THE USE OF DIRECT CURRENT TO CAUSE SELECTIVE BLOCK OF LARGE FIBRES IN PERIPHERAL NERVES

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SUMMARY

The effect of direct current on the propagated compound action potential in a cutaneous branch of the radial nerve of the dog was studied and a convenient method for applying electrical current to a nerve is described. Changes in the flow of blocking current, even when these were made slowly during a period of 5–10 sec, caused stimulation of the nerve. The method was unsatisfactory for producing differential nerve block within the myelinated fibres. It was confirmed that direct current could be used to eliminate selectively the group II/III potentials. When these potentials had been eliminated for a period of 5 min the mean height of the group IV potentials was reduced to 65% of the control value, and their conduction velocity was decreased by 10%. Relatively small variations in current flow caused a marked change in conduction. In the early stages of block, frequent relatively large reductions in current flow were necessary to produce a constant response and it was impossible to cause a stable effect on conduction until the blocking current had been applied for at least 1 min. Because of nerve damage the method is unsuitable for clinical use.

It is a common clinical experience that during local analgesia, such as subarachnoid or extradural nerve block, it is possible to block selectively conduction in small pain fibres while retaining some other sensory modalities and motor function (de Jong and Wagman, 1963).

Chemical methods of nerve block have a relatively greater effect on the smaller fibres in a nerve. This has been demonstrated for local anaesthetic drugs (Gasser and Erlanger, 1929; Matthews and Rushworth, 1957; Nathan and Sears, 1961), phenol (Nathan and Sears, 1960), sodium-deficient solutions (Nathan and Sears, 1962) and the veratrum alkaloids (Lorente de Nó, 1947).

Hypoxia also has a greater effect on small fibres which have a greater surface area in relation to energy stores (Lorente de Nó, 1947; Davies, 1953). The effect of ischaemia on a peripheral nerve is complex. In any particular section of a nerve the smallest and most slowly conducting fibres are the most sensitive to a reduction in blood flow. However, the proximal part of a large nerve appears to be more vulnerable than the more distal parts (Fox and Kenmore, 1967).

In order to block selectively conduction in the largest and most rapidly conducting fibres in a nerve it is necessary to use physical methods, for example, pressure, reduction in temperature or electrical current. Pressure block (Gasser and Erlanger, 1929) is difficult to control and is not easily reversible. Cold block is useful for causing total reversible nerve block (at temperatures of 1–2 °C), but is unselective between the different groups of myelinated fibres (Paintal, 1965a) and produces very little usable separation of conduction in myelinated and unmyelinated fibres even at low temperatures (Paintal, 1965b).

For these reasons, methods for rapid reversible selective block of conduction in large myelinated fibres depend on the use of electric current (anodal block).

When stimulating a nerve electrically with bipolar electrodes, if the anode lies in the direction of impulse propagation, some of the faster fibres, activated at the cathode, may be blocked by the brief flow of current at the anode. Kuffler and Vaughan-Williams (1953) have used this technique to block differentially the faster fibres in frog nerve at room temperature. However, the speed of conduction of mammalian nerve fibres makes this method impractical (Mendell and Wall, 1964). It is necessary to apply polarizing current through a separate pair of electrodes, situated at a distance from the stimulating electrodes.
Three methods for the application of current have been used: (1) repetitive application of stimuli to polarize the nerve (Bishop and Heinbecker, 1935); (2) the application of direct current immediately before each propagated impulse (Zimmerman, 1968; Schmidt and Weller, 1970); (3) the application of continuous direct current to produce and maintain the required degree of differential block (Kuffler and Gerard, 1947; Mendell and Wall, 1964; Shealy, Tyner and Taslitz, 1966; Fussey, Kidd and Whitwam, 1968; Collin, Kaufman and Koizumi, 1969; Coote and Perez-Gonzalez, 1970; Guz and Trenchard, 1971).

The use of direct current to cause block of conduction in peripheral nerves has proved to be an important experimental technique. For example, Mendell and Wall (1964) were able to show the interaction between large and small fibres and dorsal root potentials, and hence to contribute physiological evidence for the "gate" theory of sensation. In spite of this, there has never been published a systematic study of the effect of direct current on conduction in peripheral nerves.

