in which studies were carried out acutely in the operating room). After the patient recovered from the acute effects of the surgical procedure for intracranial implantation of electrodes, usually in two to three days, the responses to electrical stimulation at each electrode site were checked for the actual placement with respect to the intended structures.

The initial experimental phase usually consisted of a brief `training' period. This consisted of 15 to 25 trials with temporally-coupled pairs of two peripheral stimuli; these were similar to trials to be used in the `control' series except that, after his report of subjective order for the P<sub>1</sub>-P<sub>2</sub> stimuli in each training trial, the subject was told the `correct' answer (that is, the order in which the two peripheral stimuli were actually delivered in that trial). In addition to providing some familiarity with the procedure, the training series often quickly improved the consistency of responses obtainable in the following control series portion of the experiment when no information was given to the subject. Trials in the experimental series, with the temporally-coupled peripheral vs. cerebral stimuli, were subsequently started without further training; subjects were never given any information about the actual order of stimulus deliveries for peripheral-cerebral couplings.

In most series of trials with temporally-coupled stimuli, three different time intervals were employed for delivery of one stimulus of the pair relative to the P<sub>1</sub>-peripheral stimulus, usually -200, 0 and +200 ms. For a number of subjects additional intervals were used (as in Tables 1-3). The particular coupling interval used in each given trial of a series was set by the operator just before each trial on the basis of a randomized sequence of numbers. Inter-trial intervals were kept to about 20 s with tests involving n.VPL or LM, 30 s with C (SI cortex), and 10-15 s when both coupled stimuli were purely peripheral.

For each individual trial, the subject was pre-alerted by the word `ready', given orally by the observer who was in the room with the subject. Within a second or two, the actual trial period was initiated by an operator who was located in a control booth just outside the closed room in which the subject and the observer sat. The trial was initiated by a brief alerting tone signal and was followed by the two test stimuli which were separated by the preset coupling time interval. A fixed time period of 600 ms between the alerting tone and the P<sub>1</sub> test stimulus helped the subject to focus his attention during the required time. Neither the observer nor the subject were given any indication (either before or after a trial) of the specific coupling time interval used in any of the tests. However, the subject was told in advance that the time intervals, between each pair of test stimuli, might be changed in a random manner for each succeeding trial in the series; and, that he was therefore to try to ignore and not be influenced by any particular pattern of the reports that he might make. Guessing about the sequential order of the two sensations was discouraged; the subject was asked to report his actual conscious experience of the order. When a subject occasionally `missed', that is, found himself unable to report the timing order without guessing, because of a lapse in attention or memory, the same trial was repeated. The latter procedure conforms to our objective of studying the relative subjective timings of reportable awarenesses, not the ability to detect a timing order without necessarily consciously experiencing the order.

#### *Establishment of Stimulus Values for Tests in an Experiment*

The procedure for determining the threshold intensity (I) and minimum train duration (TD) at a given cerebral site were similar to those previously employed (Libet *et al.*, 1964; Libet, 1973). (Liminal I is the lowest peak-current level for a train of stimulus pulses which can elicit any conscious sensory experience; for SI cortex, n.VPL or LM, a minimum train duration of `utilization TD' [U-TD] of about 0.5 s is required with liminal I-see Libet *et al.*, 1964; Libet, 1973). For stimuli to SI cortex, liminal I and U-TD values remain consistent (to within about ±10 per cent or less) when individual stimulus tests are repeated, if the intervals between tests are about 30 s or more (Libet *et al.*, 1964). However, when the stimulus to one of the cerebral sites was temporally coupled with a peripheral stimulus, as required in the present study, and when such paired stimuli were presented repeatedly at regular intervals in an experimental series, the subject's conscious responses to the cerebral stimulus tended to drop out (reversibly). In order to retain positive responses in the series without intolerable interruptions,

intensity was raised somewhat above liminal I, to a level which reduced the minimum TD requirement to 200 to 300 ms. (Increases in TD above the U-TD of about 500 ms, when using a liminal I train, did not appear to eliminate this difficulty).

In most experimental series, therefore, the pulse intensity 'I' for the cerebral stimulus was set at a value such that the minimum required train duration was reduced to (but not below) a value of 200 ms; this minimum peak current for a 200 ms train is termed  $I_{200}$ . It should be recognized that a cerebral stimulus with intensity of  $I_{200}$  and with TD of 200 ms produces the same near-threshold subjective experience as does one with TD of 500 ms at the somewhat lower, liminal I current (*see* I-TD relationship; Libet *et al.*, 1964; Libet, 1966, 1973). The difference is that the 200 ms stimulus train obviously becomes adequate earlier than does the 500 ms one.

The minimum TD was judged to be at least 200 ms only when reduction of TD to 150 ms produced flatly negative (as opposed to 'uncertain') responses in every test. There were thus often instances in which the adopted minimum TD (of 200 ms) produced an inconsistent and uncertain subjective response ('maybe something was there'), and when consistent and not uncertain responses ('I felt it even though very weak') might require minimum train durations of 300 ms or more. In order to retain positive responses, suitable for subjective timings during a series of trials, it was found necessary to employ a TD of 500 or 600 ms, rather than the minimum effective one of 200 ms for the intensity of  $I_{200}$ . The use of such cerebral *test stimuli* (peak current intensity of  $I_{200}$  but TD of 500 or 600 ms) would imply the following: (a) the test stimulus produces a conscious sensory experience that is somewhat stronger than threshold, and it lasts longer than one produced by a stimulus with  $I_{200}$  and TD of 200 ms (*see* Libet *et al.*, 1964); (b) the test stimulus however *cannot become adequate before at least a 200 ms portion* of the total train duration of 500 to 600 ms has elapsed. (With some 'bobbling' of threshold effectiveness some test stimuli might require up to about 300 ms for adequacy, as noted above.)

It was not possible to match precisely the temporal and spatial features of the P-induced sensations with those of the cerebrally-induced sensations. The peak current of the 0.2 to 0.5 ms pulse to the skin could be set so that the subjective intensity of its sensation roughly matched the relatively weak subjective sensory experience produced by the test cerebral stimulus. However, the peripherally-induced sensation was sharper both in its spatial localization and onset, as well as briefer in duration and different in quality. The area of subjective spatial referral for the cerebral test stimuli (whether at SI cortex, n.VPL or LM) was not only larger but, not uncommonly, it could shift to some degree in successive tests of a given series (*see also* Libet *et al.*, 1964). It was also not uncommon (for example, subject G.S. in Table 2) for each cerebrally-induced sensation to have a 'spreading' character, i.e., it could start in a given smaller referral area and quickly extend to a wider referral area before terminating. Subjects in fact reported feeling that it was distinctly easier to perceive and report timing orders for P<sub>1</sub>-P, rather than for P<sub>1</sub>-cerebral couplings; in accordance with this there was a greater scatter (degree of inconsistency of reported timings for the same coupling interval) for the subjective timing orders reported with P<sub>1</sub>-cerebral couplings than with P<sub>1</sub>-P<sub>2</sub> Couplings. In addition, a less sharp onset for a cerebrally induced sensory experience might tend to bias the reported timing order in the direction of this experience starting relatively later than its actual time of onset might warrant. It should be noted that, in tests in which the P stimulus is coupled with one in n.VPL or LM (as in Table 2), any such bias would alter the reports in a direction contrary to that predicted by our modified hypothesis (*see* Results and Discussion); that is, it would tend to weaken the support for the hypothesis. However, in tests coupling a P with a cortical (SI) stimulus, such a bias would operate in the same direction as the hypothetically predicted one, and could thus provide some measure of false support for this particular prediction.

The longer duration of the cerebrally-induced test sensation, and to a lesser extent the less sharp onset, can be roughly matched by the peripherally-induced one if a suitable train rather than a single pulse is applied to skin. (Intensity of the pulse train to skin is also adjusted so that subjective intensities of the two different sensations also match). For such peripheral stimulus trains, the (skin TD) - (total TD of the cerebral test stimulus) minus (min TD required by cerebral test stimulus); for example, with a cerebral stimulus employing a test TD of 500 ms but requiring a minimum TD of 200 ms, the TD for the peripheral stimulus should be 500 minus 200, i.e., 300 ms. (This assumes that the peripheral stimulus requires a negligibly small minimum TD; *see* Libet *et al.*, 1964; Libet, 1973, and below). This arrangement (*see* Table 2) in fact did make the duration of the two sensations (skin vs. LM stimulus) appear subjectively similar, and it seemed to reduce the inconsistency of reported timings.

#### *Data Analysis*

The useful data that could be obtained with a given subject were limited in amount and scope in most cases. The first part of the study, reported in Section I of Results, was carried out in the operating room, during second stage acute procedures in which therapeutic electrodes were inserted and used for treatment of dyskinesias in the awake, responsive patients (Feinstein, Alberts, Wright and Levin, 1960). A

number of the earlier cases involved in Section III of the Results were also studied in the operating room. Most of the studies in Section III, however, were carried out in sessions outside the operating room, with patients in whom therapeutic procedures required the electrodes to remain implanted for approximately a week (Feinstein *et al.*, 1969). Even in this group of ambulatory but in-hospital patients the quality and number of the rather demanding experimental test series that could be achieved with each subject was limited by their condition (recovering from the intracranial implantation procedure and undergoing therapeutic procedures during the week); in most cases it was not feasible to evolve and employ a fully adequate and standardized experimental series of tests. The latter became more readily possible in only a few of a small group of patients, most recently available, in whom stimulating electrodes were chronically implanted in LM for treatment of intractable pain (Feinstein *et al.*, in preparation). Two of this group of patients, in whom the implanted electrodes were still retained with apparent therapeutic benefit after some two to four years, were alert, younger men (H.S., G.S.) whose pain was now generally under control and of negligible significance, and who were able to return and participate adequately in suitably complete experiments (*see* Table 2). Even under optimal conditions, however, the total number of suitable trials in a given session of a few hours is limited by the nature of the subject's task in the experiment. The required attention to very weak sensory experiences itself imposes a considerable 'information load' (*see e.g.*, Desmedt and Robertson, 1977); in the present experiments the weak and brief sensations induced by the cerebral test stimuli were even more elusive and required greater concentration by the subject than did the weakest effective peripheral stimuli. In addition, there was the task of remembering and reporting the temporal order for two experiences closely coupled. Even our normal subjects, who had to deal only with coupled peripheral stimuli, found each session somewhat demanding, and the total number of trials were kept to a minimum for best results (*see* Table 1). Therefore statistical evaluation of results under even the best obtainable conditions required development of a statistical procedure that could deal successfully with the relatively small numbers both of different time intervals (for coupled stimuli) and of trials at each time interval. The statistical treatment was developed by Dennis Pearl, in consultation with Prof. Elizabeth Scott of the Department of Statistics, University of California at Berkeley; a discussion of the treatment is given below in connection with the data in Tables 1, 2, and 3. For the large number of other subjects, we had to rely on in-depth evaluation of more limited data in each case to make qualitative judgments of what such data appeared to demonstrate.

