Equivalence of radio frequency and electrolytic lesions in producing septal rage¹

Robert W. Reynolds²

UNIVERSITY OF CALIFORNIA, SANTA BARBARA

Abstract

Radio frequency and electrolytic lesions were placed in the septal region in the rat. Daily ratings of emotionality failed to show any postoperative differences between groups as a function of type of lesion. In both groups, however, "septal rage" was temporary, giving place within six to ten days to docility. It was suggested that this syndrome may not be a result of the lesions as such, but may instead be attributable to the trauma of the surgical procedure producing a temporary sensitization of the nearby "affective defensive reaction" zone of Hess.

Introduction

In a previous study (Reynolds, 1963) it was suggested that the dramatic symptoms of hyperphagia and viciousness seen following electrolytic destruction of the ventromedial nuclei of the hypothalamus were artifacts of the electrolytic process rather than release effects following tissue removal. This suggestion was based on the fact that the symptoms failed to appear when the lesions were produced through radio frequency thermocoagulation. In view of the equally dramatic consequents of septal forebrain lesions (Spiegel et al., 1940; Brady & Nauta, 1953, 1955) it was decided to investigate the effect of radio frequency lesions in this structure. If septal rage is, like hypothalamic hyperphagia, an irritative artifact of the lesioning process, it should not appear after radio frequency lesions.

Subjects

The Ss were 47 adult male albino rats of the Sprague-Dawley strain.

Surgical and Histological Method

Operations were performed using Nembutal anesthesia. Lesions were placed stereotactically using coordinates which had previously been determined to produce septal lesions. The electrodes for all lesions were 00 gauge stainless steel insect pins (Clay-Adams). In half of the animals the lesions were made electrolytically using anodal DC current at 2 ma for 15 sec. In the rest of the animals, the lesions were made by thermocoagulation using radio frequency current at two megacycles per second derived from a Grass LM-3 lesion maker. Lesions were in bilateral pairs, 0.5 mm on each side of midline. In order to insure complete destruction of the septal region lesions were placed at three antero-posterior levels at

0.5 mm steps in some Ss. In others, the lesions were placed at two levels and at one level.

After testing, the animals were perfused intraventricularly with saline followed by 10% formalin. Frozen sections were taken at 30 micra through the region containing the lesions and every fourth section was mounted and stained with the Kluver-Barrera stain (1953). A parallel series was stained with a Perl stain for iron.

Behavioral Testing

The Ss were tested for relative emotionality prior to surgery and then daily following surgery until they were sacrificed. The rating scale was the same as that used by Brady & Nauta (1953). Ss received a score ranging from zero (no response) to four (maximum response) on seven different points: resistance to capture, resistance to handling, muscular tension, squealing, urination and defecation, reaction to presentation of a blunt probe in front of its nose, and reaction to prodding with the probe. Rating was normally done independently by two observers. The inter-rater reliability was approximately .92. On two occasions, three additional raters were used, and again the inter-rater reliability was about .92.

Results

It should be noted that the emotionality rating scale is not a true interval scale. The statistical procedures used below, therefore, are in violation of several basic assumptions. The results, however, are sufficiently clear cut that such violations need not be cause for alarm. It must be noted, nevertheless, that the statistics are indicative rather than definitive. Individual "t" tests for each day showed no differences when the animals were grouped according to lesion technique. In both groups lesion size ranged from negligible to complete destruction of the septal region. The largest lesions were bounded laterally by the lateral ventricles and extended from the genu of the corpus callosum to and including the descending columns of the fornix, ventrally to the anterior commissure, and dorsally to the corpus callosum (Fig. 1). Considering only the first few days following surgery, the emotionality ratings also ranged from extreme viciousness and reactivity (over 20 points out of a possible 28) to extreme docility (below 3). Rank correlations between lesion size and emotionality rating for the first day following surgery were 0.50 for the electrolytic lesion

Fig. 1. Coronal sections through lesions in representative animals. A, section through greatest extent of radio frequency lesion in Rat No. 38. Emotionality ratings for this animal for the first four days following surgery were 12, 4, 0, and 0. B, section through electrolytic lesion in Rat No. 10. Emotionality ratings for the first four days postoperatively were 16, 10, 8, and 5. C, section through radio frequency lesion in Rat No. 32. Emotionality ratings were 20, 11, 2, and 2.

Fig. 2. Emotionality ratings as a function of days after surgery. Solid line is exponential decay function $R = 12.7 e^{-t/4.6}$. Open circles are means of observed data for combined groups.

group, 0.58 for the radio frequency lesion group, and 0.57 for both groups combined. By the sixth day after surgery the mean rating for both groups had fallen to less than four, and by the tenth day to less than two. The combined means for the two groups conform well to an exponential decay function as shown in Fig. 2. The equation for the function is

$$R = 12.7 e^{-t/4.6}$$

where R is the emotionality rating and t is the number of days postoperative. A test for goodness of fit yields

$$\chi^2 = 0.695; p < .85$$

Discussion

This study failed to demonstrate any difference in the septal rage syndrome as a function of the procedure used in producing the lesions. The data for both groups, however, indicate very strongly that the designation "septal rage syndrome" is a misnomer insofar as it implies a relatively chronic condition. The fact that it is dissipated within a week suggests that it is a transient after effect of surgery. The approximation of the data to an exponential decay function is also highly suggestive. In any case, the syndrome is obviously not a permanent effect of destruction of tissue in the septal region. It should also be noted that in Reynolds' (1963) study of the ventromedial hypothalamic syndrome, there was a similar transient effect after the placement of massive radio frequency lesions. Harrison & Lyon (1957) report no consistent relationship between destruction of parts or all of the septal region and post-operative rage behavior, and suggest that "septal rage" is really a function of incidental damage to other structures. Their Fig. 1 (p. 126), however, shows that the animals in their study with a "well developed behavior syndrome" also returned to normal in a little over a week. Brady & Nauta (1953, 1955) and King (1959) also show a decline in the post-operative emotionality rating, although the decline in these studies was not as rapid as in the present study.

Zeman & King (1958) implanted a rat sarcoma cell

suspension in the septal region. They found that although the typical rage syndrome appeared, it subsided in 14 days, and its time course "correlated with the growth period of the tumor." They concluded that the hyperemotionality so induced "may be more closely associated with the dynamics of the expansion of the neoplasm than merely with its space occupying effect."

The fact that the region giving rise to this transient phenomenon is close to, but does not include, the "affective defensive reaction" zone of Hess (see Akert, 1961) is highly suggestive. Electrical stimulation of this latter region gives rise to the same sort of directed viciousness which appears in "septal rage." Surgical trauma might very well produce a temporary sensitization of this zone. It might be possible to produce a chronic sensitization, and, hence, persistent viciousness, by placing electrolytic lesions even closer to this zone. One difficulty with this procedure, however, might be the approximation of such lesions to the region in which lesions were found to produce fatal pulmonary edema by Gamble & Patton (1953). This would tend to prevent the observation of the syndrome.

Harrison & Lyon (1957) have pointed out that on theoretical grounds septal lesions should produce either "no behavioral change or a slight placidity" rather than rage. The present study suggests that the theoretical prediction is indeed correct, but is normally obscured by the much more striking, but transitory, rage.

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Notes

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2. Special Neurophysiology Training Fellow, Department of Physiology and Biophysics, University of Washington School of Medicine, Seattle, Wash., 1961-1962.