DYNAMICS OF CHANGES IN SOMATOSENSORY INPUT TO THE MOTOR CORTEX FOLLOWING LESION OF SOMATOSENSORY CORTICAL AREAS IN DOGS

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The pattern of change produced in somatosensory evoked potential (EP) in the forelimb projection area within the motor cortex (MI) following lesion of the projection area of the same limb in the somatosensory cortex (SI) or in parietal cortex area 5 was investigated during chronic experiments on waking dogs. Amplitude of the initial positive – negative wave of EP declined to 28-63% of preoperational level in all cases. No significant recovery of EP was noted for three weeks. Thus, a correlation between change in EP and spontaneous recuperation of the precision motor response occurring within two weeks after lesion of the SI did not exist. Nor was EP reinstated in the MI after ablation of area 5, despite complete but gradual reinstatement of EP (after an initial decline to 53%) in the nearby SI region. This protracted depression of EP seems to have been associated with breakdown of somatotopic sensory input from the SI or from area 5 to the MI, since EP in the motor cortex of the intact hemisphere and the hindlimb projection area within the MI on the lesioned side either remained unchanged or recovered within a week or two.

INTRODUCTION

The motor cortex (MI) has already been shown to play a major part in the production of precision motor response during experiments performed on dogs [2]. Protracted and severe impairment of these movements occurs in the MI after localized removal of the representation area associated with the working limb. Lesion of the somatosensory cortex (SI), as distinct from damage to the MI, undermines precise defensive movements as soon as the first postoperative week, however. Gradual, volitional reinstatement of response and precision of this movement follows in the second week [4].

The structures SI, parietal cortex area 5, SII, and direct thalamocortical input combine to transmit somatosensory afferents to the MI, according to recent theory [6, 8, 9, 11-13]. It was therefore thought worthwhile to establish whether temporary impairment of precision movement induced by SI lesion is associated with removal of sensory input from the SI to the MI and whether recuperation of this movement is connected with compensation for lost input.

It was established during experiments on anesthetized cats and monkeys [7, 8] that removal of the SI induces an abrupt decline in the amplitude of somatosensory evoked potentials (EP) in the MI, viewed as an indicator of attenuated sensory inflow into the MI. We obtained similar findings from comparable experiments performed on dogs [5]. This study set out to evaluate changes in EP occurring in the MI following SI lesion in chronic experiments on waking animals and to find whether recuperation of EP amplitude occurs in the MI and, finally, whether this recovery shows a time correlation with that of precision movements. Findings from lesioning the SI were compared with the consequences of damage to area 5, another cortical area sending sensory input to the MI.

METHODS

Chronic experiments were performed on 4 waking dogs (dogs Nos. 1-4) weighing 10-15 kg. Different projection zones of the MI had each been previously implanted with 2 chronic recording (epidural or interosseous) silver spherical electrodes spaced 2-3 mm apart, all animals having been previously anesthetized with 35 mg/kg Nembutal, i.p. Readings were mainly taken from the forelimb representational area in the MI on the same side as the lesioned SI or

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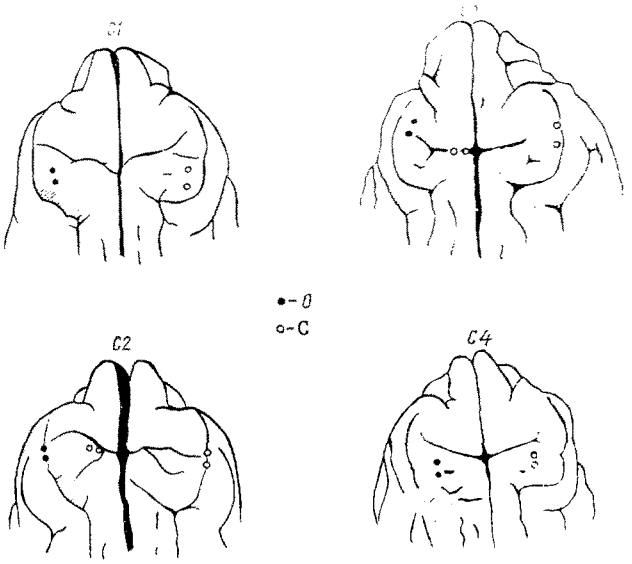

