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Comparison of the mode of action of succinylcholine and succinylmonocholine on rat skeletal muscle after denervation

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The effects of equimolar concentrations ($3{\cdot}0 \times 10^{-5}$ M) of succinylcholine (SCh) and succinylmonocholine (SMC) were studied in-vitro at 20 °C in rat extensor digitorum longus muscle (EDL) 0–147 days after common peroneal nerve section. Analysis of simultaneous measurements of K^+ efflux (mmolL^{-1} g^{-1}) and contracture tension (mN) to SCh showed that there was a rapid increase in the mean values of both parameters up to 22–28 days after denervation (7·7 mmolL^{-1} g^{-1}, 36 mN). At the end of the period studied, the contracture response declined to 4·0 mN whilst the capacity for K^+ efflux remained relatively high (4·8 mmolL^{-1} g^{-1}) in comparison with normal contralateral EDL muscle (n = 82) K^+ efflux measurements (0·62 mmolL^{-1} g^{-1}). A significant correlation ($r = 0{\cdot}86$, $P \leq 0{\cdot}001$) was found between SCh-induced K^+ efflux and contracture tension 1–56 days following nerve section which indicated that the development of the contracture response and K^+ efflux were concomitant during the period specified. The ratios of maximum contracture tension/K^+ efflux in response to SCh and SMC, 18–22 days after denervation were similar, 4·9 and 5·0, respectively. Results indicated that the mode of action of each agent was similar in denervated rat skeletal muscle, and that they were equally potent in their hyperkalaemic potential. Results of comparative measurements of membrane depolarization and contracture tension in response to SCh and SMC showed that both agents produced quantitatively similar responses at 7 and 14 days after denervation; 23 mN c.f. 20 mN/17 mV c.f. 15 mV, and 32 mN c.f. 33 mN/20 mV c.f. 19 mV, respectively. It is proposed that SMC would not be a suitable substitute for SCh for use with either normal or denervated skeletal muscle.

The action of succinylcholine in normal muscle in-vivo is relatively short, being hydrolysed to succinylmonocholine (Whittaker & Wijesundera 1952). Previously succinylcholine has been shown to act mainly as a depolarizing agent on normal skeletal muscle in man at 37 °C (Zaimis 1953), but in the rat the depolarizing characteristics are more distinct at lower temperatures (Whittaker 1962a, b; Harris & Leach 1968). Succinylmonocholine (SMC), however, demonstrates competitive features (Whittaker 1974). Results of experiments on denervated rat skeletal muscle, in which simultaneous measurements were made of SCh-induced membrane depolarization and contracture tension, showed that, during the first 28 days after denervation, depolarization increased and that from 7–35 days following denervation, depolarization was directly proportional to contracture tension (Andrews 1984). The depolarizing action of SCh intensified, therefore, after nerve section and was proportional to the contracture response in the period specified. Measurements of serum potassium ion concentrations in-vivo and brief SCh-induced contracture responses in-vitro have been used in a study by Carter et al (1981) to estimate the changes which follow spinal cord transection in the rat.

The aim of this investigation is to establish the onset and duration of SCh-induced K^+ efflux from rat extensor digitorum longus (EDL) muscle after peripheral denervation, to study the relationship between the contractile response and K^+ efflux, and to compare membrane and contractile responses of denervated fast twitch muscle to SCh and SMC.

METHODS

Young adult male Wistar rats from a homogeneous group were divided into two sets: 87 rats (223 g, s.d. ± 39) were used to investigate the contractile response and K^+ efflux from the EDL muscle during 20 min exposure to SCh and SMC 1–147 days after denervation, and 51 rats (217 g, s.d. ± 32) were used for simultaneous measurements of membrane depolarization and contracture tension in response to SCh and SMC 1–35 days after denervation.

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Denervation procedure
Rats were anaesthetized by intraperitoneal injection of pentobarbitone sodium (Sagatal), 40 mg kg^{-1}, made up in sterile sodium chloride solution (0·9% w/v). Operative procedures for common peroneal nerve section were performed under aseptic conditions. At specific periods following nerve section rats were anaesthetized and EDL muscles were removed.