## RESULTS AND DISCUSSION

### *1. Subjective Timing Order for Couplings of a Threshold Peripheral Stimulus (P) with a Liminal Cortical (C) Stimulus Train*

When train duration of a cerebral stimulus with liminal intensity is reduced by 10 to 20 per cent below the average value of about 500 ms for the minimum or 'utilization' train duration (U-TD), the subject reports with certainty that he feels nothing (Libet *et al.*, 1964, 1972). It seemed justifiable, therefore, to assume that the conscious experience for a liminal C stimulus could not begin before the end of the U-TD, though it might begin afterwards (*see* fig. 1). The end of the U-TD is an empirically determinable value for a given subject. Consequently, the onset of the conscious sensory experience elicited by the liminal C stimulus appeared to be utilizable as a 'reference' time. The timing of a peripherally-induced sensory experience might then be meaningfully compared to the 'reference' time provided by the onset of such a cortically-induced sensation. (It should be recalled that conduction delays for the arrival of the peripherally-initiated neural message at the sensory cortex are trivial, in the context of the hundreds of milliseconds required for the 'reference' stimulus at cortex. The latency for the primary evoked potential, recorded on SI cortex in response to a stimulus on the hand, is about 15 ms or so).

On our original hypothesis (Libet *et al.*, 1964, 1972; Libet, 1966, 1973), a single pulse stimulus to the skin at just above threshold level should also be followed by a period of about 500 ms before cerebral neuronal adequacy for the conscious sensation would be achieved. If such a *skin pulse (S)* were to be applied some time (say 200 ms) *after* the beginning of the C stimulus train, then neuronal adequacy for the peripherally-induced sensation should be achieved after the end of the U-TD of the C train (in this example, at about 700 ms after the beginning of the C train; *see* fig. 1). If the *subjective experience* were to occur at the same time as the achievement of *neuronal adequacy* in the case of either stimulus, one would expect the subject to report that the conscious sensory experience for the C stimulus began before the appearance of that for the threshold S pulse (fig. 1).

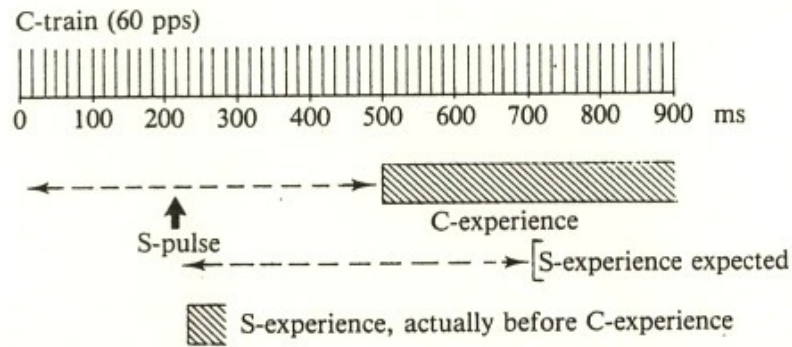


FIG. 1. Diagram of experiment on subjective time order of two sensory experiences, one elicited by a stimulus train to SI cortex (C) and one by a threshold pulse to skin (S). C consisted of repetitive pulses (at 60 pps) applied to postcentral gyrus, at the lowest (liminal) peak current sufficient to elicit any reportable conscious sensory experience. The sensory experience for C ('C-experience') would not be initiated before the end of the utilization-train duration (U-TD, average about 500 ms), but then proceeds without change in its weak *subjective* intensity for the remainder of the applied liminal C train (see Libet *et al.*, 1964; Libet, 1966, 1973). The S-pulse, at just above threshold strength for eliciting conscious sensory experience, is here shown delivered when the initial 200 ms of the C train have elapsed. (In other experiments, it was applied at other relative times, earlier and later.) If S were followed by a roughly similar delay of 500 ms of cortical activity before 'neuronal adequacy' is achieved, initiation of S-experience might have also been expected to be delayed until 700 ms of C had elapsed. In fact, S-experience was reported to appear subjectively before C-experience (see text).

Actual tests of this kind, with S delayed for variable times after the start of the C train, were carried out with six patients. In each of these subjects only a limited number of observations could be made. However, the pooled reports were predominantly those of sensory experience for the C (cortical) stimulus beginning *after*, not before, that for a delayed threshold S pulse; this was true even when the delivery of the S pulse was delayed from the start of the C stimulus train by almost the full value of the U-TD (that is, by up to 400 to 500 ms when U-TD was 500 ms). These findings indicated that the subjective experience of the skin stimulus occurs relatively quickly after delivery of the S pulse, rather than after the expected delay of up to about 500 ms for development of neuronal adequacy following the S input.

Study of this point in this way was carried out chiefly at a time (before 1969) when chronic implantations of therapeutic electrodes were not being made. Thus, only a relatively small number of tests could be made during the surgical procedure (with local anesthesia) in the operating room, with each of the 5 subjects involved (4 parkinsonians, 1 spasmodic torticollis). A sixth subject, an amputee being treated for intractable pain in 1970, was tested via implanted electrodes outside the operating room. However, the results were qualitatively consistent among the different cases in this group.

## II. Modified Hypothesis, to Relate Subjective Timing to the Timing of Neuronal Adequacy for an Experience

There were now two possible alternative conclusions that might be drawn from the experimental result in Section I, above. Alternative (1): the substantial delay empirically required to achieve neuronal adequacy with the cortical stimulus might not apply to the case of a sensory experience elicited by a peripheral stimulus. However, our previous evidence strongly supported the hypothesis of such a cerebral delay for eliciting even a peripherally-induced sensation (Libet *et al.*, 1972; Libet, 1973), and it argued against adopting this alternative (see also General Discussion). Alternative (2): there is a discrepancy between the subjective timing (of a conscious sensory experience) and the expected time at which 'neuronal adequacy' for eliciting the experience is achieved. In considering the apparent paradox posed by alternative (2) it was necessary to recognize that the original hypothesis dealt directly only with the time to achieve the *adequate neuronal state* that elicits the experience. The two timings, for subjective experience vs. neuronal adequacy, might not necessarily be identical. But if there were a

discrepancy between the two kinds of timings, why should it appear in the case of peripheral skin stimuli and not with a cortical stimulus? A possible answer to this question lay in the difference between the initial cortical responses elicited by peripheral vs. cortical stimuli. The S (skin) pulse leads to a volley in the ascending specific projection (lemniscal) system; the latter elicits a relatively localized 'primary' (initially surface-positive) evoked potential in the SI cortex, with an onset latency of about 15 ms after a stimulus to the hand (*see*, Fig. 2; *see also* Jasper, Lende and Rasmussen, 1960; Desmedt, 1971; Goff, Matsumiya, Allison and Goff, 1977). The liminal C stimulus, applied subdurally at SI cortex (postcentral gyrus), does not elicit a similar type of response (*see* Libet *et al.*, 1967, 1972; Libet, 1973). With these considerations in mind we developed the following postulates, to be added as modifiers to our original hypothesis on the cortical processing time for a conscious sensory experience:

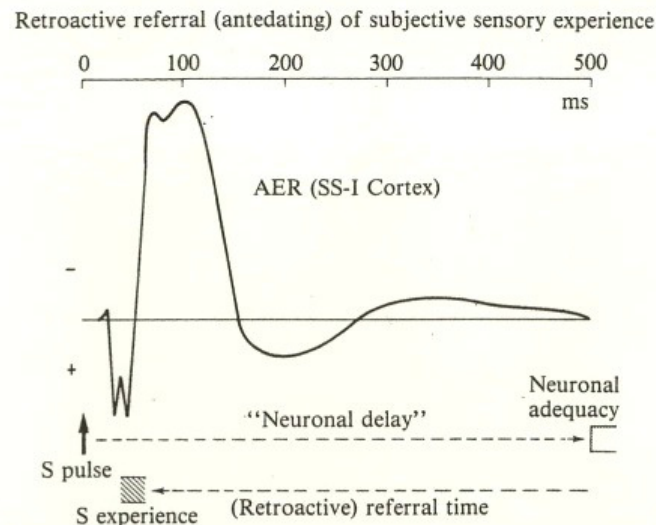


FIG. 2. Diagram representing the 'averaged evoked response' (AER) recordable on the surface of human primary somatosensory cortex (SI), in relation to the modified hypothesis on timing of the sensory experience. Below the AER, the first line shows the approximate delay in achieving the state of 'neuronal adequacy' that appears (on the basis of other evidence) to be necessary for eliciting the sensory experience. The second line shows the postulated retroactive referral of the subjective timing of the experience, from the time of 'neuronal adequacy' backwards to some time associated with the primary surface-positive component of the evoked potential. The primary component of AER is relatively highly localized to an area on the contralateral postcentral gyros in these awake human subjects, as had been shown in anesthetized patients (Jasper, Lende and Rasmussen, 1960). The secondary or later components, especially those following the surface negative component after the initial 100 to 150 ms of the AER, are wider in distribution over the cortex and more variable in form even when recorded subdurally (*see, e.g.*, Libet *et al.*, 1975). It should be clear, therefore, that the present diagram is not meant to indicate that the state of 'neuronal adequacy' for eliciting conscious sensation is restricted to neurons in primary SI cortex of postcentral gyros; on the other hand, the primary component or 'timing signal' for retroactive referral of the sensory experience would be a function more strictly of this SI cortical area.

