tinating antibody to the $Rh_0(D)$ antigen in agglutinating antiserums for the $Rh_0(D)$ factor (*8*). The prozone phenomenon can be reproduced artificially by mixing saline-agglutinating with non-agglutinating-incomplete antibody to the $Rh_0(D)$ antigen (*9*). Zoning which has been observed with the agglutination of Rh-sensitized cells when serial dilutions of rheumatoid serums are used has been attributed to the agglutinating phase of the reaction and not to any effect which implicates the primary binding of antibody to the red cell (see *10*).

The results obtained in this study are not accounted for by the explanations based on serological studies which have attributed the prozone phenomenon to the secondary, agglutinating stage of the hemagglutination reaction. Only the primary binding of the non-agglutinating, incomplete antibody was followed in this study so that the inhibition observed in antibody excess was independent of any agglutination phenomena. Furthermore, the antiserum, as well as the labeled eluate, did not contain any demonstrable agglutinating activity against $Rh_0(D)$ red cells.

The phenomenon of zoning is more easily understood in precipitating antigen-antibody systems. Three zones have been delineated in a precipitating system, an antibody excess zone, equivalence zone, and an antigen excess zone. The precipitate formed in both antigen and antibody excess zones is decreased because of the formation of soluble complexes which interfere with lattice formation. As in the hemagglutination system, zoning has been associated with a secondary stage in the precipitin reaction rather than with the primary immunochemical phase, the interaction of the antibody combining site with the corresponding antigenic determinant. Zoning often occurs with horse antibodies (*11*) and has been demonstrated with precipitating rabbit antibodies. Inhibition of rabbit antibody precipitation in antibody excess has been shown (*12*) by using an antigen readily detected in low concentrations (dog intestinal phosphatase) and also by controlling the addition of antigen to antibody so that a high antibody to antigen ratio is maintained during the initial phase of the reaction (*13*).

No explanation is provided for the apparent paradox revealed by this study, whereby in antibody excess there is apparent inhibition of antibody binding to the red cell. It is conceivable that this effect may be due to the nonuniform distribution of the iodine label on the antibody molecules in the preparation. If sufficient unlabeled antibody molecules were present in antibody excess the unlabeled antibody would compete with the labeled antibody for the red cell antigen sites. Under these conditions there would be no decrease in total cell-bound antibody, but only an apparent decrease due to the displacement of the labeled antibody by the unlabeled antibody. The available data are inadequate to rule out this possibility, although it appears unlikely since zoning has been observed with more heavily labeled preparations (up to 3.3 moles of iodine per mole of γ-globulin).

Another possibility that deserves consideration is that this is a property peculiar to the antiserum obtained from this donor (REZ). Antiserums produced by other individuals will have to be tested for this property before this possibility can be evaluated.

The available evidence suggests that the paradoxical phenomenon of inhibition in antibody excess is due to some interaction between antibody molecules which interferes with the sensitization of the erythrocytes. Such an explanation is consistent with the observation that reduced antibody uptake does not occur if the excess antibody is added in two or more increments. In addition, the inhibition in antibody excess observed with papain-modified red cells suggests that zoning involves the antibody rather than the antigenic determinant in the red cell.

The immediate significance of these observations concerns the estimation of the red cell $Rh_0(D)$ antigen content. Previous studies (*6*) were based on the assumption that the maximum red cell antibody uptake would occur if the reaction were carried out in antibody excess. In view of the inhibition of antibody binding in antibody excess, previous estimates of the red cell $Rh_0(D)$ antigen content will require re-evaluation. It is also evident that the quantitative aspects of both red cell sensitization and the hemagglutination reaction require critical study.

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Simultaneous Recordings of Scalp and Epidural Somatosensory-Evoked Responses in Man

Abstract. *The calvarium and scalp markedly attenuate the amplitude, but do not alter the latency or frequency, of somatosensory responses evoked by electrical stimulation of the contralateral median nerve in man. With scalp electrodes no significant potentials are obtained that are not also present in the epidural recordings when proper averaging techniques are used. The somatosensory-evoked response recorded with scalp electrodes in man appears to be the result of brain activity.*

Electrical stimulation of mixed peripheral nerves, such as the median or ulnar, evoke an electrical response in the cerebral cortex of various vertebrates, including man. While such responses are of sufficient amplitude that they may be recorded easily and directly from the somatosensory cortex of animals, attenuation by the skull and scalp necessitates special averaging techniques for recording these potentials in intact human beings (*1*). The early components of somatosensory responses in man show the expected

latencies of rapid conduction to the cerebral cortex. However, the recent demonstration by Bickford *et al.* (*2*) of predominant artifacts in skeletal muscle potentials shown in scalp recordings of auditory, somatosensory, and visually evoked responses necessitates an examination of the components of all sensory-induced responses directly from the cerebral cortex of man. Jasper *et al.* (*3*) and Hirsch *et al.* (*4*) already have recorded evoked responses directly from the exposed somatosensory cortex during various neurosurgical procedures.