Removal of EDL muscles for in-vitro preparation
Isolated muscles were secured in a small calibrated muscle bath, total volume 2 mL, in Krebs-Henseleit solution (Perry 1968) made up from deionized water and aerated with 95% O_2 and 5% CO_2. Muscle length was adjusted to that measured in-vivo. At the end of the experiment muscle weights were recorded and atrophy was estimated from the percentage weight loss with respect to contralateral control muscles.

Estimation of K^+ efflux
Spectrophotometric estimation of SCh-induced K^+ efflux was made from a pipetted sample (0·5 mL) of the total drug solution (1·5 mL) collected from the muscle bath after 20 min exposure to SCh ($3·0 \times 10^{-5}$ M), or SMC ($3·0 \times 10^{-5}$ M) in experiments with EDL muscles in Set 1. The samples were diluted 1:47 with deionized water for comparison with control solutions. $[K^+]$ was measured using the Instrumentation (I.L.151) acetylene/air flame emission method at 766·5 μm. A calibration curve was constructed for $[K^+]$ within the most sensitive range of the machine.

K^+ efflux estimations were calculated from the difference in $[K^+]$ in the control samples, and those taken after exposure to the drug and were expressed as mmolL^{-1} g^{-1} of the EDL muscle tissue.

Measurement of contracture tension
Contracture tension was measured by a 2 oz strain gauge (Dynamometer U.F.I.) and recorded on a Washington oscillograph (MDI 400). A 1 mV calibration was used to standardize the oscillograph record. Contracture tension was measured at 15 s intervals during the first minute of contracture and then at 2 min intervals during the 20 min exposure to the drug. Also, tension was measured during the Krebs wash until residual tension returned to the baseline. Muscle bath temperature was thermostatically controlled by a water jacket and heat lamp at 20 °C. Muscles were washed in Krebs-Henseleit solution for 60 min between drug applications. Pilot experiments indicated that this wash was sufficient.

Measurement of membrane potentials
Membrane potentials were recorded in batches of 10, taken in progressive 5 min sample blocks, throughout the 20 min exposure to SCh or SMC. Measurements were made using glass microelectrodes, 10 Mohms, filled with 3 M KCl solution. Microelectrode input signals were amplified by an M 701 preamplifier (W. P. Instruments). A silver/silver chloride earth plate completed the circuit through a DC calibrator (Epil 116A) to a Tektronix 502 oscilloscope. A 10 mV pulse was used to standardize the oscilloscope record. The equipment was screened in the conventional manner and connected to a common earth. Membrane depolarization was calculated with reference to the baseline resting potential measurement. A large muscle bath, total volume 25 mL, was used for the simultaneous measurement of membrane potential and contracture tension in EDL muscles in Set 2. Microelectrode placement in the muscle fibres was monitored visually using a microscope.

RESULTS

The relationship between SCh-induced K^+ efflux and atrophy in EDL muscles after denervation
Muscle atrophy increased throughout the period studied but was rapid 1–14 days after denervation, followed by a progressive loss up to 56 days which continued at a slower rate up to the end of the period studied (Table 1). The correlation coefficient, $r = 0·72$, indicated that the relationship was statistically significant ($P \leq 0·001$), 1–56 days following nerve section (Fig. 1). Also the coefficient, $r = 0·46$, calculated for the whole period indicated that the relationship between K^+ efflux and atrophy remained significant ($P \leq 0·001$) even at late stages after denervation when the contracture response had declined (Table 1).

The relationship between SCh-induced K^+ efflux and maximum contracture tension in EDL muscles after denervation
Contracture tension was recorded during 20 min exposure to SCh ($3·0 \times 10^{-5}$ M) in muscles denervated between 1–147 days before experiments, but was not observed in normal contralateral muscles. Analysis of the mean values of K^+ efflux (mmolL^{-1} g^{-1}) and maximum contracture tension (Newtons^{-3}, mN) showed that there was a rapid increase in both parameters (Table 1), 1–7 days after denervation (2·3 mmolL^{-1} g^{-1}/6·5 mN) which continued to rise up to 22–28 days after denervation (7·7 mmolL^{-1} g^{-1}/33·6 mN). During later stages of