Fig. 1. Location of recording sites of evoked potentials and cortical lesion in trial animals (Nos. 1-4); o and c) basic and control readings. Recording locations hatched.

area 5. Control readings were taken from the hindlimb projection area in the MI on the lesioned side in animals Nos. 2 and 3 in order to evaluate the nonspecific traumatic effects of surgery, as well as from the forelimb projection area within the MI of the intact hemisphere in all trial animals. Reference electrodes were located below the frontal sinuses.

It was found that EP occurred in response to electrocutaneous stimulation (ECS) of the contralateral fore- or hindlimb according to the area studied. This involved cradling the pre-trained animal in such a way that the stimulated limb hung freely while ECS was applied via cup-shaped electrodes centrally located to the rear of the lower limb surface. Sequences of 15 squarewave current pulses of 0.2 msec duration were applied, succeeding at varying intervals of roughly 1 sec. Current intensity was gradually raised from one sequence to the next, starting at the minimum level required for EP and up to the point at which near-maximum response occurred (saturation EP) – a range of 0.1-10.0 mA. Intervals between sequences measured 0.5-3.0 min; EP were recorded on magnetic tape and data processed by computer. Mean total amplitude of the initial positive – negative (peak-to-peak) complex was calculated, as well as latency of the initial positive peak and standard error of the mean. The EP were recorded over a 3-4 week period at the rate of 2-3 experiments per week both prior and subsequent to surgery.

Localized cortical lesion was produced under Nembutal-induced anesthesia and sterile conditions by sub-pial suction. The projection area of the right forelimb with the SI was removed in dogs Nos. 1 and 2 [10] and the projection area of the same limb in area Pc_1 [1] in the other two animals (Nos. 3 and 4) corresponding to area 5 [3, 9] (see Fig. 1). A lethal dose of Nembutal was administered putting an end to these experiments. Markers of electrode projections on the cerebral cortex were introduced via the osseous openings by a cauterizing needle once the recording electrode had been removed. The staining so produced served to verify correct location of 17 out of the 20 electrodes used. two electrodes were found not in the MI but more caudally – in the SI (to the right in dog No. 1 and to the left in dog No. 4); one was situated in the premotor cortex (to the left, in dog No. 3 – see Fig. 1). Results of these readings were also included in processing and subsequent analysis. Histological monitoring of the depth at which extraction had been performed in serial brain slices stained by Nissl's technique showed that focus of the lesion took in all cortical layers. The frontal slices shown in Fig. 2 serve as an indication of the extent of the lesion in the SI region and area 5.

RESULTS

Amplitude of EP (from peak-to-peak) in intact animals gradually increased in the forelimb projection area within the MI to match intensification of ECS, to reach its highest