The AER shown here is a composite drawing, based on actual recordings by us in several unanaesthetized patients, in whom a subdural metal contact was located on the pia-arachnoid surface of the postcentral gyros (SI cortex) at a 'good spot'; the latter was defined by the low intensity required by a direct cortical stimulus train at this site in order to elicit a relatively localized somatic sensation (*see* Libet, 1973; Libet *et al.*, 1964), and by the fact that stimulation of another contact, located 5 to 10 mm anterior to it, could elicit the localized pyramidal-type motor response typical with primary motor cortex. In each case the evoked potentials were recorded (relative to an indifferent electrode usually on ear lobes) in response to single pulse stimuli (S). The latter were applied to a contralateral area of skin within the referral area for the sensation elicited when stimulating via the recording SI cortical electrode. Skin stimuli were just above the threshold for eliciting a sensation in 100 per cent of the trials. The AER for each subject was the average of SI evoked potentials from usually 256 such stimuli, delivered at about 1/s. (The later components of these AERs are probably relatively minimal in their amplitudes, compared to what could presumably be obtained if the rate of stimulus repetition were lower than 1/s and if the subjects had *been* asked to perform some discriminatory task in relation to the



series of 256 stimuli, as in Desmedt (1971). The composite form of these AERs to skin stimuli may be compared with those obtainable as responses to stimulating the median nerve, both with intracranial recordings (Hirsch, Pertuiset, Calvet, Buisson-Ferey, Fischgold and Scherrer, 1961) and with scalp recordings (*see, e.g.,* Desmedt, 1971; Goff, Matsumiya, Allison and Goff, 1977)).

- (1) Some neuronal process associated with the early or primary evoked response, of SI (somatosensory) cortex to a skin stimulus, is postulated to serve as a 'time marker'.  
 (2) There is an automatic subjective referral of the conscious experience backwards in time to this time-marker, after the delayed neuronal adequacy at cerebral levels has been achieved (see fig. 2). The sensory experience would be 'antedated' from the actual delayed time at which the neuronal state becomes adequate to elicit it; and the experience would appear subjectively to occur with no significant delay from the arrival of the fast projection volley. Fortunately, it was possible to put these newly added postulates to experimental tests that could potentially falsify them.

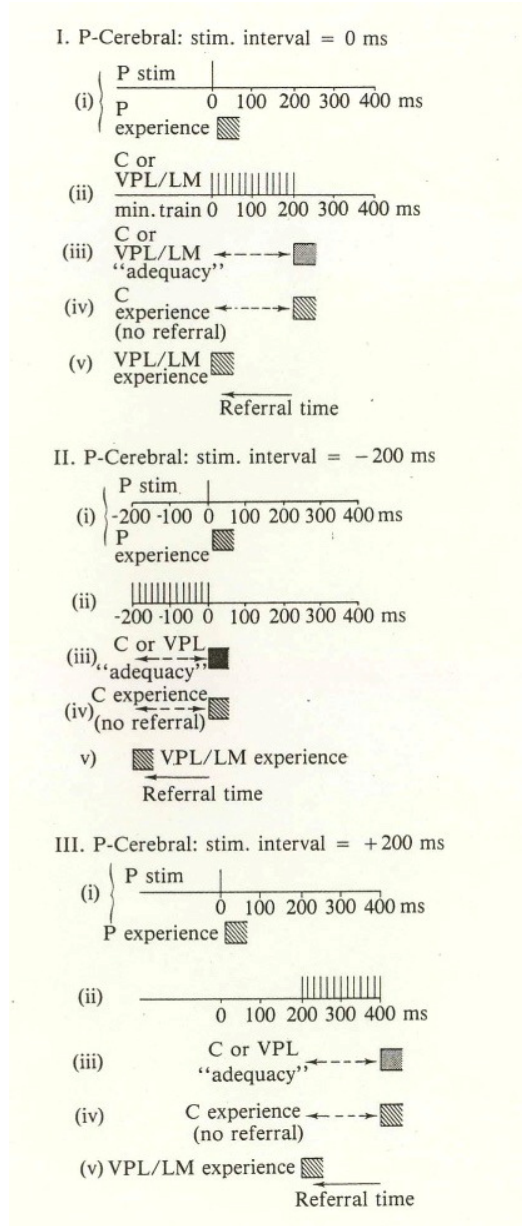


FIG. 3. Diagram of timing relationships for the two subjective experiences when a peripheral stimulus (P) is temporally coupled with a Cerebral stimulus, as predicted by the modified



hypothesis. The Cerebral stimulus train is located either at SI cortex (C) or in n.VPL (or LM). Therefore, timing relationships may be compared for two types of coupled pairs: (a) P paired with SI; and (b) P paired with n.VPL/LM. In set I, the *time interval* between (i) P stimulus and (ii) onset of a cerebral train (whether C or VPL/LM) = 0; in set II, this interval = -200 ms (i.e., cerebral stimulation starts 200 ms before P); in set III, the interval = +200 ms.

P usually consisted of a single pulse applied to skin of the hand (but trains used for experiments in Tables 1 and 2) on the side of body opposite to that in which a referred sensation was elicited by the cerebral stimulus. The P-experience (*see (i)*) is timed subjectively to appear within 10 to 20 ms after the P stimulus (*see also* fig. 2). Each cerebral stimulus (in (ii)) is a train of pulses, usually 60 pps, with peak current adjusted so that a minimum train duration of about 200 ms is required in order to produce any conscious sensory experience; this means that the state of 'neuronal adequacy' (*see (iii)*) with either C or VPL/LM stimuli could not be achieved before 200 ms of stimulus train duration had elapsed. The subjective timing of the experience of C stimulus (iv) should be delayed for a time similar to this minimum TD of 200 ms. But the experience of VPL/LM(v) should be timed earlier; i.e., it should be subjectively referred retroactively, to a time associated with the primary evoked cortical response that is elicited even by the first pulse of a stimulus train in the VPL/LM portion of the specific projection pathway.

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*Predictions from the hypothesis.* The chief test of the modified hypothesis was based on the unique conditions associated with a cerebral stimulus applied to LM or n.VPL, as contrasted with one to SI cortex. As already noted, a stimulus applied to LM or n.VPL requires the same kinds of minimum train durations as one applied to SI cortex, in order to elicit a conscious sensory experience. However, unlike SI cortex, each volley in LM or n.VPL should and does elicit a primary evoked response in SI cortex equivalent to the early components in the response to a skin pulse, which are seen in fig. 2 (Libet *et al.*, 1967). The primary cortical response to an LM volley should supply the same putative timing signal as does the single skin pulse. Consequently, the modified hypothesis would lead to a startling prediction: the subjective timing of a sensory experience elicited by a stimulus train in LM (or n.VPL) should be essentially similar to that for a skin pulse (i.e., as if there were no perceptible delay from the onset of the LM train); this should occur in spite of the experimental fact that the stimulus to LM or n.VPL does not become adequate until its train duration has achieved a substantial value of up to about 500 ms, depending on the intensity employed.

A diagram of the experimental paradigm for these tests with pairs of temporally coupled stimuli is shown in fig. 3. For the cerebral stimulus train at 60 pps, whether cortical (C) or subcortical (LM or n.VPL), the intensity (peak current per pulse) is adjusted so that a minimum train duration of about 200 ms is required in order to elicit any conscious sensory response (*see Methods*).

For *P-Cerebral stim. interval = 0* (fig. 3-I). When a P stimulus pulse or train (to skin or nerve) and a stimulus train to LM (or n.VPL) are begun synchronously (i) and (ii), the patient should report that the *subjective* onsets of both conscious experiences are very close together or synchronous (i) and (v). This should occur even though it is empirically established that stimulus adequacy for the LM/n.VPL stimulus cannot become adequate until after its minimum TD of 200 ms has elapsed, while the P stimulus is adequate either after 1 pulse, or within 33 ms or less when a train is used to elicit a sensation matching both the subjective intensity and duration of the LM-induced one (*see below*). *Neuronal adequacy* for the experience (as distinguished from stimulus adequacy for inducing this neuronal response) would be achieved after a roughly similar delay for both LM and P (as well as for C), as in fig. 3-I (iii) and in fig. 2, according to the hypothesis. On the other hand, with a similar coupling between P and C stimuli, sensory experience for C should be reported to appear after that for P (i) and (iv), as in experiments of Section I above. This should occur even though it is empirically established that C stimulus becomes adequate after the same minimum TD of 200 ms as does LM stimulus.

For *P-Cerebral stim. interval = -200 ms* (fig. 3-II). When LM/n.VPL stimulus train is begun 200 ms before P stimulus (ii) vs. (i), the patient should report that the experience for LM/n.VPL starts before that for P(i) and (v); whereas for a similarly coupled C stimulus the onset of the experience should be reported to come either at the same time or possibly after that for P (i) and (iv).

For *P-Cerebral stim. interval = +200 ms* (Fig. 3-III). When cerebral stimulus train is begun 200 ms after P stimulus (ii) vs. (i), patient should report that the experience for either LM/n.VPL or C stimuli (v) and (iv) appears after that for P (i).

### *III Subjective Timing Orders, Experimentally Determined, for Couplings of P,-P,, P,-LM, and P,-C*

A. *Couplings of two peripheral stimuli (P,-P,).* In order to assess the significance of the relative subjective timings for couplings of peripheral and cerebral stimuli, it is necessary to have an appropriate 'control' series in which the cerebral stimulus is replaced by another suitable peripheral one (P,). Indeed, the experimental question becomes one of directly comparing the reported timing orders for a block of trials with P<sub>1</sub>-P<sub>2</sub> couplings with those for a block of trials with P<sub>r</sub>-cerebral couplings (both types of pairings temporally-coupled by similar intervals). Any *difference* between the two sets of subjective timing orders (for Pr-P<sub>2</sub> vs. P<sub>r</sub>-cerebral couplings) would indicate the presence or absence of a delay in subjective timing for the cerebral stimulus relative to a comparable peripheral one (*see* Tables 2B and 3B). In this method each subject provides his own individual control or comparison data, in the patterns of his reports of subjective timing orders for two peripheral stimuli which should be processed with no differences which are significant in the present context.

