

## **Early and late effects of median nerve injury on Meissner's and Pacinian corpuscles of the hand of the macaque (*M. fascicularis*)**

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### INTRODUCTION

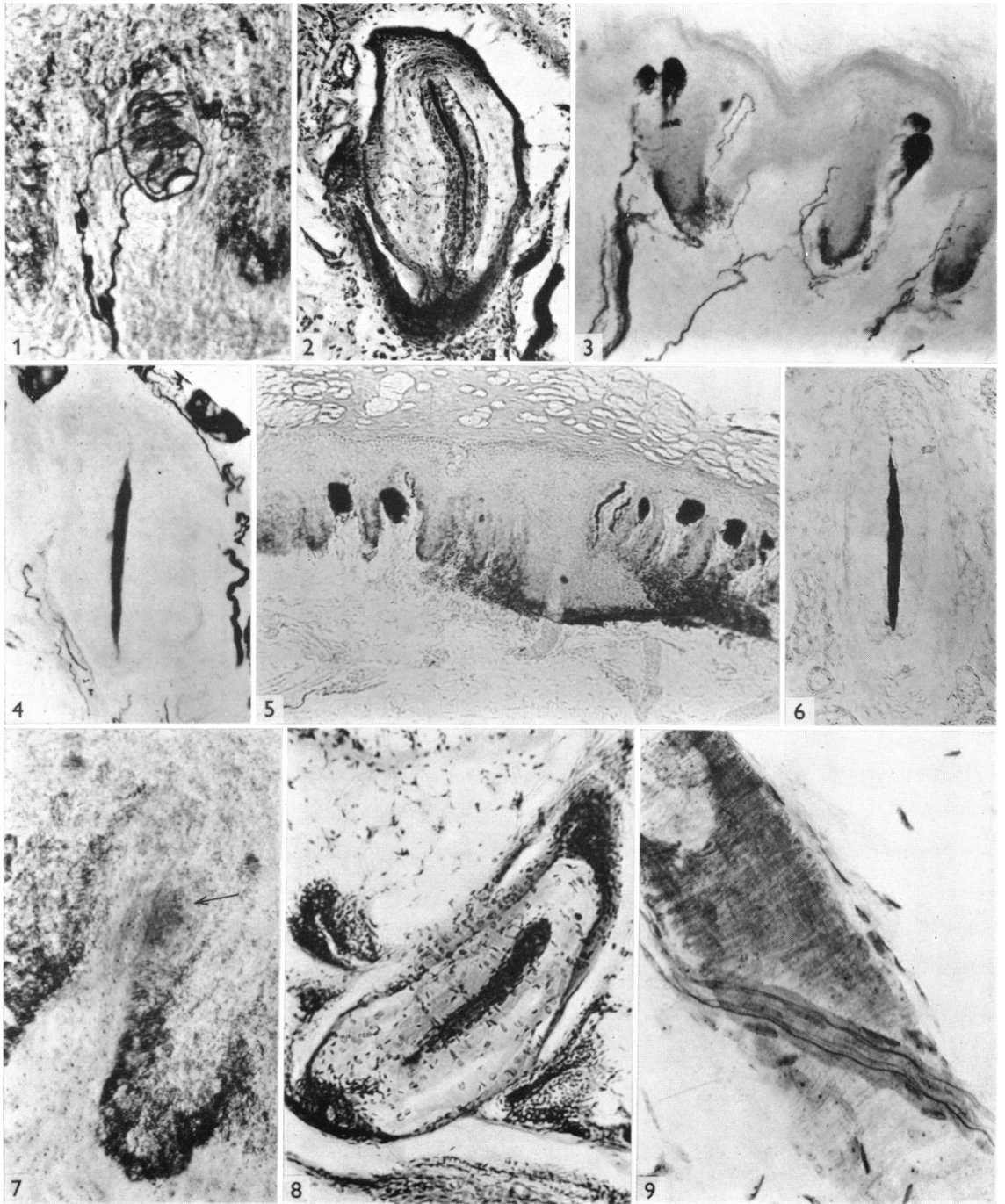
Despite much histological and histochemical work on the normal digital skin of numerous primates, including man, relatively little is known of the changes that the digital sensory corpuscles undergo after denervation and during reinnervation. Recently, Wong & Kanagasuntheram (1970) showed that during degeneration specific cholinesterase (AChE) activity in Meissner's corpuscles was diminished or absent but that it became abundant during early regeneration and slowly declined to normal during late regeneration. On the other hand, non-specific cholinesterase (ChE) activity remained relatively unchanged during early degeneration but subsequently showed a progressive decline until regeneration occurred, when it became progressively more intense once again. The nerve dependence of these receptor enzymes was thus clearly established. The present study is not only an extension of our previous work on Meissner's corpuscles but also includes observations on the Pacinian corpuscles following nerve injury.