Table 1. The relationship between K^+ efflux and contracture tension in chronically denervated rat EDL muscles in response to succinylcholine at 20 °C. Simultaneous measurements of maximum contracture tension (T_{max}) and K^+ efflux ($mmolL^{-1}g^{-1}$) were made in isolated rat EDL muscles in response to SCh ($3{\cdot}0 \times 10^{-5}$ M) at specific periods of denervation (n = 82). EDL muscles were assigned to groups 1–6 according to similarities in maximum contracture tension recorded in response to 20 min exposure to SCh ($3{\cdot}0 \times 10^{-5}$ M). Contracture tension was measured with respect to the baseline tension ($Newtons^{-3} \equiv mN$). T_{max} ≡ maximum contracture tension. Groups 0 and ∅ ≡ contracture tension absent, K^+ efflux was measured as the extracellular $[K^+]$ in excess of the normal contralateral muscle. K^+ efflux recorded from normal contralateral muscles was 0·62 (s.d. ± 0·1) $mmol^{-1}g^{-1}$ (n = 82). Atrophy was estimated as the % weight loss compared with the contralateral normal muscle.

			SCh ($3{\cdot}0 \times 10^{-5}$ M) 20 min			
EDL muscle groups	Duration of denervation days (mean ± s.d.)	EDL % wt loss (atrophy) (mean ± s.d.)	T_{max} mN (mean ± s.d.)	K^+ efflux $mmolL^{-1}g^{-1}$ (mean ± s.d.)	Ratio of T_{max}/ K^+ efflux	EDL n
0	1·5 ± 0·7	1·9 ± 6·1	–	1·5 ± 0·5	–	11
1	2·0 ± 1·0	3·9 ± 6·4	5·1 ± 3·2	2·0 ± 0·8	2·5	7
2	5·5 ± 1·6	11·2 ± 6·4	18·3 ± 10·6	3·5 ± 2·4	5·2	7
3	8·0 ± 4·3	24·5 ± 13·5	16·5 ± 6·6	4·3 ± 2·6	3·8	6
4	43·6 ± 25·3	56·0 ± 11·2	32·9 ± 13·2	6·8 ± 2·7	4·8	22
5	58·1 ± 22·0	62·4 ± 11·2	23·8 ± 13·3	7·6 ± 3·5	3·2	14
6	124·0 ± 2·3	75·2 ± 4·7	10·3 ± 9·1	4·7 ± 1·4	2·3	11
∅	147·0 ± 0	72·4 ± 5·9	–	4·3 ± 6·4	–	4

denervation a marked reduction was recorded 99–105 days (16·1 mN) and 141–147 days following nerve section (4·0 mN). Conversely, an increase in K^+ efflux was recorded up to 51–56 days after denervation (10·9 $mmolL^{-1}g^{-1}$), followed by a moderate decline at 141–147 days after denervation (4·8 $mmolL^{-1}g^{-1}$). The capacity for K^+ efflux from denervated rat skeletal muscle was present even at late stages of denervation and remained above the contralateral control value (0·62 $mmolL^{-1}g^{-1}$).

The correlation (r = 0·86) between the K^+ efflux and maximum contracture tension was statistically significant ($P \leq 0{\cdot}001$) 1–56 days after denervation (Fig. 2). Therefore the contractile changes and the development of excessive K^+ efflux were concomitant and the magnitude of the contracture response could be used as an indicator of hyperkalaemic potential.

EDL muscles were divided into groups 1–5 according to the similarities in maximum tension recorded during 20 min exposure to SCh ($3{\cdot}0 \times 10^{-5}$ M) for further analysis (Table 1). K^+ efflux was greatest in conjunction with SCh-induced contractures in groups 4 and 5, at 43·6 (s.d. ± 23) and 58·1 (s.d. ± 22) days after denervation, when the mean K^+ efflux was 6·8 and 7·6 $mmolL^{-1}g^{-1}$, respectively (Table 1). The ratio of T_{max}/K^+ efflux in groups 2–5 showed that maximum contracture tension could be used as an indicator of hyperkalaemic potential in these muscle groups.