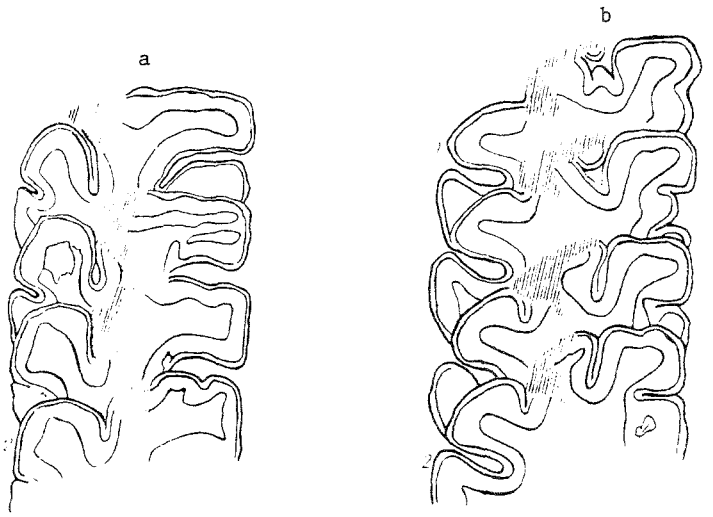

Fig. 2. Frontal brain slices reconstructing volume of cortical lesion into dogs – Nos. 1 and 3 (a and b) respectively; Nos. 1 and 2: slices in rostral and caudal sections of lesion respectively. Remaining notations as for Fig. 1.

(saturation) point, which varied between 21 and 85 μV from one animal to the next. Latency of the initial positive peak measured 9-13 msec and hardly depended on intensity of the stimulating current.

Figure 3a shows amplitude plotted against intensity of ECS applied prior to surgery in dog No. 1 (rostral recording) and Fig. 3b gives mean amplitude of response induced by stimulation at a fixed minimum and maximum intensity (0.2-1.0 and 3-6 mA respectively) in dogs Nos. 1 and 2 (caudal and rostral recording). Averaging for each stimulus intensity was performed from the results of 3-6 trials (with 15 EP per trial).

Localized lesion of the projection area of the right forelimb in the SI in dogs Nos. 1 and 2 led to a sharp decline in peak amplitude of EP in the representation region of this limb within the MI (see Fig. 3a and b). Meanwhile, latency of the initial positive peak did not change significantly. Amplitude of saturating EP declined to 28-33% of control level over three recordings in these animals and to 55% in one of the dogs (No. 2; rostral recording). Response to mild stimulation declined to a far lesser extent (see Fig. 3b). This change was only significant in one instance (dog. No. 1, rostral recording). It will thus be seen from Fig. 3a that the steep upward slope turned downwards abruptly. The findings presented in this diagram from three experiments carried out during the first, second and third week of the surgery respectively point to a gradual and insignificant rise in peak amplitude. No significant rise in amplitude was revealed in any of the recordings, indicating that marked depression of somatosensory saturating EP in the MI persisted after lesion of the SI.

Similar changes in EP were also observed in the MI after lesion of area 5 in dogs Nos. 3 and 4. Accordingly, amplitude of response to stimuli of peak intensity in dog No. 3 declined to 63 and 60% of control level respectively in the motor and premotor areas compared with 55% (in the MI) in dog 4. The reduction in amplitude of response to mild stimulation was not significant. Figure 4 sets mean amplitude of EP recorded for three weeks before against those obtained three weeks after removal of area 5.

Peak amplitude of EP after surgery declined significantly (to 53% of control level) in area SI of the fourth animal (caudal recording) as it had done in the MI (see Fig. 4) although here, in contrast with the neighboring MI, EP returned completely to normal by the start of week 3 (upper unfilled section of column).

Findings from control recordings in dogs with lesioning of the SI and field 5 were similar. In most instances, neither EP in the representation region of the forelimb within the MI of the intact hemisphere nor in the projection area of the hindlimb in the structure on the lesioned side showed any significant change (see Table 1). Amplitude of response to ECS of peak intensity did decline in some readings, although EP would then be reinstated. Accordingly, a significant reduction in amplitude was seen in the MI of the intact hemisphere