The present investigation was concerned particularly with the effect of direct current on conduction in the larger peripheral nerves of the dog, and more specifically with the possibility of producing block of conduction of the faster myelinated fibres, while retaining conduction in the slower myelinated (group III) and group IV fibres. In addition, the stability of the block and changes induced in the group IV potential were studied.

METHODS
Experiments were performed on the lateral branch of the superficial branch of the radial nerve of the dog; observations were made on 22 nerves and the effect of direct current was studied on 120 occasions.

Anaesthesia was induced with a single i.v. injection of thiopentone sodium (Intraval Sodium, May and Baker Ltd) 30 mg/kg, followed by 75–80% nitrous oxide in oxygen. The animals were immobilized with intermittent i.v. injections (1–2 mg/kg/hr) of suxamethonium chloride (Soline, Allen and Hanbury Ltd). They were ventilated artificially through two polythene tubes (i.d. 3 mm) with lateral holes, placed one along each side of the nerve. The large vein adjacent to the nerve was tied distally and the leg was lagged in cotton wool except for the surface of the pool. The mean temperatures in the pool adjacent to the nerve at the recording, blocking and stimulation sites were 37.3 °C (SEM 0.23 °C), 37.2 °C (SEM 0.21 °C) and 36.8 °C (SEM 0.17 °C) respectively. The mean temperature decrease along the nerves, using paired data for each nerve, was 0.59 °C (SEM 0.08 °C), representing a mean gradient of 0.06 °C cm⁻¹.

Nerve lengths were measured to the nearest millimetre between the stimulating cathode and the proximal recording electrode by a piece of thread placed close to the full length of the nerve. The mean nerve length between the stimulating cathode and the proximal recording electrode was 9.4 cm (SEM 0.41 cm; range 6.7–15.2 cm).

Single square-wave stimuli of appropriate duration and intensity, supramaximal for unmyelinated fibres, were applied at a frequency of one every 2 sec through silver–silver chloride electrodes. The compound action potential recorded with bipolar silver–silver chloride electrodes was amplified by a preamplifier (Tektronix 122 band width 0.8–10.000 Hz) and displayed on an oscilloscope (Tektronix 565). Recordings of the compound action potential were made on
film and measurements were taken from the projected film magnified 12 times. The compound action potential showed three principal components, allowing classification of the nerve fibres into groups II, III and IV (Lloyd, 1943). The myelinated fibres caused two major deflections, referred to as groups II and III respectively. The conduction velocity of the fibres representing the beginning of the group III potential varied between 27 m sec\(^{-1}\) and 34 m sec\(^{-1}\) in different preparations. Unmyelinated fibres are referred to as group IV and the fastest fibres in this group had conduction velocities of 1.9 m sec\(^{-1}\).

Direct current was applied to the nerve from a dry battery with electrodes which consisted of felt pads soaked in 0.9% saline, mounted on 16-gauge stainless steel needles. The needles were attached to 2-ml plastic syringes filled with 0.9% saline. The preparation is illustrated schematically in figure 1 and has been demonstrated and described previously (Kidd and Whitwam, 1967; Whitwam, 1971). This system ensures a large area of contact between each electrode and the nerve which can be flushed with 0.9% saline. Alternatively, excess saline or accumulated serum can be aspirated from the area of the blocking electrodes without disturbing the preparation.

(b) Production of a constant response

In these experiments a current was applied which would produce a particular degree of block of conduction in the nerve as indicated by the compound action potential. This level of block was maintained constant for a period of 5 min by manual adjustment of the current flow which was recorded every 15 sec. Responses were recorded in the control period, at 1-min intervals during application of the current and thereafter at 1-min intervals for 4 min.

RESULTS

The application and withdrawal of current, and also the minor adjustments to the current intensity required to produce a constant effect on the compound action potential, stimulated individual nerve fibres whose action potentials were superimposed on the compound potential. This activity lasted 10-15 sec after a step change in the level of current flow.

Two levels of nerve block and subsequent recovery of conduction were studied. First, the current was applied to just eliminate the group II/III potentials and the effect on the group IV potential was observed. Second, partial block of conduction of the group II/III potential was produced in an attempt to eliminate the group II while retaining the group III potentials.