Skin stimulus trains which elicit a sensation matching the subjective intensity and duration of that induced by the test cerebral stimuli (*see* Methods) were found to be below the threshold I for a single pulse and to require a minimum TD of 17 or 33 ms, that is, 2 or 3 pulses at 60 pps. When such an S train is coupled with an LM stimulus train which has a minimum requirement of 200 ms TD, the difference between the required stimulus durations for S vs. LM could, therefore, be reduced from 200 ms down to 167 ms. The possible impact of such a 33-ms reduction in the effective coupling intervals, on the pattern of reported subjective timing orders, was tested in normal subjects (Table 1).

In these, the P<sub>1</sub> \_P<sub>2</sub> stimuli were applied to skin of the right and left hands respectively, becoming S<sub>R</sub> (right) and S<sub>L</sub> (left) stimuli. Stimulus intensity in each case was reduced to a level that required a minimum of 2 or 3 pulses at 60 pps (TD = 17 or 33 ms) to elicit any sensory experience; but actual TD of each test stimulus was 300 ms, to simulate both the subjective intensity and duration of cerebrally-induced sensations (*see* Methods). For the A-blocks of trials, S<sub>R</sub>-S<sub>L</sub> coupling intervals ranged from -200 to +200 ms (and were similar to the 'control' series with S<sub>1</sub>-S<sub>2</sub> couplings in Table 2). For the 'experimental' B-block series in Table I, delivery times of S<sub>R</sub> stimuli were modified by delaying onset of each S<sub>R</sub> stimulus by 33 ms. This reduced each S<sub>R</sub>-S<sub>L</sub> coupling by 33 ms, from what the interval had been in the first or A series of the session with that subject; for example, an S<sub>R</sub>-S<sub>L</sub> interval of -200 ms (that is, S<sub>R</sub> started 200 ms after S<sub>L</sub>) in series A would now become -233 ms in B, while an interval of S<sub>R</sub>-S<sub>L</sub> = 0 (synchronous delivery) in A would now become -33 ms (S<sub>R</sub> started after S<sub>L</sub>) in B, etc. In all Tables the value of the coupling time interval between test pair of stimuli was varied in a random manner in successive trials. However, all the subjects' reports in those trials using a given coupling time interval in a given block of trials are collected together in the Table under 'Subject's timing'. In block A of Table 1, for example, subject D.A. was presented with an S<sub>R</sub>-S<sub>L</sub> interval of 0 in 10 trials which were randomly distributed among the total of 50 trials in block A. Of these 10, she reported experiencing S<sub>R</sub> (skin of right hand) 'first' in 3 trials; she reported S<sub>R</sub> and S<sub>L</sub> sensations starting 'together' (T) or at the same time in 7 trials; and there were no reports of 'S<sub>L</sub> first' in any of these 10 trials.

The comparison of timing orders in block A with those in block B trials of Table 1 simulates the design for the experiments in Tables 2 and 3. But in Table I the known delay imposed on one of the stimuli (S<sub>R</sub> in block B) should theoretically produce a similarly defined shift in subjective timing of the sensation elicited by that stimulus; whereas in Tables 2 and 3 the possibility of a shift in subjective timing relative to onset of a stimulus train in LM or SI cortex constitutes the unknown point. Therefore, the experiment in Table 1 serves as at least a partial check on the validity of this design and of the statistical method employed in the analysis, as well as to test the specific question of what effect a 33-ms shift may have on overall pattern of reports of subjective timing.

Comparing block A with block B for each subject in Table IA, it is seen that the extra 33-ms delay for S<sub>R</sub> stimuli produced no change in subjective timing orders for the 200- and 150-ms coupling intervals (that is, the orders remained essentially the same as the actual order of stimuli delivered). However, small differences between blocks A and B did appear for shorter S<sub>R</sub>-S<sub>L</sub> intervals; these indicated qualitatively that in series B there was a slight shift of reported timing orders in the expected direction of a small delay in the experience of S<sub>R</sub> relative to that for S<sub>L</sub>. Statistical evaluation of the data in Table 1 was carried out by the same procedure that was developed for treatment of experimental data obtained with the patients, as in Tables 2 and 3 (*see* discussion of statistical terms, etc.). The 'mean shift', in the subjective timing for S<sub>R</sub> relative to S<sub>L</sub>, should be close to 0 for each A-block, since the coupling intervals are grouped symmetrically, + and -, around 0. (In fact, however, the mean shift was close to 0 only for subject M.L.; the -30 ms shift for D.A. indicates a slight 'bias' in the direction of reporting S<sub>R</sub> first, and the + 100 ms shift for R.J. indicates a bias in the opposite direction. All three subjects were right-handed).

The *change in mean shift*, when block B ( $S_R$  delayed by 33 ms) is compared with block A, is given for each subject in Table 1B. The changes in mean shift are not far from -33 ms for all three subjects ; the changes all indicate a statistical tendency to experience  $S_R$  as delayed, relative to  $S_L$ , by a time not far different from the actual delay imposed on  $S_R$  in the  $S_R$ - $S_L$  couplings in block B.

*Statistical treatment.* In this treatment, the responses for all the stimulus-coupling intervals in a given series or block of trials are used to estimate a 'mean shift'. The mean shift is, qualitatively speaking, the best time delay to use for one of the stimuli in order to get close to the centre around which the subject is reporting the relative orders for the other stimulus in all the temporally-coupled pairs in that block. (A value of zero for the mean shift would indicate no shift, in the subjective timing 'centre' of the first stimulus relative to the second stimulus of each pair, from the actual relative positions of the coupled stimuli as delivered. A negative value for the mean shift indicates that subjective timing 'centre' for the first stimulus of the pair is shifted retroactively away from the timing for the second; that is, the timing for the second stimulus is delayed from that of the first by this value).

TABLE IA. SUBJECTIVE TIMING ORDERS OF EXPERIENCES FOR TEMPORALLY COUPLED PAIRS OF SKIN STIMULI, RIGHT VS LEFT HANDS, IN NORMAL SUBJECTS

Subject	$S_R$ - $S_L$ interval (ms)	No. of trials	Subject's timing			Estim. 'mean shift' (ms)	Approx. SD
			$S_R$ first	T	$S_L$ first		
D.A. (female, aged 26 y)	A	10	0	0	10	-30	10
			0	3	7		
			3	7	0		
			10	0	0		
			10	0	0		
	B	10	0	0	10	18	16
			0	1	9		
			0	10	0		
			8	1	1		
			10	0	0		
R.J. (male, aged 29 y)	A	10	0	0	10	100	21
			0	0	10		
			0	3	7		
			3	6	1		
			8	1	1		
	B	10	0	0	10	122	25
			1	0	9		
			0	1	9		
			2	7	1		
			6	3	1		
J.Wl. (male, aged 31 y)	A	6	0	1	5	-5	14
			0	0	6		
			0	0	6		
			1	0	5		
			2	1	3		
			5	1	0		
	B	6	0	0	6	22	14
			0	0	6		
			0	0	6		
			1	1	4		
			1	0	5		

Effect of added 33 ms delay for one stimulus of each pair, see text.

The *difference* between the mean shifts for two blocks of trials, carried out in the same or in a closely comparable session, gives the estimated change in shift. For each such change in shift, the standard deviation (SD = square root of the variance) and the approximate '95 per cent confidence interval' is

given. The latter consists of two values (in parentheses, Tables 1B, 2B, 3B) each of which is equal to two standard deviations on either side of the estimated change in shift; that is, we are about 95 per cent certain that the true value of the change in shift lies between these two values. The estimated 'change in shift' in the appropriate direction for all three subjects (Table 1B) is surprisingly close to the relatively small imposed shift of 33 ms, and it provides a kind of confirmatory test of the validity of the statistical procedure.

In Tables 2 and 3, of course, the comparisons for change in shift are between a block of trials for P,-P, couplings and a block of P,-cerebral couplings ('cerebral' stimuli being those to LM in Table 2, and to SI cortex in Table 3). When P, is common to both blocks, the change or difference in mean shifts between the two blocks reflects the difference between subjective timings for the second stimuli of the couplings in each block, for example, between the timings for  $S_L$  and for C (see Table 3s). When the mean shift for block B is subtracted from that for block A, a positive value for the resulting 'change in shift' indicates a delay for timing of the second stimulus in block B (C in Table 3B) relative to the timing for the second stimulus in block A ( $S_L$  in Table 3B).

TABLE 1B. COMPARISON OF TIMING ORDERS FOR TWO BLOCKS OF  $S_R$ - $S_L$  PAIRS, WHEN ONE BLOCK OF STIMULUS COUPLING INTERVALS IS SHIFTED BY 33 MS.

Subject	Comparison	Estim. change in shift (ms)	Approx. SD	Approx. 95% confidence interval
D.A.	A vs. B	-48	19	(-86; -9)
R.J.	A vs. B	-22	33	(-87; 43)
J.WI.	A vs. B	-27	20	(-68; 13)

$(S_R - S_L)_A - (S_R - S_L)_B$

A fuller, rigorous description and analysis of the statistical treatment is beyond the scope of the present paper. An alternative statistical approach which could have been adapted to our needs has since been published (Dempster, Laird, and Rubin, 1977). Three assumptions involved in formulating the statistical model employed were as follows: (i) for a particular block of data the shift function is roughly constant from trial to trial, and (ii), each trial is independent. Both of these assumptions appear to be reasonable and warranted on the basis of the care taken to maintain constant conditions within a given session, keeping the total load on the subject at levels well below any apparent fatigability, etc., and randomizing the presentation of the coupling time intervals in successive trials; in addition, data of the exact sequence of responses were examined for subjects H.S. and G.S. in Table 2, and they showed no significant deviation from the assumption of independence of trials; (iii) the distribution function of the responses is roughly linear within the experimental range even for coupling time intervals which were not tested, and also for the range of intervals extending where necessary on either side of the experimental range. This assumption introduces a possible 'interpolation error'. This potential error tends to be reduced by the use of more different time intervals for coupling, for example, at least five intervals for the series in Tables 1 and 2 instead of the three employed in most of our other experiments. The probable actual interpolation error, due to linearizing the estimated shift function, appeared to be no more than 10 ms in the experiments using five different time intervals (as in Table 2A) and no more than 30 ms in experiments using three. Fortunately, the amounts in such errors would not seriously affect the significance of the data in relation to the hypothesis being investigated.