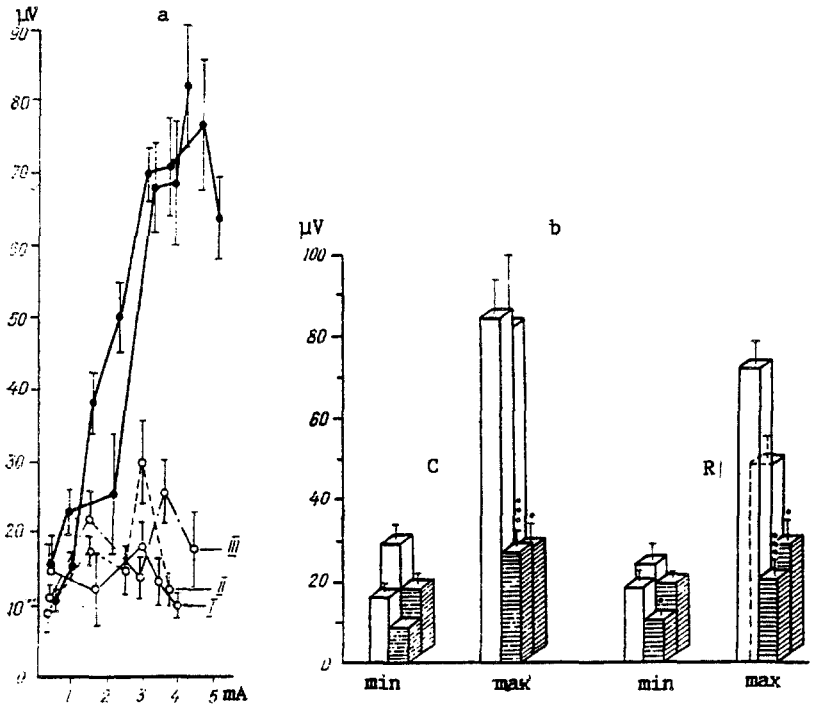

Fig. 3. Alteration in the amplitude of evoked potentials (EP) in area MI after lesioning the ipsilateral SI; a) EP amplitude plotted against intensity of electrocutaneous stimulation prior to surgery (thickened lines) and during the first, second, and third week afterwards (slender lines) in dog No. 1 (rostral opening). Each point on plot represents mean amplitude of 15 EP. Abscissa: intensity of stimulating current, mA; ordinate: amplitude of EP, μV; b) mean amplitude of EP under minimum and maximum stimulation recorded caudally (C) and rostrally (R) before and after surgery (unfilled and hatched columns respectively) in dog No. 1 (first series) and No. 2 (second series). Significance of differences indicated by 1, 2, and 3 dots respectively ($p < 0.05$; $p < 0.01$, and $P < 0.001$).

TABLE 1. Amplitude of Evoked Potentials in Control Recording Made Prior and Subsequent to Cortical Lesion

Trial animals	Recordings	Mean amplitude in the MI area of the intact hemisphere		
		prior to surgery	No. of weeks after surgery	
			week 1	week 3
1	R	82,1±5,9	24,1±2,5	76,9±4,6
	C*	84,3±6,0	24,8±3,2	76,6±6,3
2	R	46,4±5,9	44,7±5,6	
3	R	34,4±4,3	27,0±3,4	
	C	27,4±4,5	27,3±2,9	
4	R	38,5±6,9	26,3±1,0	39,7±3,8
	C	56,9±7,4	51,8±2,3	
Mean EP amplitude in the hindlimb projection area within the MI on lesioned side				
2	L	27,4±3,0	23,6±4,4	
	M	25,0±6,3	26,9±6,4	
3	L	21,2±2,7	14,9±2,8	23,3±4,0
	M	22,1±1,9	23,4±2,4	

R) rostral, C) caudal, L) lateral, and M) medial recording (see Fig. 1, n = 15); asterisk: recording of evoked potentials in area SI.