(1) Block of conduction in myelinated fibres (groups II and III) while retaining conduction in unmyelinated (group IV) fibres

In the radial nerve of the dog it was possible to eliminate the compound potential resulting from
myelinated fibres while retaining a large group IV potential thus confirming the observation of previous workers in the cat (Mendell and Wall, 1964). The experiments were performed either by applying a constant current or by adjusting the current to produce a constant response as described in the section on methods.

(a) Constant current. The current applied to the radial nerve of the dog in these experiments varied from 27 μA to 350 μA.

Several preliminary experiments were performed and responses from one are illustrated in figure 2a in which 320 μA was applied to the radial nerve of a dog. After 0.5 min the group II potential was eliminated and there was a small residual group III potential; the group IV potential remained virtually unchanged. At 4 min the group II/III potentials were eliminated, and, while the form of group IV potential remained essentially the same, the conduction velocity of the fibres representing the earliest phase of this potential had decreased by 10%; 30 sec after removal of the current recovery of all the potentials was observed. Subsequently, a series of 21 experiments was performed, on nine radial nerves in seven dogs, in which the response was standardized so that a constant current was applied for 5 min which just eliminated the group II/III potentials after 3 min. After 5 min the group IV potential showed a mean decrease of approximately 10% in both peak height and conduction velocity (fig. 3A). After removal of the current recovery of the group II and group IV potentials was complete in 2 and 3 min respectively, and the mean height of the group II/III potential returned to the control value within 1 min. The mean conduction velocity, timed to the beginning of the group II potential, was still decreased by 5% 3 min after removal of the current.

(b) Constant response. In nine experiments on six radial nerves in five dogs, a current of intensity just sufficient to eliminate the potentials resulting from group II/III fibres was applied for 5 min, and the effect on the group IV fibres was observed. Single responses recorded during such an experiment are illustrated in figure 2b. Responses at 2 min and 5 min show complete elimination of the group II/III potentials. The group IV potential recorded at 2 min showed a 3% decrease in initial conduction velocity, a 30% reduction in peak-to-peak height and an increase in the width of the potential indicating temporal dispersion. At 5 min, apart from a further decrease in conduction velocity of 2%, the size and form of the potential remained relatively unchanged. Two minutes after the current was removed, the group III and group IV potentials had recovered but the height of the group II potential was still reduced by 14% from the control value. In figure 3b can be
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Fig. 3. Effect on group IV potential of eliminating group II/III potentials with direct current in the radial nerve of the dog. • • Conduction velocity of the early part of the group IV potential. ○ ○ Peak-to-peak height of group IV potential. A. Constant current. Mean values from 21 experiments on nine nerves in seven dogs. B. Current adjusted continuously to just eliminate potentials from myelinated fibres (constant response). Mean values from nine experiments on six nerves in five dogs.

seen the effect on the latency and peak height of the group IV potential during these nine experiments. There was a gradual reduction in the mean height of the group IV potential so that after 5 min it was only 65% of the control value, while the conduction velocity of the early part of the potential was reduced by 10%. After withdrawal of the current, the group III and group IV potentials recovered completely within 1–2 min and in 3 min respectively. The conduction time of the group II potential returned to the control value in 2 min, but at 3 min there was still a mean loss of 5% of the peak height of the potential.

(2) Differential block of conduction in myelinated fibres (within fibres of groups II and III)

Observations were made on a total of 18 nerves during this part of the study.

(a) Constant current. The range of current flow applied varied from 30 μA to 125 μA. Fourteen preliminary experiments were carried out on four nerves in four dogs in which current was applied for periods of 2–4 min. In a further 20 experiments on eight nerves in seven dogs, current was applied for a duration of 5 min in which the response was standardized (see section on methods). Thus the effect of constant current was studied in a total of 12 nerves. Seven nerves showed a similar change in response when a current of constant intensity was applied and a series of responses from a typical experiment is shown in figure 4. The conduction velocity of the fastest fibres in these nerves was 67 m sec⁻¹ (SD 4.9 m sec⁻¹). No allowance was made for the activation time in calculating these velocities, and hence the true value is likely to be 5–10% greater (Erlanger and Gasser, 1937). At first that part of the group II potential resulting from fibres with the highest conduction velocities was eliminated while at the same time there was a progressive loss in height of both this potential and the potentials resulting from myelinated fibres with slower conduction velocities. The loss of signal height was most marked in the
potentials from the fast myelinated fibres, so that when the conduction velocity of the start of the group II potential had been reduced to 75% (SD 5.9%) of the control value, corresponding to a mean conduction velocity of 50 m sec\(^{-1}\), the amplitude of the group II potential was reduced to the same height as the following group III potential, and a clear distinction between the two potentials was no longer possible. Then as the current caused further block of conduction, there was a loss of height of all the potentials simultaneously. Thus, once the conduction velocity of the start of the group II potential had been reduced from a mean value of 67 m sec\(^{-1}\) to 50 m sec\(^{-1}\), in this particular group of seven nerves, no further differential loss of the group II/III compound action potential occurred.