'Accuracy' of timing orders for paired peripheral stimuli. The degree of 'accuracy' (the similarity of the reported to the actually applied order of P,-P<sub>2</sub> stimuli) had to be virtually 100 per cent for P,-P, coupling intervals of 200 ms, in order to be useable for the comparisons with the P,-Cerebral couplings. Experimental tests of the hypothesis required that the subject be capable of subjectively distinguishing timing orders for intervals equal to or less than the minimum TD of 200 ms that was required by the test cerebral stimuli. Fortunately, subjective timing orders for  $S_R$   $S_L$  coupling intervals of 200 ms did turn out to be essentially 100 per cent 'accurate' for almost all the patients tested. The 'accuracy' was often somewhat reduced with 150-ms intervals, and distinctly poorer with 100-ms intervals (for which some patients could not report consistent orders). The examples in Tables 2 and 3 illustrate this point. The use of brief trains of pulses (300 to 400 ms TD's) for skin stimuli, rather than the single pulse stimuli used in most of the subjects, did not appear to affect the reported timing orders.

TABLE 2A. SUBJECTIVE TIMING ORDERS OF EXPERIENCES FOR TEMPORALLY-COUPLED STIMULI: COMPARE SKIN (S<sub>1</sub>) AND MEDIAL LEMNISCAL (LM) PAIRINGS WITH S<sub>1</sub>-S<sub>2</sub> PAIRINGS

Subject	LM stim.		S <sub>1</sub> -S <sub>2</sub>	Subject's timing					Estim. 'mean shift' (ms)	Approx. SD	
	Min. TD	Test TD		Interval (ms)	No. of trials	S <sub>1</sub>		S <sub>2</sub> /LM			
	(ms)	(ms)	first			T	first	LM			
H.S. (male, aged 62 y)	A		S <sub>L</sub> -LM	-200	9	0	1	8	-41	9	
				-100	9	0	8	1			
				0	10	0	10	0			
				+100	11	9	2	0			
				+200	10	10	0	0			
	B	200- 300	600	S <sub>L</sub> -LM	-200	10	0	0	10	1	18
					-100		1	6	3		
					0		1	9	0		
					+100		1	8	1		
					+200		10	0	0		
C			S <sub>L</sub> -S <sub>R</sub>	-250	5	0	0	5	-91	23	
				-150	6	1	3	2			
				0	5	0	4	1			
				+150	5	5	0	0			
				+250	5	5	0	0			
D	300	600	S <sub>L</sub> -LM	-250	6	0	0	6	-109	39	
				-150	4	1	0	3			
				0	4	0	4	0			
				+150	5	3	2	0			
				+250	5	5	0	0			
G.S. (male, aged 57 y)	A		S <sub>R</sub> -S <sub>L</sub>	-200	10	0	0	10	-35	8	
				-100	11	0	10	1			
				0	10	0	10	0			
				+100	10	8	2	0			
				+200	10	10	0	0			
	B	200	500	S <sub>R</sub> -LM	-200	8	0	2	6	-25	25
					-100	8	0	8	0		
					0	9	4	2	3		
					+100	7	4	2	1		
					+200	10	8	1	1		
C	200- 300	500	S <sub>R</sub> -LM	-200	10	0	4	6	-12	28	
				-100		0	8	2			
				0		2	6	2			
				+100		6	3	1			
				+200		8	1	1			
D			S <sub>1</sub> -S <sub>2</sub> (both on R. side)	-200	9	0	1	8	-19	24	
				-100	11	0	4	7			
				0	10	2	7	1			
				+100	10	8	2	0			
				+200	10	10	0	0			

TABLE 2B. COMPARISONS OF TIMING ORDERS FOR (S<sub>1</sub>-S<sub>2</sub>) vs. (S<sub>1</sub>-LM)

Subject	Min. TD for LM (ms)	Comparison	Estim. 'change in shift' (ms)	Approx. SD	Approx. 95% confidence interval
H.S.	200-300	A vs. B (S <sub>L</sub> -S <sub>R</sub> )-(S <sub>L</sub> -LM)	-42	20	(-82; -2)
	300	C vs. D	18	46	(-74; 110)
G.S.	200	A vs. B (S <sub>R</sub> -S <sub>L</sub> )-(S <sub>R</sub> -LM)	-10	26	(-63; 43)
	200	A vs. (B+C)	-30	24	(-78; 18)

The foregoing was also applicable to 'normal' subjects (non-patients); some of these exhibited considerable 'accuracy' even with a 50-ms interval, but almost none with a 25-ms interval. Four normal subjects with ages in the 40's and 50's were tested with single pulse  $S_R$  and  $S_L$  stimuli. In 4 subjects the S stimuli were trains of weak pulses to better simulate the cerebrally-induced sensations (data for 3 of these are given in Table 1A, with similar results for the fourth, a female aged 40 years). The weaker S-induced sensations in this second group appeared to be more demanding of effort and alert attention by the subjects; indeed, in two additional subjects who were studied at the end of their regular eight-hour working period as nurses, the reported timing orders for given coupling intervals exhibited considerable variability and the 'accuracy' was poor. This factor probably helps explain some of the inconsistency of results obtained with P,-Cerebral couplings in the patients; most of the patients were not in an optimal physical and mental state when they were studied with P,-Cerebral trials in which the cerebrally-induced sensation was always, because of the experimental requirements, similarly weak in subjective

*Negative 'mean shifts' for S,-S, in Table 2A.* For subject H.S., blocks A and C, estimated 'mean shifts' are -41 and -91 ms respectively; for subject G.S., block A, it is -35 ms even though the left-right order is reverse of that for H.S. The mean shifts for comparable blocks of trials were -21 and -9 ms for patients J. W. and C.J. in Table 3A; and -30, + 100, and -5 ms for the normal subjects in Table 1A. To the extent that the negative shifts in Table 2A may be significant, they would imply that, for these patients, a stimulus to skin on the normal side ( $S_L$  for H.S., and  $S_R$  for G.S.) tended to be subjectively timed somewhat earlier than a comparable stimulus on the abnormal side (that was treated for pain). Most of this estimated negative mean shift appears to be associated with an asymmetry between the responses for the smaller time intervals, that is, for -100 ms (or -150) compared to those for + 100 ms (or + 150 ms). For both subjects, the reported timing orders were predominantly  $S_1$  and  $S_z$  'together' for the -100 (-150) ms intervals; whereas, they were predominantly 'S, first' for the +100 (+ 150) ms intervals, in accord with the actual order of delivery. This asymmetry is in fact associated with a modest but definite deficit in epicritic sensibilities on the abnormal side (right side for H.S., and left for G.S.). The deficits are ascribable to losses in the specific projection pathway probably at thalamic levels, due either to their own pathological disorders, or to small heat lesions in n.VPL or just subthalamic sites (which were made to treat their pain some years prior to implanting the present stimulating electrodes in LM), or to both. The results obtained for S,-S, couplings when both stimuli were located on the normal side in subject G.S. (Table 2A, block D) are in accord with this interpretation; the smaller estimated mean shift of -19 ms has a standard deviation of  $\pm 14$  and the designation of + vs. - direction was an arbitrary one in block D, in which either of the S stimuli could have been called  $S_n$ . For the  $S_{\text{normal}} - S_{\text{abnormal}}$  couplings in these patients, negative mean shifts are in fact explainable by our modified *hypothesis*; if a small deficit in specific projection pathway were present on one side, the reduction in putative early 'timing signal' delivered by this system to the cerebral cortex should tend to reduce the degree of retroactive subjective referral of the timing for that abnormal side.

*B. Couplings of a peripheral stimulus ( $P_1$ ) with a medial lemniscus stimulus (LM).* The technically most satisfactory experimental series of this type are presented in Table 2 (see further details in small print section below). They were carried out with two subjects (H.S. and G.S.) who were able to return for study a few years after the permanent implantation of electrodes in LM. (The implantation was made for the therapeutic relief of intractable pain of central origin by self-stimulation (Feinstein *et al.*, in preparation). The subjects were now outpatients with their pain controlled and presenting no interference to studies. They were in relatively good physical and psychological condition, and they were able to tolerate well a more concentrated period of successive morning and afternoon study sessions for two days each. Peripheral stimuli were matched in the best obtainable manner to the LM stimuli (see Methods). The experiments could be designed and completed in a manner making them as amenable to statistical evaluation as were the experiments with the normal subjects (in Table 1).

The distribution of reported subjective timing orders is seen in Table 2A to be roughly similar for both the S,-S, and the S,-LM couplings. For example, with a coupling interval of -200 or -250 ms for either  $S_1-S_2$  or for S,-LM pairs, most or all the reports were either 'S<sub>2</sub> first' or 'LM first' respectively, as seen in the appropriate blocks. If the subjective timing for LM had actually been delayed an extra 200 ms, in accordance with the minimum TD requirement of 200 or more ms for the LM stimulus employed, one would have expected that the  $S_1$ -LM couplings at -200 ms should have produced more reports of 'together' (both sensations experienced about the same time) or even of 'S<sub>1</sub> first'.

This qualitative impression of overall similarity between the subjective timing orders for  $S_1-S_2$  vs. S,-



LM couplings is substantiated by the results of the statistical evaluation. The following should be noted in Table 2B: (a) each 'estimated change in mean shift' is relatively small, far less than the minimum TD of 200 ms or more required by the LM stimulus to elicit any sensory experience. Furthermore, most of the changes in shift are negative, although probably not significantly so. If valid, a negative change would indicate that subjective timing for LM is slightly earlier than, rather than delayed after, that for  $S_1$  (each relative to  $S_1$ ). (Such an earlier timing might even be additionally explainable by the shorter latency time for the primary cortical response to an LM volley than to an S volley, although there are other possible small modifiers in both directions); (b) the 95 per cent confidence intervals do not contain the value of the minimum TD of 200 ms or more that is required by the LM stimulus; consequently it is very unlikely that the data can be explained by a shift or delay in subjective timing equal to or determined by this minimum TD of the LM stimulus. Rather, the data are most reasonably explained on the basis of the prediction from the hypothesis, that subjective timing for an LM stimulus was roughly similar to that for a peripheral S stimulus, in spite of the empirically determined extra 200 ms or more that was required by the LM stimulus to be effective at all.

