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Abstracts

## SHORT- AND MIDDLE-LATENCY SOMATOSENSORY EVOKED POTENTIALS IN CALLOSAL AGENESIS

Michel Vanasse,<sup>1</sup> Luc Forest,<sup>2</sup> and Maryse Lassonde<sup>2</sup>

<sup>1</sup>Service de Neurologie, Département de Pédiatrie  
Hôpital Sainte-Justine pour les Enfants,  
Université de Montréal  
3175, Chemin Côte Sainte-Catherine, Montréal  
Qué., H3T 1C5, Canada.

<sup>2</sup>Groupe de Recherche en Neuropsychologie Expérimentale  
Département de Psychologie  
Université de Montréal, C.P. 6128, Succ. A  
Montréal, Qué., H3C 3J7, Canada

### INTRODUCTION

Experimental transection of the corpus callosum in animals and callosotomy practiced in human adults for therapeutic purposes have led to the description of the disconnection syndrome. Typically, adult patients or animals who undergo a callosal section show a permanent deficit in interhemispheric transfer and integration of sensory and motor functions (for reviews, see Sperry et al., 1969; Gazzaniga, 1970). By contrast, few of these deficits are seen in individuals with agenesis of the corpus callosum when there are tested in certain tasks requiring intermanual comparisons. For example, whilst callosotomized patients are unable to cross-match objects held in both hands out of view, acallosal subjects have no difficulties in performing this task although their response times may be longer than in callosally-intact subjects (Ettlinger et al., 1972, 1974; Saul and Gott, 1973; Jeeves, 1979; Sauerwein et al., 1981). The same is true when callosotomy is performed before puberty (Lassonde et al., 1986, 1991).

The mechanisms used by acallosal subjects to compensate for the absence of the callosal commissure are still a matter of speculation. Several hypotheses have been proposed, including bilateral speech representation (Sperry, 1968; Ettlinger, 1972, 1974; Saul and Gott, 1973) or the use of behavioral strategies (Gazzaniga, 1970). Reviews by Chiarello (1980) and Sauerwein et al. (this volume) tend not to confirm these two propositions. In fact, it has often been suggested that an enhanced proficiency of the ipsilateral components of the somatosensory system is a more likely explanation for the absence of disconnection syndrome in acallosal subjects, at least in the tactuomotor modality (Nebes and Sperry, 1971; Dennis, 1976; Gazzaniga and Ledoux, 1978; Sauerwein et al., 1981). Hence, by relying on information provided by both ipsi- and contralateral somesthetic pathways, acallosal subjects would perform a bimanual matching task using an *intra-*, rather than an *inter-*, hemispheric comparison process.

This hypothesis has received some support from electrophysiological studies carried out in both hemispherectomized and acallosal patients. For instance, Arnott et al. (1982) reported that stimulation of the hand contralateral to the decorticated hemisphere could still evoke ipsilateral somatosensory potentials in hemispherectomized patients. Similarly, by recording evoked responses to wrist stimulation, Laget et al. (1977) demonstrated a greater responsiveness of the ipsilateral pathway in acallosal subjects as compared with normals where the ipsilateral component was negligible or totally absent. The latter results were not replicated, however, when using vibratory stimulation in an acallosal subject (Gott et al., 1985). Although a difference in stimulation site and procedure might explain the discrepancies, other technical problems such as the use of a cephalic reference and/or a limited amount of trials, make all of these studies difficult to interpret. Clearly, better methodological controls are required in order to confirm the existence of bilateral cortical connections of the lemniscal pathway in acallosal subjects.