In three out of the 12 nerves, the application of current blocked conduction in all the myelinated fibres simultaneously and there was no differential loss of conduction in the fastest fibres as outlined above, so that a potential produced by the fastest group II fibres persisted until the group III potential was abolished.

In two nerves, differential block of conduction of the faster fibres did occur: the early part of the combined potential was eliminated, leaving a residual potential with clearly defined limits, the conduction velocity of the fastest recorded fibres being less than 25 m sec\(^{-1}\).

In 20 experiments on eight nerves in which the response was standardized (see section on methods) and the current was applied for 5 min, when the current was removed the group III and group IV potentials returned to control values in 2 and 3 min respectively. The mean height of the group II potentials returned to 90%, 95% and 98% of the control values at 15 sec, 3 min and 4 min respectively; the mean conduction velocity of the start of the potentials recovered to 96% and 99% of the control values at 4 sec and 4 min respectively.

(b) **Constant response.** In nine experiments on six nerves in five dogs, an attempt was made to produce partial or total elimination of the group II potential for a period of 5 min. In five out of these six preparations the current blocked conduction in all myelinated fibres simultaneously and it was not possible to eliminate partially the group II potential without eliminating the group III potential also. When the current was withdrawn, the conduction time of the group II potential recovered in 2 min, but the mean peak height returned to only 91% (SD 4%) of control value at 3 min. The conduction time of the group IV and group III potentials returned to control values at 1 min and 3 min respectively, while the mean height of these potentials returned to only 96% and 98% of initial values at 4 min.

**Effect of current with time**

In figure 5 the current values have been plotted during a series of experiments for partial and total elimination of the group II/III potentials. It is seen that frequent relatively large reductions in current flow were required for the 1st min in order to maintain a constant block of nerve conduction, and hence it was impossible to produce an afferent volley passing through the blocked area which was stable until current had been applied to the nerve for 1 min. Even then, progressive small reductions in current flow were essential to maintain a constant response and these were associated with the activation of
Fig. 5. Current flow to maintain a constant effect on conduction in the radial nerve of the dog. ● — ● First experiment on the nerve. Current flow applied in an attempt to eliminate selectively conduction in group II fibres. ○ — ○ Second experiment on the nerve (5 min allowed for recovery). Current flow required to eliminate the group II/III potentials. ○ · · · · ○ Fourth experiment on the nerve. Current flow required to eliminate the group II/III potentials after one further experiment in which an attempt was made to eliminate selectively the group II potential for 5 min, with 5 min allowed for recovery. The time between the last two experiments was 15 min, during which period current was applied for 5 min in an attempt to eliminate selectively the group II potential.

individual nerve fibres whose propagated action potentials were recorded. The need for a rapid reduction of current to maintain a constant degree of block immediately after application of the current was a feature of all these experiments, and the period during which the block was regarded as unstable varied from 30 sec to 2 min. In general 1 min was regarded as the minimum time before the effect of the current could be regarded as constant, after which only small reductions of current flow were required to maintain a constant degree of block of conduction. The need to reduce the current flow to produce a constant degree of block was also noted by Kuffler and Gerard (1947).

**Effect of repeated applications of current and duration of preparation**

Progressively less current was required to produce the same effect on the compound action potential following repeated application of current during a series of experiments which is in keeping with the observations of Bishop and Heinbecker (1935). Even a small change in current flow could cause a large change in conduction, and in preparations in which nerve conduction was starting to deteriorate, a flow of current which might eliminate only partially the group II/III potentials in one experiment would, when applied only a few minutes later, eliminate totally this potential.