Comparative effects of SCh and SMC on K^+ efflux and contracture tension in denervated EDL muscles

Comparative experiments on the effects of SCh and SMC were carried out on EDL muscles denervated 18–22 days previously (n = 5) and the contralateral normal control muscles. The period of denervation was selected with reference to the data presented in Table 1 so that SCh-induced K^+ efflux would be near

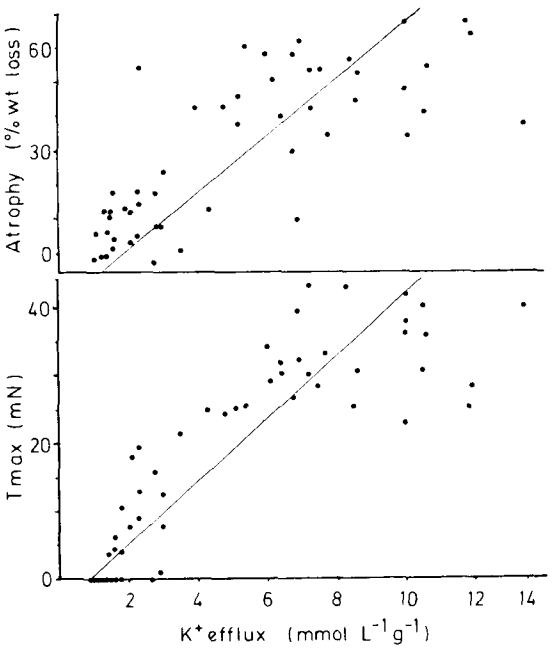

FIG. 2. Correlations between succinylcholine-induced K^+ efflux/maximum contracture tension (T_{max}), and K^+ efflux ($mmolL^{-1}g^{-1}$)/muscle atrophy (% weight loss) in rat extensor digitorum longus muscles (n = 52) calculated 1–56 days after denervation. Values for r were; K^+ efflux/T_{max} r = 0·86, $P \leq 0{\cdot}001$: K^+ efflux/atrophy r = 0·72, $P \leq 0{\cdot}001$. (mN ≡ $Newtons^{-3}$).

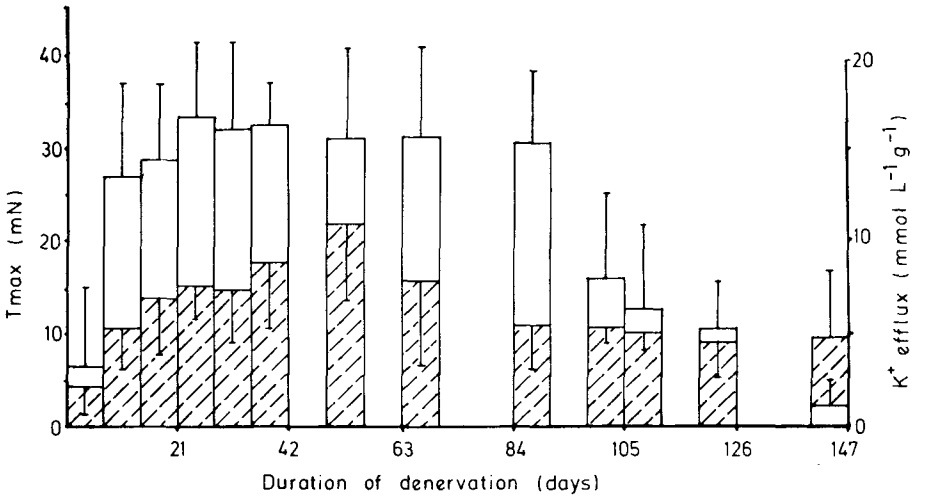

Fig. 1. Simultaneous measurements of K^+ efflux ($mmolL^{-1}\,g^{-1}$, hatched) and maximum contracture tension (T_{max}, white) were made in rat extensor digitorum longus muscles (n = 82) in response to SCh ($3{\cdot}0 \pm 10^{-5}$ M) at specific periods of denervation as described in the text. Contracture tension was absent in contralateral normal muscles (n = 82) but the mean K^+ efflux recorded was 0·62 (s.d. ± 0·1) $mmolL^{-1}\,g^{-1}$. Denervated EDL muscles were assigned to groups according to the duration of denervation as follows: 1–7 DPD, N = 12; 8–14 DPD, n = 6; 15–21 DPD, n = 5; 22–28 DPD, n = 5; 29–35 DPD, n = 5; 36–42 DPD, n = 5; 50–56 DPD, n = 5; 64–70 DPD, n = 5; 85–91 DPD, n = 5; 99–105 DPD, n = 4; 107–112 DPD, n = 5; 120–128 DPD, n = 5; 141–147 DPD, n = 6. (DPD = days post denervation, mN ≡ $Newtons^{-3}$).