### MATERIALS AND METHODS

Ten monkeys (*M. fascicularis*) weighing 1.2–3 kg were used in this study. Six of the animals were used for short-term and the remaining four for long-term observations. In the short-term experiments the left median nerve was crushed, sectioned or ligatured at the wrist. A pair of animals was used in each type of experiment. Palmar digital skin from the median nerve territories on the operated side was biopsied at approximately weekly intervals between 3 and 8 weeks after the nerve injury while skin biopsies taken at the same time from the digital skin of the unoperated hand were used as controls. At the last biopsy the animals were sacrificed.

The long term experiments consisted of a section (1 specimen) crush (1 specimen) and ligature (1 specimen) of the right median nerve at the wrist; in the fourth specimen of this series, the left median nerve was ligatured in the arm region. The respective times of sacrifice in this series were 32, 40, 40 and 47 weeks after the nerve injury. Again palmar digital skin from the median nerve territories of the operated and unoperated sides were removed for study.

Each piece of skin was divided sagittally into two halves. One half was fixed immediately in 10% formol saline and subsequently treated by a modified Bielschow-



sky-Gros (BG) technique (Garven & Gairns, 1952). From the other half fresh frozen sections of 25  $\mu\text{m}$  thickness were processed by a modified Koelle's technique for the demonstration of cholinesterase as adopted by Kanagasuntheram, Wong & Chan (1969).

## OBSERVATIONS

*Normal material*

*Bielschowsky preparations.* Meissner's corpuscles were found in the majority of the dermal papillae. Each corpuscle was innervated by a number of nerve fibres varying from 2 to 6. Within the corpuscle the nerve terminals ended in a spiral pattern of varying complexity (Fig. 1). Pacinian corpuscles occurred mostly in the deeper part of the corium but were also found in a superficial position, especially at the finger tips. They were usually solitary (Fig. 2), but were occasionally distributed in clusters. The nerve terminal innervating the inner core was single.

*Cholinesterase preparations.* The AChE reaction for Meissner's corpuscles (Fig. 3) and the inner core of Pacinian corpuscles (Fig. 4) was usually moderate, but occasionally weak and very rarely intense. The ChE activity of both types of corpuscles (Figs. 5, 6) was strong to intense in the majority of cases.

*Early effects of injury*

*Nerve crush.* In BG preparations 3–4 weeks after a nerve crush, Meissner's corpuscles (Fig. 7) and the inner core of Pacinian corpuscles (Fig. 8) were devoid of nerve terminals. However, even in these early stages thin nerve fibres had reinnervated some of the empty nerve bundles in the corium (Fig. 9). Moreover, in the subepidermal region solitary nerve fibres were occasionally seen, and some had reached the base of the dermal papillae. AChE preparations of comparable stages revealed similar positive fibres. The AChE reaction in individual Meissner's corpuscles and the inner core of Pacinian corpuscles varied, but taken as a whole was much reduced when compared with the controls (Figs. 10, 11).

At 6 weeks, though the majority of Meissner's corpuscles were uninnervated, a few showed early reinnervation, by thin transversely running fibres inside the corpuscle (Fig. 12) or by a solitary fibre running a fairly straight course within the dermal papillae. The inner core of Pacinian corpuscles remained uninnervated. The

Fig. 1. A normal Meissner's corpuscle, BG technique.  $\times 340$ .

Fig. 2. A normal Pacinian corpuscle. BG technique.  $\times 85$ .