A much larger number of less adequate experimental series was carried out prior to those in Table 2 (*see Methods*). These included preliminary studies in four subjects, in which controls and experimental procedures were being developed. There were also previous extensive studies with H.S. and G.S. that were conducted under less favorable conditions than those in Table 2; these included 12 sessions with H.S., some five years earlier (during a prolonged stay of two and a half months in the hospital) plus a few sessions two years after that during a revisit, as well as 5 sessions with G.S. some two years earlier. Additionally, there were sessions of variable numbers and durations with two other patients with chronically implanted electrodes in LM. Our own in-depth analyses of each case convinced us that, when experimental conditions were at least partially adequate, the results obtained were qualitatively in support of the hypothesis, that is, they tended to show patterns of subjective timing qualitatively resembling those in Table 2.

In Table 2, the stimulus to LM (medial lemniscus) consisted of a train of 0.2 ms-pulses at 60 pps. Peak current intensity was set so that a minimum train duration (TD) of 200 or 300 ms was required (*see 'min TD' column*) in order for the stimulus to elicit any reportable sensory experience. The actual test stimulus applied to LM, in each trial with an S<sub>1</sub>-LM coupling, was at this same intensity ( $I_{200}$ ) but had a TD longer than the minimum required one (*see values under 'test TD' column*), and explanation in *Methods*). The peripheral stimuli,  $P_1$  and  $P_2$ , were applied to the skin and are called S<sub>1</sub>-S<sub>2</sub>. Since the LM-induced sensation (that replaces S<sub>2</sub>) was referred to the right side for subject H.S. and to left side for subject G.S., S<sub>1</sub> and S<sub>2</sub> were actually  $S_L$  and  $S_R$ , respectively, for subject H.S., but  $S_R$  and  $S_L$ , respectively, for subject G.S. Each test stimulus to skin (whether S<sub>1</sub> or S<sub>2</sub>) consisted of a train of 0.2 ms-pulses, 60 pps, with peak current set so that subjective intensity of the sensation approximated that elicited by the test LM stimulus; and TD was set at 400 ms in block A for H.S. and at 300 ms in all the other S<sub>1</sub>-S<sub>2</sub> blocks, so as to approximate the subjective duration of the sensation elicited by the LM test stimuli.

Reports of 'subject's timing' for either S<sub>2</sub> or LM 'first' refer, respectively, to whether a block of S<sub>1</sub>-S<sub>2</sub> couplings or S<sub>1</sub>-LM couplings is involved. In block D for G.S., S<sub>1</sub> and S<sub>2</sub> were both located on the normal right hand (S<sub>1</sub> on back of hand near digits 4-5, and S<sub>2</sub> on ventral aspect of wrist). *See small print section above on 'Negative mean shifts . . .'* for comparison of these results in block D with those in block A,  $S_R$ -normal side vs.  $S_L$ -abnormal. Because of this, it was not appropriate to compare blocks C and D for subject G.S. in the same way as the other comparisons in Table 2B. Instead, the two blocks with  $S_R$ -LM trials (blocks B and C) were combined and then compared to block A ( $S_R$ - $S_L$  trials) for subject G.S. In any case, however, a comparison of the D vs. C blocks in subject G.S. in fact produces a result qualitatively similar to that for A vs. B.

*C. Couplings of a peripheral stimulus (P) with an SI cortical stimulus (C).* These experiments were similar in principle to those in section 111-B above, but with the cerebral stimulus applied subdurally to somatosensory, SI cortex (C), rather than to LM. Blocks of trials with paired P<sub>1</sub>-C stimuli were compared in each subject with blocks of P<sub>1</sub>-P<sub>2</sub> stimuli, with coupling intervals for each trial that overlapped for the two blocks. P<sub>1</sub> was either a single pulse to the skin (S<sub>1</sub>) of the hand opposite to that in which C-induced sensation was referred, or in many cases it was a brief but weak flash of light (F). P<sub>2</sub> was a single pulse to skin ( $S_2$ ), usually placed within the referral area of the C-induced sensation. As with LM, the C stimuli (pulse trains, 60 pps) were set at intensities somewhat above liminal levels so that a *minimum* TD of at least 200 ms or more was required to elicit any sensory experience; and, with these same intensities, the *test* TD's used in the actual trials were longer than the required minimum (*see actual values in columns under 'min TD' and 'test TD'*). The results obtained with C trains of unidirectional cathodal pulses ('cath') were distinctly different from those with C trains of pulses that successively alternated or reversed in polarity ('PR'). The two kinds of P<sub>1</sub>-C couplings are



therefore considered separately.

In Table 3 subjects J.W., C.J., W.M. and A.E. were parkinsonians; subject O.K. had 'basal ganglion disease' and M.T. had spasmodic torticollis. The S<sub>1</sub> and S<sub>2</sub> stimuli were single pulses, whose intensities were matched subjectively but were at levels distinctly above the threshold. Therefore, unlike those in Table 2, the sensations elicited by these S stimuli were not optimally matched, for subjective intensity and duration, with the cortically-induced sensations. Subjects in Table 3 were inpatients who were less able, than those in Table 2, to maintain consistency of reported sensory experiences in a long series of trials when S stimuli were set very close to threshold intensities for a conscious sensory experience. The use of a suprathreshold single pulse for S stimuli could have to some unknown degree biased the reported subjective timing orders for S<sub>1</sub>-C couplings in the direction of S<sub>1</sub> first. However, any such bias would appear not to have determined the qualitative overall pattern of timing orders, as illustrated by the following: in subject C.J., the same S stimuli produced quite different results for C-cathodal (block B) when compared to C-polarity reversed pulses (block C). On the other hand, the use of a weak flash of light in place of S<sub>1</sub> (in P<sub>1</sub>-C couplings with C-cathodal) produced a pattern of subjective orders (subject M.T.) qualitatively similar to those using S<sub>1</sub> and C cathodal (as in J.W., C.J. and O.K.).

TABLE 3A. SUBJECTIVE TIMING ORDERS OF EXPERIENCES FOR TEMPORALLY-COUPLED STIMULI: (i) PERIPHERAL (S<sub>1</sub> OR FLASH F) AND SOMATOSENSORY CORTEX (C) PAIRINGS, AND (ii) S<sub>1</sub> (OR F)-S<sub>2</sub> PAIRINGS

Subject	C stim.		S <sub>1</sub> (F)-S <sub>2</sub>		Interval (ms)	No. of trials	Subject's timing			Estim. 'mean shift' (ms)	Approx. SD	
	PR	cath	Min. TD (ms)	Test TD			S <sub>1</sub> (F)-C	S <sub>1</sub> (F) first	T			S <sub>2</sub> /C first
J.W. (male, aged 54 y)	A				-200	5	0	0	5			
					-150	12	0	3	9			
					0	12	1	11	0			
					+150	9	9	0	0			
					+200	4	4	0	0			
	B cath 200 500					-400	6	0	1	5		
						-300	11	0	8	3		
						0	12	11	1	0		
						+300	5	5	0	0		
						+400	4	4	0	0		
C.J. (male, aged 60 y)	A				-200	3	0	0	3			
					-150	8	0	0	8			
					0	8	1	7	0			
					+150	6	6	0	0			
					+200	4	4	0	0			
	B cath ~300 700					-200	9	5	4	0		
						0	7	5	2	0		
						+200	9	9	0	0		
	C PR ~200 700					-200	6	0	6	0		
						0	4	1	3	0		
+200						6	1	5	0			
O.K. (male, aged 53 y)	A				-200	11	0	1	10			
					0	7	1	5	1			
					+200	10	9	1	0			
	B cath ~400 500					-500	10	9	1	0		
						-400	7	7	0	0		
						-200	5	5	0	0		
						0	14	11	3	0		
						+200	4	4	0	0		
	M.T. (male, aged 42 y)	A				-100	10	0	0	10		
						0	13	1	9	3		
+100						7	6	1	0			
B cath 200- 400 300						-200	11	0	7	4		
						-150	11	0	7	4		
						0	15	6	8	1		
						+150	10	9	1	0		
						+200	9	8	0	1		

Subject	Cath	C stim.		$S_1(F)-S_2$	Interval	No. of trials	Subject's timing			
		Min. TD	Test TD				$S_1(F)$ first	T	$S_2/C$ first	
	PR	(ms)	(ms)	$S_1(F)-C$	(ms)					
W.M. (male, aged 47 y)	A				-300	15	0	1	14	
					-200	33	0	4	29	
					0	31	1	26	4	
					+200	24	12	10	2	
					+300	12	11	1	0	
	B	PR	200 300	400 500		-400	7	1	1	5
						-300	11	0	6	5
						-200	17	1	6	10
						0	23	2	17	4
						+200	8	2	6	0
A.E. (female, aged 57 y)	A				-200	25	1	2	22	
					-150	23	3	2	18	
					-100	13	3	10	0	
					0	41	2	38	1	
					+100	10	2	7	1	
	B	PR	~300	700		+150	19	11	6	2
						+200	18	16	1	1
						-400	22	2	12	8
						-200	16	3	12	1
						0	18	5	13	0

TABLE 3B. COMPARISONS OF TIMING ORDERS, FOR PAIRS OF PERIPHERAL STIMULI VS. PERIPHERAL-CORTICAL PAIRS (C=CATHODAL PULSES)

Subject	Min. TD for C (ms)	Comparison	Estim. 'change in shift' (ms)	Approx. SD	Approx. 95% confidence interval
J.W.	200	A vs. B ( $S_R-S_L$ )-( $S_R-C$ )	220	25	(169; 271)
C.J.	~300	A vs. B ( $S_R-S_L$ )-( $S_L-C$ )	454	156	(143; 765)
M.T.	200-300	A vs. B ( $F-S_L$ )-( $F-C$ )	95	25	(45; 145)

For subject O.K.,  $S_R$  was applied to back of right hand, while the C-induced sensation (stimulus to left SI cortex) was referred to the same right side but to the vicinity of the ear. The coupling of this  $S_R$  (instead of  $S_O$  with C would result in the processing of the initial responses to  $S_R$  and C at separate sites in the same, left postcentral gyrus. However, this did not prevent the subject from maintaining a clear distinction between the timings for the two sensations, as he reported a preponderance of ' $S_R$  first' (in block B) compared to the reports for  $S_L-S_R$  couplings (in block A). It may be added that trials (in some other subjects) with S, and S, on the same side have generally produced timing orders with an 'accuracy' comparable to series using  $S_R$  and  $S_L$  analysis (for example, Section III, block D for G.S. in Table 2A). However, there tended to be less confusion and less effort required on the part of the subject with comparisons of one side vs. the other.