## TECHNICAL FACTORS IN SOMATOSENSORY EVOKED RECORDINGS

Sensory or mixed nerve (such as the median nerve) stimulation produces or evokes a series of potentials along the lemniscal sensory pathway. Several technical factors can influence the recording of somatosensory evoked potentials (SEPs) and therefore their latency and morphology (Chiappa et al., 1980; Mauguiere et al., 1981). Active and reference electrode locations, low and high frequency filters, time of analysis (or sweep time) and number of stimulations are probably the most important of these factors. When stimulating the median nerve, one records potentials originating from the roots of the brachial plexus (at Erb's point), cervical cord, brainstem and cerebral cortex. These potentials are designated according to their polarity and mean latency in normal adults. For instance, N20 is a negative potential with a mean latency of 20 msec in normal adults (Donchin et al., 1977). SEPs are further subdivided into short, middle- and long-latency potentials. Short-latency potentials are those generated within the first 40 msec after the stimulation while middle- and long-latency responses are recorded between 40 and 100 msec, and after 100 msec after stimulation, respectively.

SEPs are potentials of low amplitude which can only be extracted from baseline cortical activity by averaging a large number of responses to the electrical stimulation. Each stimulation produces a series of potentials which have the same latency on each occasion. By electronically averaging or adding these potentials, it becomes possible to extract these fixed-latency responses from random cortical activity. The number of nerve stimulations is thus extremely important and in most laboratories at least 500, and frequently 1000 to 2000, stimulations are recorded (Mauguiere et al., 1981). High and low frequency filters are used to eliminate different artifacts. However, the filter bandpass may also have an influence on the morphology of evoked potentials, especially when it is too narrow (Desmedt et al., 1974).

Finally, in most laboratories, SEP recording is done using an algebraic summation of the difference in potential between the active and reference electrodes. It is therefore important that the reference electrode be as neutral as possible. A frontal or cephalic reference electrode is frequently used but it has the disadvantage of picking up, at least partially, the potentials recorded by the active electrode located over the central or parietal head regions. This technique can thus create a distortion of the recorded potentials (Desmedt and Cherron, 1982). Following Desmedt's and Mauguiere's technique (Desmedt and Cherron, 1981, 1982; Mauguiere, 1983), we have used a non-cephalic reference electrode, located over the shoulder or on the ear lobe contralateral to the stimulated limb. Only when using this technique can two types of potentials be distinguished: the far- and near-field potentials (Desmedt and Brunko, 1980).

As their name indicates, far-field potentials are generated within the peripheral or central nervous system and can be recorded over all head regions. They originate from the brachial plexus (P9), the cervical cord (P11 and P13) and the brainstem (P14 and

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N18). These potentials are probably generated by a change in volume conduction and are recorded bilaterally, which is an important factor to consider in a study such as the present one (Desmedt and Chéron, 1981, 1982; Mauguire, 1983; Mauguire et al., 1983). By contrast, near-field potentials are much more localized and they have to be picked by an electrode close to the potential's source. Thus, for short-latency SEPs, N20s and P27s are best recorded with an active electrode located over the parietal head region whereas P22s and N30s are better seen over the central head region. Middle-latency SEPs may also best be visualized when recorded over the central region although in some individuals, N60s are better seen over the frontal head regions (Bastuji, 1988).

It has been shown conclusively that N20s and P22s are the potentials generated by the arrival of the electrical volley in the primary sensory and motor cortex, respectively. As yet, the generators of subsequent potentials are not known precisely (Desmedt et al., 1987; Bastuji, 1988). These technical factors are of utmost importance especially in a study aimed at verifying the bilaterality of cortical evoked responses to a unilateral stimulation.

## THE STUDY

### Subjects

The sample consisted of four acallosal subjects. The first two subjects, a 21-year-old left-handed subject (M.G.) and his 29-year-old right-handed sister have been extensively described elsewhere (e.g. Lassonde et al., 1988). Briefly, both subjects were diagnosed as having complete callosal agenesis, first by pneumoencephalography and later by CT scan. In L.G., the diagnosis was further confirmed by MR imaging, which also indicated the presence of an intact anterior commissure in this subject. Both siblings have a global IQ of 78.