Inasmuch as investigators from numerous disciplines such as psychology, physiology, pharmacology, neurology, and psychiatry are now using computer averaging techniques for recording somatosensory responses with scalp electrodes in man, it is important to simultaneously record and compare the scalp and epidural potentials under identical conditions. To date, Giblin (*5*) has come closest to obtaining such recordings, although further data are necessary.

We have had a unique opportunity to make simultaneous comparisons of somatosensory-evoked potentials with epidural and scalp electrodes in awake patients undergoing neurosurgery for various dystonias. Most of the patients had Parkinson's disease and came to surgery to have cryogenic lesions made in selected thalamic nuclei as a means of relieving incapacitating dyskinesias. To maintain wakefulness and cooperation during the surgical procedures, none of the patients received prior medication. After a pneumoencephalogram was obtained, the patient was placed on the operating table. A small incision was made in the scalp under local anesthesia and a burr hole made in the skull over the premotor area for placing the cryogenic cannula. Before the cryogenic lesions were made in the thalamus, somatosensory-evoked responses were obtained by cathode-electrical stimulation of the contralateral median nerve with a monopolar electrode.

The parameters of electrical stimulation were: 0.2-msec square waves at 1, 2, and 3 times the sensory threshold at a frequency of 4 cy/sec. Preamplifiers with a bandwidth of 0.3 to 10 kcy were used in conjunction with a CAT computer for recording the somatosensory-evoked response from a monopolar scalp needle-electrode placed over the sensory area and an epidural electrode directed toward the same site through the burr hole. The monopolar recordings were made with the nasion as reference. A total of 200 stimuli were averaged and the evoked response, for 125 msec after the stimulus, was written out on a *T-Y* (time versus amplitude) plotter. So far we have recorded these responses from 67 different subjects.

Figure 1, which shows the results obtained from two different subjects, indicates that scalp recordings do reflect the activity of the somatosensory cortex. As might be expected, the scalp potentials are markedly attenuated. Of considerable importance is that the major components of the somatosensory-evoked response resemble those reported by others (*1*, *5–7*) using scalp electrodes. At the patient's sensory threshold, the scalp responses are just barely visible while the epidural responses are distinctly evident. Our data are in agreement with those obtained by Schwartz and Shagass (*7*), who showed with scalp electrode recording techniques that at sensory threshold the somatosensory-evoked response is just identifiable.

It should be emphasized that scalp and epidural recordings are similar (when conventional electroencephalographic techniques are used) only if a sufficiently large area of cerebral cortex is involved. Discrete cortical electrical stimulation and simultaneous recordings with scalp and epidural electrodes do not show similarity (*8*), indicating that scalp recordings do not reflect the events of small populations of neurons. Presumably, much larger neuronal populations participate in somatosensory-evoked responses so that scalp and epidural recordings show qualitatively similar electrical activity. The scalp does not appear to distort the frequency in the range of 1 to 1000 cy/sec, but merely attenuates the voltage, as determined by separate studies with a sine-wave generator. The voltage attenuation is approximately 20, depending upon conditions. Although epidural recordings are far more satisfactory, one obviously can use scalp recordings for studying somatosensory-evoked responses in man when only these are available.

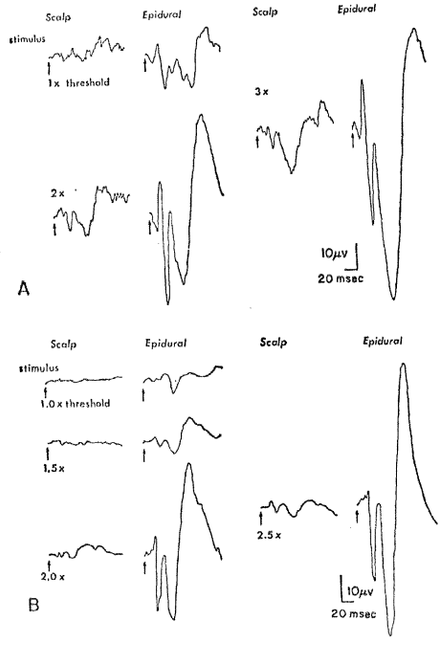

Fig. 1. Averaged somatosensory-evoked responses in two patients under local anesthesia. A monopolar scalp needle and an epidural stainless steel ball electrode were placed over the hand area of the somatosensory cortex. The nasion served as the reference. The patient was fully awake, having received no prior medication except for local anesthesia at pressure points for the head holder and at the site of the scalp incision over the premoter area. The contralateral median nerve was stimulated at the wrist at a frequency of 4 cy/sec with monopolar cathodal square-wave pulses of 0.2 msec duration at stimulus threshold and various increments as shown. The analysis time of 200 averaged response was 125-msec. The stimulus was applied at the arrow. The time base and microvolt calibration are as indicated. Negativity is upward. The records of two different subjects (*A* and *B*) are shown to illustrate some of the variability of the responses.

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