Fig. 3. Normal Meissner's corpuscles giving moderate AChE reaction. Modified Koelle's technique, 21 h incubation.  $\times 85$ .

Fig. 4. A normal Pacinian corpuscle giving moderate AChE reaction. Modified Koelle's technique, 21 h incubation.  $\times 85$ .

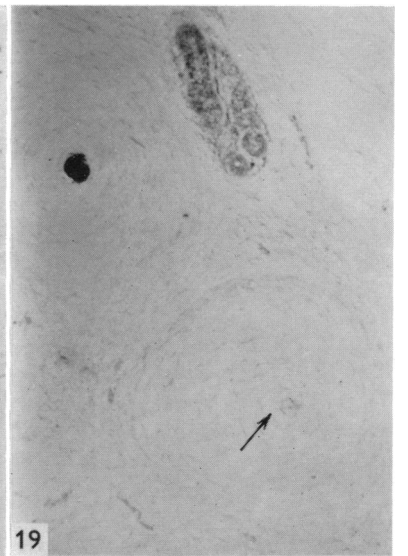
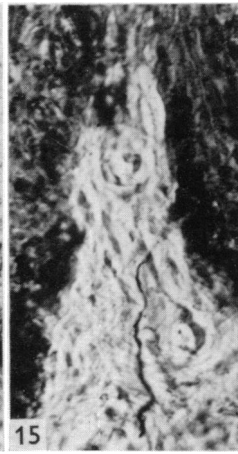
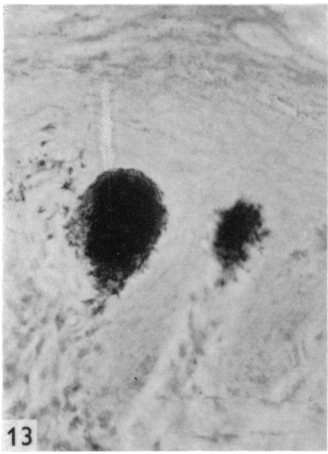
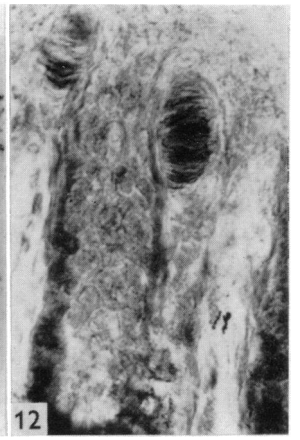
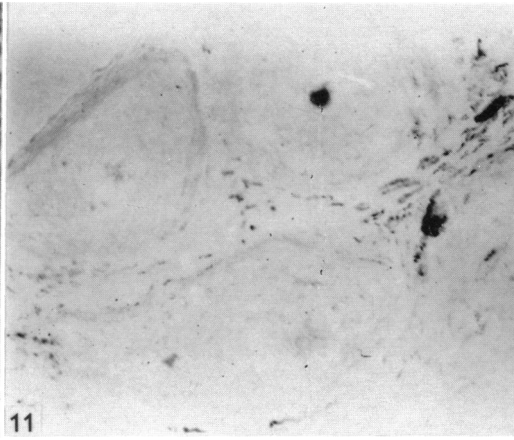
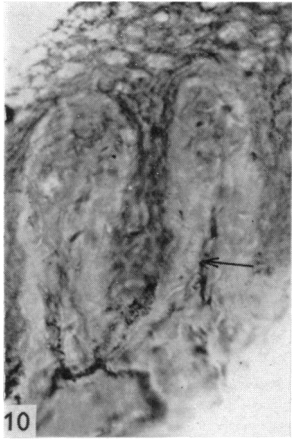
Fig. 5. Normal Meissner's corpuscles giving intense ChE reaction. Modified Koelle's technique, 21 h incubation.  $\times 85$ .

Fig. 6. A normal Pacinian corpuscle giving intense ChE reaction. Modified Koelle's technique, 21 h incubation.  $\times 85$ .

Fig. 7. A denervated Meissner's corpuscle (arrow) 3 weeks after nerve crush. BG technique.  $\times 340$ .

Fig. 8. A denervated Pacinian corpuscle, 3 weeks after nerve crush. BG technique.  $\times 85$ .