The third subject (S.G.) is the elder sister of the two subjects described above. Callosal agenesis was diagnosed in this subject after she and her parents volunteered to have a CT scan examination in order to assess the distribution of the congenital abnormality in the family. At the time of testing, S.G., a right-handed subject, was 30 years old. She has a global IQ of 84 and has no other known neurological pathology.

The fourth subject (S.B.), a right-handed 16-year-old male, started to have absence seizures at the age of six. A CT scan taken at the time revealed complete callosal agenesis. The seizures are presently well controlled with Carbamazepine. S.B. obtains a global IQ of 68.

The control group consisted of ten adult subjects without any neurological pathology.

### Methodology

Two SEP studies were conducted. In the first one, far-field and short-latency (N20 and P27) SEPs were recorded in the four acallosal subjects and in 10 normal controls of similar age. In the second study, short- (N20, P22, P27 and N30) and middle- (P45 and N60) latency SEPs were recorded in three of these four acallosal subjects (M.G., S.G., S.B.) and in four normal adults.

Both studies involved a stimulation of the median nerve at the wrist level. Electrical stimulations of 0.1msec duration at the rate of 5.1/sec were first applied on the left median nerve and then on the right side. Stimulus intensity was adjusted to produce a minimal thumb movement. Evoked potentials were picked up by surface electrodes placed at different levels. In the first experiment, the four active electrodes were placed at Erb's point, over the cervical spine (at the level of C2) and over both parietal head regions (C'3 and C'4, 2cm behind C3 and C4 respectively, as defined by the 10-20 International System). The reference electrode was located on the shoulder contralateral to the stimulation site. The time of analysis was 40 msec. In the second

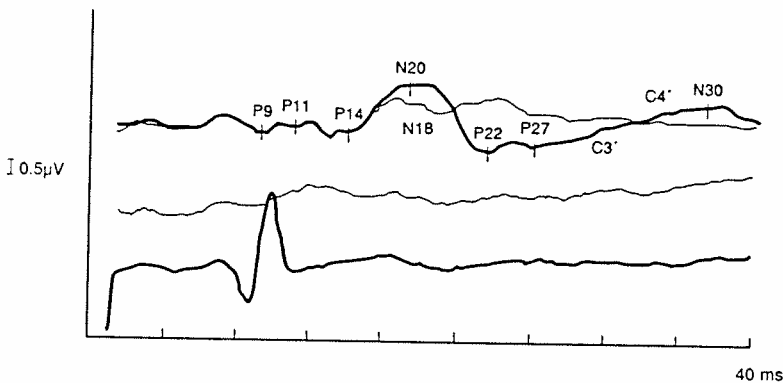
study, the active electrodes were located at F3 and F4 and C3 and C4 (again according to the 10-20 International System) and the reference electrode was placed on the ear lobe contralateral to the stimulated side. The time of analysis was 100 msec.

Electrode impedance was kept inferior to 5 kW. The grounding electrode was placed between the stimulation and recording electrodes. The electrical activity was collected, filtered (5-3000 Hz), amplified and averaged with 0.2 msec resolution. In both experiments, two series of 1000 sweeps were recorded for each stimulation site and analysis was made by comparing the outlines of the waves.

### Results

Recorded potentials were labeled by visual inspection according to the nomenclature suggested by Donchin et al. (1977). Absolute latencies were measured from the onset of the stimulus to the peak of the corresponding waves. The following latencies were analyzed: N20, P22, P27, N30, P45 and N60. Central conduction time (P14-N20 interpeak latency) was also measured as well as interside differences for all SEPs.

Statistical analysis for interside differences was carried out using a two-tail t-test. Since no statistical differences were observed between the two sides, results from left and right median nerve stimulations were combined for further analysis. The ipsi- and contra-lateral waves thus obtained were superimposed with the early components of both waves (P9, P11 and P14) having a perfect fit (see Figure 1).