For Table 311, 'changes in shift' were estimated only for those experiments in Table 3A in which stimulus C consisted of cathodal pulses.

1. P,-C couplings using a cathodal pulse train for C. Results from those experiments in which

suitable comparative blocks of trials were achieved are given for subjects J.W., C.J., O.K., and M.T. in Table 3A. Patterns of subjects' timing orders (blocks A vs. B in these subjects) show a qualitative difference from those in Table 2A (with LM stimuli). For example, J.W. reported in most of the trials with  $S_R$ -C interval at -300 ms (i.e., C stimulus train begun before  $S_R$  by 300 ms) that the  $S_R$ - and C-induced sensations subjectively started 'together'. But when two peripheral stimuli,  $S_R$ - $S_L$ , were coupled by intervals of -200 and -150 ms he reported mostly ' $S_L$  first'. Only when C stimulus was advanced to 400 ms before  $S_R$  ( $S_R$ -C interval=-400) did J.W. report mostly 'C firsts'. Similarly, with coupled stimuli initiated simultaneously (coupling interval= 0), J.W. reported mostly ' $S_R$  first' for the  $S_R$ -C couplings, but mostly 'together' for the  $S_R$ - $S_L$  couplings.

The statistical analysis of all the suitable data is in agreement with the impression of a qualitative difference. The estimated 'change in mean shift', when C stimulus (cathodal pulses) was substituted for the S, stimulus ('mean shift' for block A minus that for block B) is given in Table 3B for subjects J.W., C.J. and M.T. They all show values for a substantial delay in the subjective timing of the C-induced sensation relative to the S-induced sensation. The amount of this estimated change in shift, that is, the delay for C-induced sensation, is close to the actual required minimum train duration (TD) of 200 ms for C stimulus in J.W.; it is greater than the minimum TD of 300 ms in C.J. ; and it is less than the minimum TD of 200 to 300 ms in M.T. (on the latter difference, *see below*). Note also that the 95 per cent confidence intervals all indicate that the change in shift in each case is in the positive range only, that is, in the direction of a delay for timing of C-induced sensation. (Results for O.K. were not treated statistically because the coupling was left-right [ $S_L$ - $S_R$ ] in block A, but right-right [ $S_R$ - and C-induced sensations on the same side] in block B (*see details in small print section, above*). However, the results for subject O.K. in Table 3A are in qualitative agreement with those for J.W., C.J., and M.T.)

These findings are thus in general accord with the prediction from the hypothesis (*see fig. 3*) and also with the results described in Section I of the Results. The substantial relative delay in the subjective timing of the C-induced sensation is of course sharply different from the absence of such a delay for a sensation induced by a comparable LM stimulus train (*see Section III-B of Results, above*); for example, compare Table 2B with Table 3B. For subject M.T. the estimated change in shift of 95 ms indicated a relative delay that is less than the 200 to 300 ms minimum TD required by the C stimulus. However, subject M.T. (who was a very alert, introspective observer) reported having a 'hunch', or preconscious type of feeling, that 'something' was building up before the instant at which he himself felt that he was actually aware of a somatic sensation, when elicited with the C stimulus; this would tend to make his reported timings for onset of C earlier than warranted by the criterion for subjective experience. (This interesting phenomenon may in fact be related to an additional hypothesis, that neuronal activities which are too brief for eliciting a conscious experience may mediate unconscious mental functions, *see Libet, 1965, 1966*).

## 2. $P_r$ -C couplings using 'polarity reversals' (PR) in pulse train for C. In 'PR'

stimulus trains applied to the unifocal subdural electrode the polarity of each successive pulse, was reversed; that is, the polarity alternated between being cathodal and anodal. PR trains should potentially reduce any tendency for the stimulus to produce electrolytic damage to tissues, and so they had been previously employed by us for cerebral stimuli in which a consistent unidirectional polarity of pulses is not essential to the study. It should be noted that PR trains generally required greater peak currents than did cathodal pulse trains, in order to elicit any conscious sensory experience (*see also Libet et al., 1964; Libet, 1973*).

When PR trains were used for the cortical test stimuli in the present study, the reported subjective timings for C relative to the  $P_r$  stimulus did not show the same patterns that were seen for the unidirectional cathodal pulse trains (*see Table 3A; block C for subject C.J., and block B for W.M. and A.E.*). Instead, there tended to be a preponderance of subjective timing reports of 'together', for the  $P_1$ - and C-induced sensations, regardless of the coupling intervals between the two stimuli. This is especially convincing in the subject C.J. for whom trials with both cathodal and PR pulses can be directly compared (blocks B vs. C). It would appear that use of PR pulses for C stimuli (a) tends to confuse or blur the subjective experience of timing orders, so that distinctions are less possible; and (b) does not produce the kind of clear evidence of a substantial delay in subjective timing for C that was seen with cathodal pulses. The curious difference between the responses with PR as opposed to cathodal cortical pulse trains may be explainable in terms of the proposed modified hypothesis (*see below*).

Each cathodal pulse would tend initially to excite neuronal elements, probably conducting fibres, that lie in the surface layers of the cortex (Libet *et al.*, 1964; Libet, 1973). The electrophysiological response to each cathodal pulse begins with a large surface negative component; this 'direct cortical response' is different from the primary evoked potential elicited by a peripheral or a lemniscal stimulus pulse (Libet *et al.*, 1967; Libet, 1973). On the other hand, each surface anodal pulse should tend to excite deeper lying nerve fibres (Hern, Landgren, Phillips and Porter, 1962; Phillips, 1969; Libet,

1973), and these might include some of the afferent specific projection fibres from the thalamus which terminate chiefly in layer IV (Colonnier, 1966). This possibility is further promoted by the relatively larger peak currents that were required by PR as opposed to cathodal pulse trains, to elicit the same minimal sensory experience. Excitation of some of these ascending fibres would, according to our hypothesis, provide at least a weak timing signal for retroactive subjective referral. A train of pulses with successively alternating polarities might then provide both the surface cortical and the ascending specific kinds of input alternately, in addition to possible other kinds. In such circumstances, it would hardly be surprising for there to be a subjective confusion about the timing of the sensory experience elicited. Indeed, the nature of these results provides some indirect support for the modified hypothesis. (This analysis suggested the possibility that one or a few surface anodal pulses of sufficient intensity, delivered at a time just before a cathodal pulse train, might provide the signal for shifting the subjective timing of the experience, from the usual position at the end of a minimum TD to a position at the onset of the cathodal C stimulus train. It has, however, been possible to carry out only a few preliminary and inconclusive tests of this kind).

## GENERAL DISCUSSION

The results obtained in these experiments provide specific support for our present proposal, that is, for the existence of a subjective temporal referral of a sensory experience by which the subjective timing is retroactively antedated to the time of the primary cortical response (elicited by the lemniscal input). Subjective timing for onset of an LM-induced sensation did in fact appear to occur with no more delay than that for a peripheral (skin)-induced sensation, even though the minimum delay for the stimulus to achieve neuronal adequacy for the LM-induced sensory experience was experimentally set to be at least 200 ms. On the other hand, with cathodal cortical stimuli subjective timings appeared to exhibit relative delays similar to those required to achieve neuronal adequacy. Stimuli to LM (or n.VPL) of course excite specific projection afferents of the lemniscal system, while C-cathodal stimuli (at near liminal intensities) do not. The apparent confusion or blurring of subjective timings found when the C stimulus pulses were 'polarity-reversed' (train of cathodal pulses alternating with anodal ones) is compatible with this interpretation.

An even more startling experimental prediction remains yet to be tested: if the putative timing signal alone were to be delivered at the *onset* of a cortical-cathodal stimulus train, one might expect that the subjective timing of the *cortically-induced* sensation could be shifted or referred, *from* its usual position (at or after the end of the minimum required train duration) backwards *to* the onset of the cortical stimulus train. An 'isolated' timing signal could be generated by a single pulse stimulus in LM, which can elicit a large primary evoked response at the SI cortex with no conscious sensory experience (Libet *et al.*, 1967). However, this experiment would require the placement, in a given patient, of one electrode in LM (or n.VPL) and another over the precise area of the SI cortex that receives the projection of impulses electrically initiated by the LM (or n.VPL) electrode; these conditions are obviously difficult to achieve under the limitations of approaches that are clinically warranted.

Further testing of the proposal can also be sought in the effects of pathological destruction of the specific projection system at cerebral levels. Elimination of the putative signal required for retroactive subjective referral of timing should introduce a substantial delay for the subjective experience even of a peripherally-induced sensation. If the destruction were purely unilateral, one could test for such a delay by comparing the subjective timings for peripheral stimuli applied to homologous sites on the normal and abnormal sides of the body. For this purpose, the same experimental paradigm which was employed in the 'control' series of the present study could be employed; in this, the pattern of reports of relative timing orders for a skin stimulus on the normal side temporally coupled with one on the abnormal side is obtained. Some indications of inadvertent partial tests of this kind may be already apparent in the present study, with subjects who had sustained some partial unilateral sensory losses apparently due to damage in the specific projection system (*see* discussion of 'Negative mean shifts for S<sub>1</sub>-S<sub>1</sub>, in Table 2A' at the end of Section 111-A of Results). A more thorough study of this issue, employing purely peripheral testing in responsive patients who have incurred appropriately located cerebrovascular accidents which produced a severe unilateral 'epicritic' sensory deficit, has been initiated and will be reported separately. For the one suitable patient studied thus far, there did indeed appear to be a delay of 200 to 400 ms in the subjective timing for a peripherally-induced sensation on the abnormal side, relative to one on the normal side.