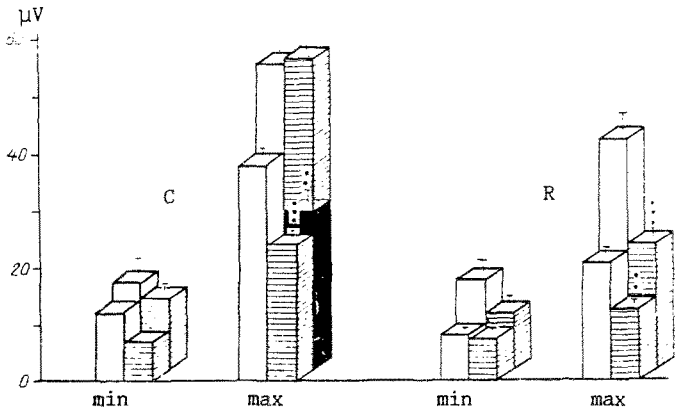

Fig. 4. Changes in the amplitude of evoked potentials (EP) in the MI area as well as the premotor region in dog No. 3 (rostral recording) and in the SI area in dog No. 4 (caudal recording) following lesion of ipsilateral area 5 in dogs Nos. 3 and 4 (first and second set of columns respectively). Filled and unfilled columns represent mean amplitude of EP in the first and third week after surgery respectively in dog No. 4 (caudal recording). Remaining notations as for Fig. 3.

in three out of seven recordings (of down to 30% of control level in two readings taken from animal 1 and down to 68% during rostral recording from animal 4). In dog No. 4, EP had returned to normal by the end of week 1 and by the start of week 3 in dog No. 1; in addition, a marked recovery in amplitude had already begun by the end of week 1. A significant decline in EP amplitude (of down to 70%) was only recorded at one of the four points (lateral recording in dog number 3) in the hindlimb projection zone within the MI (on the lesioned side) but complete recovery had already taken place by the end of week 1.

DISCUSSION

We began by postulating that spontaneous recovery of precision movements in dogs following lesion of the SI could be associated with compensation for lost somatosensory input in the MI (through sprouting from surviving MI input, for instance) or with recuperation of the functional state of the MI which had been surgically damaged. Either of these could give rise to reinstatement of EP amplitude. An attempt was therefore made to follow up changes in EP within the MI following localized lesion to the SI and (for the purposes of comparison) of field 5 by performing chronic experiments on waking animals.

These showed that in both waking and anesthetized animals [5, 7, 8] with localized damage to the hindlimb projection area within the SI or field 5, amplitude of the initial positive–negative EP complex in the corresponding MI region of the ipsilateral hemisphere declined abruptly. Amplitude of EP did not return to normal in the MI for two weeks after surgery (the period required for recovery of precise movement). This indicates a lack of correlation between recovery of motor and sensory function within the MI taking EP as a criterion.

The changes described applied mainly to EP arising in response to stimuli of peak intensity. Low-amplitude EP produced by mild subthreshold stimuli following cortical lesion showed comparatively little change, giving the impression that low- and high-threshold inputs are mediated mainly by direct thalamo-cortical and by cortico-cortical connections with the MI respectively. Impaired ability to generate high-amplitude EP could also be associated with a breakdown in MI function resulting from loss of the relevant input.

We now list some possible mechanisms for depression of EP as found in our experiments. Firstly, amplitude of EP may reflect the total afferent signals reaching the MI via different inputs, so that removal of one of these should accordingly lead to a decline in EP amplitude [7, 8]. Our findings would support this in so far as slowly developing and prolonged depression of EP (lasting more than three weeks) was only observed at the MI area receiving somatotopic inputs from the lesioned SI and area 5 sites [9, 11-13]. The decisive part played by impairment to these connections in the alterations noted in EP would be supported by the

fact that removal of the entire SI region, as earlier performed on cats [8] as well as localized lesioning of the forelimb projection area within the SI produced in our experiments brought about a similar-sized reduction in EP amplitude (to 1/3 of control level) in the forelimb representation zone within the MI.