**Figure 1.** Far-field and short-latency SEPs obtained from a normal individual after stimulation of the right median nerve. The ipsilateral and contralateral (bold) cortical responses have been superimposed in order to illustrate the measurement of the N20 and P22 potentials' amplitude in relation to N18. The two lower traces are recorded at the cervical level (N13) and at Erb's point, respectively.

Being interested in a possible bilateral representation of SEPs, we chose to measure the amplitude of the primary cortical components (N20 and P27) by subtracting the responses recorded over the parietal head region ipsilateral to the stimulated limb from the ones recorded contralaterally. With this approach, the amplitude of the "genuine" N20 (N20 - N18) and P27 (P27 - N18) could be evaluated. Other amplitude components (P22, N30, P45 and N60) were measured from baseline to peak. Table 1 presents the mean amplitude obtained by the acallosal and control groups for each of the wave components.

On visual inspection, none of the acallosal subjects obtained clear bilateral SEPs after median nerve stimulation (see Figures 2 and 3). Paired t-tests, however, revealed that the amplitude of the N20 component was smaller in acallosal subjects as compared to normal controls. No such differences were seen for any of the other components.

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Table 1. SEP amplitude in  $\mu$ Volts.

Groups	N20	P22	P27	N30	P45	N60
<b>Acallosal subjects</b>	(4)	(4)	(3)	(3)	(3)	(3)
Mean	0.73	1.41	2.28	1.47	1.05	2.05
Standard Deviation	0.54	0.26	1.04	0.63	0.55	0.77
<b>Controls</b>	(10)	(10)	(4)	(4)	(4)	(4)
Mean	1.45	0.89	1.64	0.85	1.00	2.19
Standard Deviation	0.73	0.93	0.50	0.52	0.40	0.77
p Value	<0.05	N.S.	N.S.	N.S.	N.S.	N.S.

Figures in brackets indicate the number of subjects recorded in each group. Statistical analysis was performed using a two-tailed test.

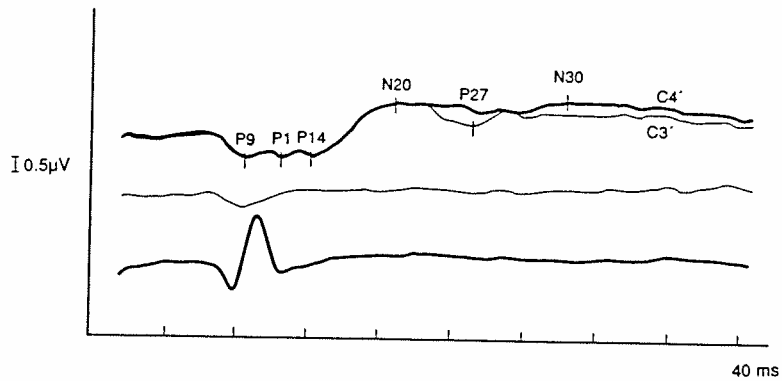


Figure 2. Far-field and short-latency SEPs obtained from an acallosal subject after stimulation of the left median nerve. The ipsilateral and contralateral (bold) cortical responses have been superimposed in order to illustrate the reduction in amplitude of the N20 potential. The two lower traces are recorded at the cervical level (N13) and at Erb's point, respectively.