Without the application of electrical current to the nerve, in similar preparations the propagated compound action potential has been observed to show little change for periods up to 8 hr. It must be assumed that the relatively rapid deterioration of conduction seen in the experiments reported here is related to the application of direct current to the nerve, and the temporal effect of current application in one preparation is illustrated in figure 5.

The longest total time during which current was applied before nerve conduction showed substantial
irreversible failure was 64 min, divided into 11 applications for partial elimination of the potentials from the myelinated fibres, each of 5 min duration, together with three 3-min "setting-up" periods. The total experimental time after completion of dissection on this occasion was 3 hr.

Deterioration tended to be slow at the start, then after a time, varying from 30 min to 3 hr from setting up the preparation, rapid progressive failure of nerve conduction occurred most marked initially in the myelinated fibres. Evidence of deterioration of conduction was seen in two ways. First, during a series of experiments there was a small percentage decrease in either the peak height or the conduction velocity of the potentials, which was most marked in the group II potential as outlined above. Second, during a series of experiments progressively less current was required to produce the same effect on conduction.

**DISCUSSION**

The results of this study confirm that the application of direct current to a nerve can be used to eliminate the compound action potential produced by the myelinated fibres while retaining much of the potential produced by conduction in unmyelinated fibres.

The problem of stimulation of the nerve when the current is applied or withdrawn has been described by previous workers (Mendell and Wall, 1964; Bower, 1966; Zimmerman, 1968). Both Bower (1966) and Zimmerman (1968) have described methods of producing relatively slow changes in current flow in an attempt to eliminate this problem, and the latter author found it difficult to avoid stimulating the nerve even when the current rise-time was 3 sec. In the present study, stimulation of the nerve was observed on occasions when the current was increased slowly from zero to the effective level during a period of 5–10 sec.

In the present study, when a blocking current just sufficient to eliminate the group II/III potentials was applied, on average the group IV potential retained 75% (SD 5%) of its peak height at 1 min and 65% (SD 13%) at 5 min (fig. 3a). When a constant current was applied, which just eliminated the group II/III potentials after 3 min, the group IV potential on average retained 90% (SD 13%) of its peak height at 5 min (fig. 3a). This is in sharp contrast with the observations of Zimmerman (1968) who found that the height of the group IV potential declined rapidly in relation to both current strength and its duration, and that there was a rapid decrease in the height of the group IV potential when a current strength which eliminated the group II/III potentials was applied for only 10 sec. The results of the two studies can be reconciled if it is assumed that Zimmerman (1968) was working on the steep part of the current graphs illustrated in figure 5. Thus he was maintaining a current flow which was necessary to eliminate the group II/III potentials initially but which, in the present study, was reduced immediately to maintain a constant response. When a constant blocking current was applied in the present study, a level was chosen which produced a given response after 3 min. Therefore it was on the flat part of the curves of current flow illustrated in figure 5.

As a reliable method of producing differential block of fibres within groups II and III, anodal block is unsatisfactory under the experimental conditions outlined above, because the current affects conduction in a wide spectrum of the myelinated fibre population simultaneously. In only two out of 18 nerves studied in the dog was it possible to produce a residual group III potential with clearly defined limits and a usable signal-to-noise ratio. These results are in keeping with those of Casey and Blick (1969) who found that the temporal order of block in single myelinated fibres of the cat, produced by direct current, was unrelated to their conduction velocity. These authors reported also that the amplitude of the large wave A (group II) increased to 120–130% of the control values at the first recorded response, 2 sec after the current was applied. Casey and Blick (1969) increased the flow of current during a period of 3–10 sec. In the present study, even when the current was applied slowly during a period of 5–10 sec, the earliest change in the compound potential was a decrease in height and an increase in latency, and we have no explanation for this difference between the two studies.