Such a considerable decline in EP was believed to indicate that the majority of sensory inputs into the MI proceed through the SI [8]. Data obtained from dog No. 4 indicating the absence of a direct connection between amplitude of EP in the SI and MI conflicts with this view to some degree: complete recovery of EP in the SI following lesion of area 5 was not accompanied by any marked recuperation of response in the adjacent MI area. It could be the case that afferent signals contributing to generation of EP in the MI do not pass via the cortico-cortical connections. (We had the opportunity of comparing latency of the positive EP peak for three pairs of matching points in the SI and MI – comparison of adjacent points. We found practically no difference or else that latency was 1-2 msec greater in the MI but apparently even such a small difference as this does not exclude the possibility of afferent signals traveling via cortico-cortical connections participating in the generation of EP). The reduced amplitude of EP could then be explained by an altered functional state of MI neurons brought about by the removal of these connections.

The third and final factor, unassociated with damage to sensory inputs, is the effect of surgical trauma. Findings from control recordings in MI zones not receiving somatotopic sensory inputs from the damaged structures enabled us to evaluate nonspecific traumatic surgical effects. A significant decline in EP amplitude was only observed in 1/3 cases in the forelimb projection area within the MI of the intact hemisphere and in the hindlimb representation zone of the MI on the damaged side. The time taken for these changes to develop roughly matched the period of acute post-trauma inflammation: depressed EP was not observed immediately after lesioning of the cortex (in anesthetized dogs) [5]; it peaked during the first few days after surgery and EP completely returned to normal within one or two weeks.

These findings are complemented by data on depression of evoked response in the SI following damage to area 5; this depression set in within the first few hours after surgery (in anesthetized dogs) but EP had fully recovered by the third week. In this case, damage to axons arriving at area 5 from the SI was probably manifesting, as well as nonspecific traumatic effects [11].

Post-operational trauma had thus led to no more than a temporary decline in EP. The persistent depression of EP observed in the motor cortex, however, may apparently be put down to breakdown of somatotopic cortico-cortical inputs.

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STATIC AND DYNAMIC ACTIVITY OF CUTANEOUS COLD RECEPTORS INDUCED BY NORADRENALINE INFUSION

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Experiments on rats showed that cutaneous cold receptors are sensitive to altered blood level of noradrenaline (NA). Both rise in and re-establishing of NA at a new, higher level exert an effect on firing activity in cutaneous cold receptors. When sustained at the raised level, NA alters both static and dynamic activity of cold receptors. The pattern of change (whether excitatory or inhibitory) depends on initial type of receptor activity.

INTRODUCTION

Response of the organism to external thermal action largely depends on the functional state of peripheral sensory structures — cutaneous thermal receptors — which can have either a static or a dynamic activity pattern. The former consists of a steady spike train at a constant cutaneous temperature; different degrees of receptor activity accompany variation in skin temperature level. Dynamic activity is an abrupt, short-lasting change in receptor firing rate resulting from a rapid change in skin temperature.

The modulatory effects of noradrenaline (NA) on static cold receptor activity has been illustrated during experiments involving intraarterial and intraperitoneal injection of NA [2, 5]. As already shown, NA injection is accompanied by continuous change in blood level of NA — an initial increase followed by a decline. The lack of any clear-cut and protracted rise in NA concentration in these experiments prevented the effects of NA on the dynamic activity of cold receptors being revealed.

Concentration of NA may not just rise or fall within the organism but can also stabilize at various steady levels [1]. The first of these effects is generally associated with the initial stage of certain factors at work on the organism and the second with continuing action of these same factors. It might thus be though that different changes in cold receptor activity would be produced by a rise in blood level of NA and with the settling of this concentration at a steady level.

This study set out to clarify the nature of the effects produced by a raised, stable level of NA concentration on static and dynamic activity in cutaneous cold receptors.

METHODS

Experiments were performed on male rats anesthetized with 100 mg/kg chloralose and 1g/kg urethane at an ambient temperature of 20-22°C.

Intravenous infusion of NA at a dose of 10 ng/g into the left saphenous vein was performed for 1 min at an infusion rate of 0.03 ml/min.

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