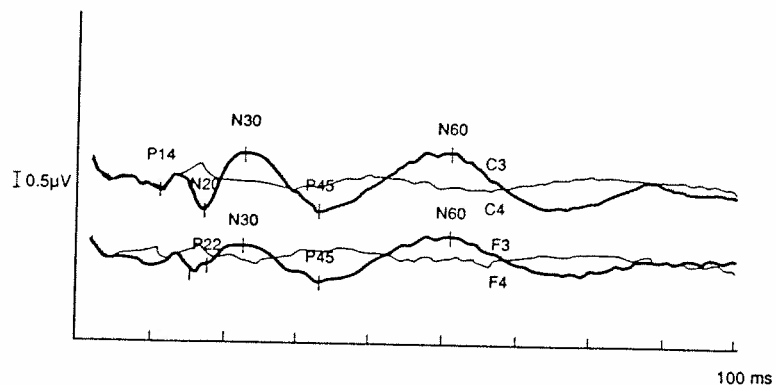


Figure 3. Short- and middle-latency SEPs obtained from an acallosal subject after stimulation of the right median nerve. The central (C3 and C4) and frontal (F3 and F4) ipsilateral and contralateral (bold) cortical responses have been superimposed. Both types of potentials are better visualized over the central head regions and are recorded only contralaterally to the stimulated side.

When latencies were compared, it appeared that the N20 and P27 components were shorter in our experimental subjects than in the normal controls. No significant differences were seen for the other SEP latencies (P22, N30, P45 and N60) or for central conduction time (P14-N20 interpeak latency).

### Discussion

Two of our findings clearly dissociated the acallosals' SEPs from those of the control subjects. Both of these findings relate to the first cortical component observed in SEPs. First, N20 and P27 latencies were significantly shorter in acallosals subjects as compared to normal controls. The signification of this finding is unclear, however, particularly in view of the fact that the central conduction time (P14- N20) was normal. Second, we observed a reduction in amplitude of the contralateral N20 potentials in the acallosals. Since this amplitude was measured by subtracting the ipsilateral response from the contralateral one, this finding could support, at least partially, the hypothesis of a bilateral cortical representation of the lemniscal pathway in these subjects. The reduction in amplitude could indeed be explained by the fact that in acallosal subjects, median nerve stimulation evokes a bilateral N20 whereas in normal individuals, this stimulation only generates sensory cortical potentials contralaterally to the stimulated side.

It is important to point out, however, that the ipsilateral response was certainly of lower magnitude than the contralateral one. Considering the way we measured the N20 amplitude, if the ipsilateral and contralateral N20s had been of the same magnitude, the calculation would have yielded a zero value. Furthermore, the fact that no such reduction in amplitude was observed for other short- (P22, P27 and N30) or middle-latency (P45 and N60) SEPs also suggests that ipsilateral lemniscal connections are not as functional as the contralateral ones in acallosal subjects. If such were the case, all SEP components should have been clearly visible both ipsi- and contra-laterally to the stimulated side.

These results suggest that an increased proficiency of ipsilateral *lemniscal* connections is not the only compensatory mechanism used by acallosals to overcome disconnections deficits. This interpretation should not be restrictive, however: other sensory ipsilateral connections may play an important role in these subjects. In fact, it has often been proposed that uncrossed *spinothalamic* pathways may be enhanced in acallosal subjects (Dennis, 1976; Sauerwein et al., 1981). In this context, it has been shown that ventral spinothalamic connections are sufficient to sustain the slow reacquisition of a size discrimination lost after transection of the dorsolateral columns and hence, of the lemniscal impulses (Mountcastle, 1984 ). Because the ventral spinothalamic pathway contains axons of smaller diameter than the lemniscal fibers and because some of these axons are unmyelinated, sensory information transmitted by this pathway cannot be recorded by standard SEP techniques, a fact which could explain why no bilateral responses were not clearly observed in our subjects. It should also be remembered that nerve transmission is slower in the ventral spinothalamic tract than in the lemniscal pathway. This would be consistent with the finding that, behaviorally, response times are often longer in acallosals subjects and in young callosotomized patients as compared to IQ-matched controls (Jeeves and Rajalakshmi, 1964; Jeeves, 1979; Sauerwein et al., 1981; Lassonde et al., 1988, 1991).

### CONCLUSION

Our results suggest that ipsilateral lemniscal connections can only partially explain the absence of a disconnection syndrome in acallosal subjects. It is quite likely, however, that the persistence of ipsilateral ventral spinothalamic connections plays a more important role as a compensatory mechanism for the absence of the largest interhemispheric commissure in these subjects.

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