Fig. 9. Regenerating nerves in the corium, 3 weeks after nerve crush. BG technique.  $\times 340$ .



AChE reaction in the majority of Meissner's corpuscles was considerably reduced when compared with the control side, but in a few corpuscles a very strong reaction was observed (Fig. 13). The inner core of Pacinian corpuscles gave very much weaker reaction than on the control side. AChE positive corial and subepidermal plexuses were frequently seen.

At 8 weeks a number of Meissner's corpuscles showed early reinnervation and in an occasional one the process had advanced considerably (Fig. 14). By contrast, the inner core of Pacinian corpuscles remained uninnervated. The AChE reaction in the majority of Meissner's corpuscles was much reduced when compared with the control side, but a number gave a moderate reaction and a few reacted intensely. The inner core of Pacinian corpuscles at this stage gave either a trace reaction or none at all.

A study of the ChE preparations in all these early stages showed that there was no difference between the experimental and the control sides in respect of the enzyme reaction in Meissner's corpuscles and in the inner core of Pacinian corpuscles.

*Nerve ligation and section.* The early effects after nerve ligation and after section were similar and will be described together. In the 3–4 week-old specimens, Meissner's corpuscles and the inner core of Pacinian corpuscles were devoid of nerve terminals, and showed either a trace reaction or more in the AChE preparations. A few AChE positive nerve fibres were found in the corium and subepidermal region.

In the 5–6 week-old specimens, occasional single fibres were seen in the dermal papillae or close to the basal part of the epidermis (Fig. 15). Meissner's corpuscles and the inner core of Pacinian corpuscles were uninnervated and showed no AChE activity.

By the 8 weeks stage BG preparations showed that the majority of Meissner's corpuscles were uninnervated; a few showed early reinnervation with transverse strands of fibres and a rare one showed an advanced reinnervation pattern (Fig. 16). The inner core of Pacinian corpuscles was uninnervated. The majority of Meissner's

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Fig. 10. Meissner's corpuscles giving trace AChE reaction 4 weeks after nerve crush. Note AChE positive nerves (arrow), approaching papilla. Modified Koelle's technique, 21 h incubation.  $\times 340$ .

Fig. 11. Pacinian corpuscles giving trace to moderate AChE reaction 4 weeks after nerve crush. Modified Koelle's technique, 21 h incubation.  $\times 85$ .

Fig. 12. Meissner's corpuscles showing early reinnervation 6 weeks after nerve crush. Note thin transverse fibres within the corpuscles. BG technique.  $\times 340$ .

Fig. 13. Meissner's corpuscles giving strong AChE reaction 6 weeks after nerve crush. Modified Koelle's technique, 21 h incubation.  $\times 340$ .

Fig. 14. A Meissner's corpuscle showing an advanced reinnervation pattern 8 weeks after nerve crush. BG technique.  $\times 340$ .

Fig. 15. A solitary nerve fibre entering a papilla 6 weeks after nerve section. BG technique.  $\times 340$ .

Fig. 16. A Meissner's corpuscle showing an advanced reinnervation pattern 8 weeks after nerve ligation. BG technique.  $\times 340$ .

Fig. 17. A Pacinian corpuscle reinnervated in an unusual manner after a long-term crush. BG technique.  $\times 340$ .

Fig. 18. Two Pacinian corpuscles after a long-term crush, one giving a weak AChE reaction while in the other there was no reaction (arrow). Modified Koelle's technique.  $\times 85$ .

Fig. 19. The same two Pacinian corpuscles as shown in the preceding figure, one giving an intense ChE reaction while in the other there was no reaction (arrow). Modified Koelle's technique.  $\times 85$ .

corpuscles were devoid of AChE reaction, a number gave a trace or a weak reaction, while a rare one showed a strong reaction.

The ChE activity in Meissner's corpuscles and the inner core of Pacinian corpuscles differed little between the experimental and the control sides in all stages except in the 8 week-old specimens where some corpuscles on the operated side showed a slightly weaker reaction than the controls.