One factor affecting the height of the compound potential is the amount of slowing of conduction which occurs through the region of the block. The effect witnessed at the recording site will depend on the relative length of the blocked area in relation to the distance between the stimulating and recording electrodes. In the present study the conduction velocity of the group IV fibres representing the start of the potential wave was reduced by 10% from the
control value after application of a constant current sufficient to eliminate conduction in the myelinated fibres of the radial nerve of the dog for a period of 5 min (fig. 3B). A reduction in the initial conduction velocity of the group IV potential of the same order of magnitude has been observed also in the sural nerve of the cat (Mendell and Wall, 1964). If it is assumed that the effect of the current on the conduction velocity of all the group IV fibres is the same, then temporal dispersion of the group IV potential wave (an increase in the width and a reduction in amplitude of the potential) would be anticipated, and evidence of such temporal dispersion was seen in several preparations (fig. 2B). However, in many preparations there was no change in the width of the group IV potential (fig. 2A), while in some the width of the group IV potential showed a slight decrease which would indicate greater effect on conduction in the faster fibres than the slower ones. One problem in interpretation is how much the shift in the early part of the group IV potential is a result of slowing of conduction and how much it is a result of block of impulse transmission. Changes in the form of this potential during the application of current also add to the problem of measurement of its width, and in the absence of studies on single fibres it is difficult to draw definite conclusions on the relative effects of direct current on conduction within the group IV fibre population.

The problems of slowing of conduction and temporal dispersion of the wave form make interpretation of residual potentials from group II/III fibres extremely difficult. Paintal (1965a) has shown that temporal dispersion of conduction during the cooling of a nerve eliminated the group III compound action potential, although some of the fibres were still conducting. Casey and Blick (1969) have shown that during anodal block, whereas single fibres conducting above 30.2 m sec⁻¹ were always blocked when the group II potential disappeared, an estimated 20% of group III fibres may continue to conduct even though the compound action potential fails to reveal activity in that part of the fibre spectrum. Thus a single recording of the compound action potential is unsatisfactory for assessing relatively low levels of conduction in a peripheral nerve. It could be suggested that the use of average transient responses might be more useful. However, some factors which make the method of anodal block difficult to apply in practice may also invalidate the use of average transient responses for interpretation of small residual potentials:

(1) The effect of a constant current increases relatively rapidly for 1–2 min, after which there is a slow progressive increase of block with time.
(2) Small changes in current flow may produce marked changes in the degree of nerve block.
(3) Conduction in the nerve gradually deteriorates so that the same current will produce a greater degree of block if reapplied after only a short lapse of time.

Thus, during any experimental procedure, it is essential to record the compound action potential continuously, and it is difficult to produce a steady state necessary for the use of average transient responses.

The damage which repeated application of electrical current causes in a nerve renders this technique unsuitable for clinical use, where complete recovery is essential.

In conclusion, the present study confirms that the results of experiments in which direct current is assumed, on the basis of observation of the compound action potential, to have produced a constant level of block and to have selectively blocked conduction in all myelinated fibres also, should be interpreted with caution.

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REFERENCES


EL USO DE CORRIENTE DIRECTA PARA PRODUCIR UN BLOQUEO SELECTIVO DE LAS FIBRAS GRANDES EN LOS NERVIOS PERIFERICOS

SUMARIO

Se estudió en perros el efecto de la corriente directa sobre el potencial de acción compuesto propagado en una rama cutánea del nervio radial, y se describe un método adecuado para la aplicación de corriente eléctrica a un nervio. Los cambios en el flujo de la corriente de bloqueo, aunque se hicieran lentamente durante un período de 5 a 10 segundos, produjeron la excitación del nervio. El método no fue satisfactorio para producir el bloqueo nervioso diferencial dentro de las fibras mielinizadas. Quedó confirmado que la corriente directa se puede usar para eliminar selectivamente los potenciales del grupo II/III. Cuando se eliminaron esos potenciales durante un periodo de 5 minutos, el pico medio de los potenciales del grupo IV quedó reducido a un 65% del valor de control y su velocidad de conducción disminuyó en un 10%. Variaciones relativamente pequeñas en el flujo de la corriente produjeron un cambio notable en la conducción. En las primeras fases del bloqueo se necesitaron grandes reducciones relativamente frecuentes en el flujo de la corriente, para lograr una respuesta constante y fue imposible producir un efecto estable sobre la conducción hasta que la corriente de bloqueo se aplicó por lo menos durante 1 minuto. El método no es adecuado para uso clínico por el deterioro del nervio.