### *Alternative Explanations of the Evidence*

Some possible alternative explanations of our findings should here be considered. One type of argument would hold that the delay in achieving 'neuronal adequacy' when stimulating LM/n.VPL or somatosensory cortex, as seen in the relatively long minimum train durations required, is simply due to the 'abnormal' route and/or pattern of these inputs. These cerebral stimuli might require a longer time to develop some special neuronal response, for example because of cortical inhibitory as well as excitatory patterns that they might produce. In this view, 'normal' inputs that do not require long minimum train durations (stimuli to skin, peripheral nerve, dorsal columns) would generate neuronal adequacy with no substantial delay; there would thus be no need to introduce the postulate of a subjective referral backwards in time for the experience of the 'normal' inputs, in order to account for their earlier, more immediate subjective timing. This kind of alternative view would seem to be untenable for the following reasons: (a) this view does not account for our experimental observation that the subjective timing for LM stimuli, requiring minimum TDs of 200 ms or more, appeared to show no delay relative to that for skin stimuli. It would still have to be conceded, therefore, that some retroactive subjective referral process can be engaged selectively by the LM stimulus, even if it does deliver an 'abnormal' input ;(b) this view would ignore other evidence already strongly indicating that input via a normal peripheral route (skin stimulus) does require a substantial period of cerebral activities before neuronal adequacy for the conscious sensory experience is achieved. The previous evidence included demonstrations (i) of retroactive effects, on the conscious sensory experience for a near threshold skin stimulus, which could be produced by a conditioning cortical stimulus that follows the skin pulse by 200 to 500 ms (Libet *et al.*, 1972; Libet, 1973) ; and (ii) of the insufficiency of the early components of the cortical evoked responses to a sensory stimulus for eliciting any conscious sensory experience (Libet *et al.*, 1967); (c) other previous findings indicate that the subjective sensory experiences elicited by a stimulus to somatosensory cortex can have 'natural-like' qualities which can resemble those elicited via normal peripheral inputs (Libet, 1973; Libet *et al.*, 1975), although the temporal and spatial features are different (*see* Methods). Also, if the train duration of the cortical stimulus is extended to one longer than the minimum required 'utilization TD' of about 500 ms, the conscious sensory experience is found to continue but with no progressive increase in subjective intensity above that at its onset; this is different from primary motor cortex where any effective stimulus, no matter how weak, elicits a progressively increasing motor response if the stimulus train duration is extended (Libet *et al.*, 1964; Libet, 1966, 1973).

Another alternative explanation accepts our proposal that there is substantial delay in achieving neuronal adequacy with all inputs, peripheral or central; but it would argue that, in those cases where there is apparent antedating of the subjective timings of the sensory experience, the subjective referral backwards in time may be due to an illusory judgment made by the subject when he *reports* the timings. This possibility was raised by Professor Donald M. MacKay in a discussion with the senior author, B.L. On such a basis, the timings of the subjective experience and of the achievement of neuronal adequacy could be actually identical at the time each sensation is elicited, that is, they would both be delayed. However, in those cases in which the neuronal response includes a component due to the fast specific projection, the subject's later report of how he perceives the timing of the sensory experience is assumed to be affected by the previous presence of the primary cortical response. For example, it could be argued that during the recall process, cerebral mechanisms might 'read back' via some memory device to the primary evoked response and now construe the timing of the experience to have occurred earlier than it in fact did occur. Such a possibility cannot be excluded at present, but it requires added assumptions and appears to be less satisfactory than our own hypothesis: (a) for example, if any 'read back' to the primary timing signal does occur, it would seem simpler to assume that this takes place at the time when neuronal adequacy for the experience is first achieved, when the 'memory' of the timing signal would be fresher; such a process would then produce the retroactive subjective referral we have proposed. Whether the later report of antedated timing of the experience is due to an immediate referral (as postulated by us) or to a later 'illusory judgment', the processes involved would be unconscious and 'automatic' in nature and would not be distinguishable by the subject; (b) the alternative explanation based upon later, illusory judgment of timing has a serious deficiency with respect to an important feature of subjective sensory experiences. By retaining delays for the immediate subjective sensory experiences, when they initially and actually occur, this alternative explanation becomes unable to explain the absence of subjective 'jitter' or asynchrony in our experience, when a variety of peripheral sensory stimuli are applied synchronously. At least one factor that should produce differences in the delays for achieving neuronal adequacy with different stimuli, is the strength of the stimulus. (This is based upon the intensity/train-duration relationship for stimuli to LM (or n.VPL), as well as to SI *cortex-see* Libet *et al.*, 1964, 1972; Libet, 1966, 1973; and on the tendency for the subjective timing of a cortically-induced sensation to approximate the end of the

minimum train duration, whether the latter is set at 500 or at 200 to 300 *ms-see* Sections I and III-C in Results). One attractive feature of our modified hypothesis is in fact its ability to deal with this difficulty. Subjective referrals, that are retroactive to the early primary evoked response to each sensory input, would make irrelevant any differences among the timings for neuronal adequacy in a group of synchronously initiated inputs; delays for the primary evoked potential are short (10 to 20 ms), and the differences produced by differing intensities of peripheral somatic stimuli are known to be so small as to be negligible for the purpose of subjective timing (*see* Desmedt, 1971).

#### *Roles of Specific Projection System*

The specific projection system is already regarded as the provider of localized cerebral signals that function in fine spatial discrimination, including the subjective referral of sensory experiences in space. Our present hypothesis expands the role for this system to include a function in the temporal dimension. The same cortical responses to specific fast projection inputs would also provide timing signals. They would sub serve subjective referral in such a way as to help 'correct' the subjective timing (relative to the sensory stimulus), in spite of actual substantial delays in the time to achieve neuronal adequacy for the 'production' of the conscious sensory experience. The temporal functions of the specific projection system need not be restricted to the one postulated here for subjective referral; for example, the fineness of temporal information it provides is probably utilized in behavioral responses to stimuli that involve spatiotemporal sequences (*see, e.g.,* Azulay and Schwartz, 1975).

The role at present postulated for the specific projection system would presumably be significant in the subjective awareness of the timing *order* of two inputs (that is, which one appeared first), and not merely of the existence and duration of some time interval between the inputs. In our studies, even young alert normal subjects were not subjectively aware of the order of two somatosensory inputs when the time interval between them was less than 25 to 50 ms; i.e., with these short intervals most of the timing reports tended to be 'together' or 'same time'. This suggests that even if latencies differed by as much as 25 ms or so for primary evoked cortical potentials elicited by two different peripheral stimuli, the two stimuli would be consciously experienced as being either synchronous or having an ambiguous order. Conscious experience of temporal order should be distinguished from forced-choice judgments of order; for example, in the forced choice paradigm the subject is not given the options of reporting that two sensations appear to be either simultaneous or subjectively not definable as to their order. However, even with forced-choice judgments of order the 'difference threshold' for two temporally coupled stimuli of the same modality has been found to be about 18 *ms-see* Sternberg and Knoll, 1973.

#### *Some Implications for the Mind-brain Relationship*

That the time factor in neural coding and decoding of experience could raise fundamental questions for the mind-brain relationship had already been recognized (*see* Lord Brain, 1963). The presently modified hypothesis deals with the problem of a substantial neuronal time delay, apparently required for the 'encoding' of a conscious sensory experience, by introducing the concept of a subjective referral of sensory experience in the temporal dimension. This would introduce an asynchrony or discrepancy between the timing of a subjective experience and the time when the state of 'neuronal adequacy' associated with the experience is achieved. However, the concept of subjective referral in the spatial dimension, and the discrepancy between subjective and neuronal spatial configurations, has long been recognized and accepted; that is, the spatial form of a subjective sensory experience need not be identical with the spatial pattern of the activated cerebral neuronal system that gives rise to this experience. Indeed, both temporal and spatial referrals are here postulated to depend in part upon the ability to generate the same physiological signal, the primary cortical response to the specific projection input. Philosophically, a discrepancy between the 'mental' and the 'physical' in the temporal dimension can be regarded, in a manner analogous to that for the discrepancy in the spatial dimension, as not contradicting the theory of psycho-physical parallelism or correspondence. But a dissociation between the timings of the corresponding 'mental' and 'physical' events would seem to raise serious though not insurmountable difficulties for the more special theory of psychoneural identity (Popper and Eccles, 1977; Libet, 1978).

#### SUMMARY

Subjective experience of a peripherally-induced sensation is found to appear without the substantial delay found for the experience of a cortically-induced sensation. To explain this finding, in relation to the putative delay of up to about 500 ms for achieving the 'neuronal adequacy' required to elicit the peripherally induced experience, a modified hypothesis is proposed: for a peripheral sensory input, (a)

the primary evoked response of sensory cortex to the specific projection (lemniscal) input is associated with a process that can serve as a 'time-marker' ; and (b), after delayed neuronal adequacy is achieved, there is a subjective referral of the sensory experience backwards in time so as to coincide with this initial 'time-marker'.

A crucial prediction of the hypothesis was experimentally tested in human subjects using suitably implanted electrodes, and the results provide specific support for the proposal. In this, the test stimuli to medial lemniscus (LM) and to surface of somatosensory cortex (C) were arranged so that a minimum train duration of 200 ms or more was required to produce any conscious sensory experience in each case. Each such cerebral stimulus could be temporally coupled with a peripheral one (usually skin, S) that required a relatively negligible stimulus duration to produce a sensation. The sensory experiences induced by LM stimuli were found to be subjectively timed as if there were no delay relative to those for S, that is, as if the subjective experience for LM was referred to the *onset* rather than to the end of the required stimulus duration of 200 ms or more. On the other hand, sensory experiences induced by the C stimuli, which did not excite specific projection afferents, appeared to be subjectively timed with a substantial delay relative to those for S, that is, as if the time of the subjective experience coincided roughly with the *end* of the minimum duration required by the C stimuli.

The newly proposed functional role for the specific projection system in temporal referral would be additional to its known role in spatial referral and discrimination. A temporal discrepancy between corresponding mental and physical events, i.e., between the timing of a subjective sensory experience and the time at which the state of 'neuronal adequacy' for giving rise to this experience is achieved, would introduce a novel experimentally-based feature into the concept of psychophysiological parallelism in the mind-brain relationship.

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