#### *Late effects of injury*

The reinnervation of Meissner's corpuscles 40 weeks after nerve crush was almost complete, but after nerve section (32 weeks) and nerve ligature (40, 47 weeks) the process was less complete, with occasional patches of uninnervated corpuscles. Fig. 17 shows the inner core of a Pacinian corpuscle being reinnervated in an unusual manner after a long-term crush. In AChE and ChE preparations Meissner's corpuscles gave the normal pattern of reaction. The cholinesterase reaction in the inner core of Pacinian corpuscles showed variation. In AChE preparations many gave a weak to moderate reaction while some showed no activity (Fig. 18). The reaction in ChE preparations varied from nil to intense (Fig. 19).

### DISCUSSION

#### *Short term experiments*

Three to four weeks following median nerve injury the AChE activity in Meissner's corpuscles and the inner core of Pacinian corpuscles was either diminished (nerve crush) or practically absent (nerve ligature and section). This is in general agreement with our previous observations on Meissner's corpuscles (Wong & Kanagasuntheram, 1970). However, a comparison of the results during these stages suggests that, though in all the material BG preparations showed uninnervated Meissner's and Pacinian corpuscles, the decline in AChE activity in these corpuscles was relatively slower and less abrupt after nerve crush than after nerve ligature or nerve section. Whether this has any relationship with the lesser degree of injury inflicted by nerve crush than by either section or ligature merits further study.

The regeneration process in Meissner's corpuscles was more rapid after nerve crush than after either nerve ligature or nerve section, as borne out by a study of the 5-6 weeks specimens. Thus the observation in the nerve crush material of an occasional Meissner's corpuscle giving an intense AChE reaction, indicating early regeneration, correlated well with the presence of argyrophilic strands in a number of these corpuscles. None of these features was seen in the comparable stages after either nerve ligature or nerve section. By the 8 weeks stage, however, there was evidence of early regeneration of Meissner's corpuscles in the nerve ligature and nerve section specimens with a rare one showing advanced reinnervation whereas in the nerve crush material, regeneration of Meissner's corpuscles had gone on apace.

#### *Long-term experiments*

Successful reinnervation of the majority of Meissner's corpuscles occurred, but reinnervation of Pacinian corpuscles was much less common, even in these late stages. The cholinesterase studies showed that the inner core of many of these

corpuscles was devoid of either AChE or ChE activity. The successful reinnervation of Meissner's corpuscles on the one hand and the comparative failure of the process in Pacinian corpuscles on the other may be a reflexion of their respective patterns of innervation. The nerve supply of a Meissner's corpuscle is usually multiple, whereas the inner core of a Pacinian corpuscle has an exclusive supply from a single fibre which remains unbranched throughout its course (Cauna & Mannan, 1961). The probability of the former regaining a nerve supply after denervation would therefore be relatively greater than in the case of the latter. On the other hand, the failure of reinnervation may also be due to some mechanical factor preventing the re-entry of nerve fibres into the denervated Pacinian corpuscle.

*Nerve dependence of receptor enzymes*

The nerve dependence of enzymes in the mammalian taste buds has recently been demonstrated (Zalewski, 1968; Iwayama & Nade, 1969). Thus, after glossopharyngeal nerve section there is a gradual diminution and eventual loss of alkaline phosphatase in the circumvallate papilla during the period of degeneration and a return of enzyme activity during regeneration. These findings show a striking similarity to our present results, with particular reference to AChE, which showed a definite decline and disappearance following nerve injury, and a reappearance following reinnervation of Meissner's corpuscles.

SUMMARY

Following median nerve section, crush, or ligature in a series of ten monkeys, the cutaneous territory of the nerve was studied by taking biopsies at intervals. The material was stained by a modified Bielschowsky-Gros technique, and also subjected to a modified Koelle technique for the demonstration of cholinesterase. The short-term results (3–8 weeks) showed that the process of regeneration of Meissner's corpuscles was more rapid after nerve crush than after either nerve section or ligature. The results from the short-term and long-term (32–47 weeks) experiments indicated that Pacinian corpuscles were less often reinnervated than Meissner's corpuscles. Whether this lack of reinnervation of Pacinian corpuscles was a reflexion of their pattern of innervation or was due to some other cause, perhaps mechanical, is not known at present.

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