the maximum level. The mean vaues for K^+ efflux (6·59 cf. 6·7 $mmolL^{-1}\,g^{-1}$), and maximum contracture tension (32·43 cf. 33·74 mN) recorded in denervated EDL muscles in response to SCh and SMC were quantitatively similar. Contracture tension was absent in normal muscles in response to SCh and SMC and K^+ efflux was minimal, namely 0·44 and 0·63 $mmolL^{-1}\,g^{-1}$ (Table 2). Maximum contracture tension and K^+ efflux were quantitatively similar in response to SCh and SMC (32·4 cf. 33·7 mN, and 6·6 cf. 6·7 $mmolL^{-1}\,g^{-1}$). The ratio of maximum contracture tension/K^+ efflux was similar in response to SCh and SMC, 4·9 cf. 5·0 mN/$mmolL^{-1}\,g^{-1}$. Results indicated that both agents were equally potent in their ability to raise $[K^+]_0$ to an abnormal level.

The modes of action of SCh and SMC on denervated rat skeletal muscle were therefore similar.

Comparison of membrane depolarization and contracture tension in denervated EDL muscle in response to SCh and SMC

The relationship between contracture tension and membrane depolarization was recorded in 36 rats 1–35 days after denervation. Six normal rats were used for control experiments. Membrane depolarization of EDL muscle (Table 3) corresponded with the relative quantities of K^+ efflux (Table 1) during comparable periods of denervation. Measurements of resting membrane potentials (Table 3) showed that after denervation the mean potential progressively declined to −64·6 (s.d. ± 14·6) mV compared with the value recorded in normal EDL muscles, −81·8 (s.d. ± 9·9) mV. The optimum period for the measurement of SCh-induced membrane depolarization and contracture tension was at 7 and 14 days after denervation. Further experiments were carried out to compare the effects of SCh and

Table 2. Comparison of K^+ efflux from denervated rat EDL muscle in response to succinylcholine (SCh) and succinylmonocholine (SMC) at 20 °C. Simultaneous measurements of maximum contracture tension (T_{max}) and K^+ efflux ($mmol\,g^{-1}$) were made in isolated rat EDL muscles in response to SCh ($3{\cdot}0 \times 10^{-5}$ M) or SMC ($3{\cdot}0 \times 10^{-5}$ M) at 19·5 (s.d. ± 1·9) days after denervation (n = 5) and normal contralateral muscles (n = 5). Contracture tension was measured with respect to the baseline tension ($Newtons^{-3}$ ≡ mN). K^+ efflux from denervated muscles was estimated as the extracellular $[K^+]$ in excess of the normal contralateral concentration.

	Duration of denervation days (mean ± ± s.d.)	T_{max} mN (mean ± s.d.)	K^+ efflux $mmol^{-1}$ g^{-1} (mean ± s.d.)	Ratio of T_{max}/ K^+ efflux	EDL muscles n
SMC ($3{\cdot}0 \times 10^{-5}$ M)					
	19·5 ± 1·9	33·74	6·70	5·03	5
	0	–	0·63	–	5
SCh ($3{\cdot}0 \times 10^{-5}$ M)					
	19·5 ± 1·9	32·43	6·59	4·92	5
	0	–	0·44	–	5

Table 3. Comparison of membrane depolarization and contracture tension in normal and denervated rat EDL muscle in response to SCh at 20 °C. Simultaneous measurements of contracture tension and membrane depolarization were made in isolated rat EDL muscle in response to succinylcholine (SCh) 1–35 days after denervation at 20 °C. Denervated muscles were assigned to groups 1–5 according to similarities in maximum contracture tension recorded during 20 min exposure to SCh ($3{\cdot}0 \times 10^{-5}$ M). (Days post denervation ≡ DPD, mean ± s.d.).

Duration of denervation (days mean ± s.d.)	Resting membrane potential (mV mean ± s.d.)	Mean membrane depolarization (mV) Mean contracture tension (mN)	SCh ($3{\cdot}0 \times 10^{-5}$ M) Sample blocks (min) 0–5	5–10	10–15	15–20
	−81·8 ± 9·9	mV	10·6	11·9	12·9	10·6
Normal n = 6		mN	–	–	–	–
3·7 ± 1·2	−71·5 ± 5·3	mV	15·8	14·8	18·8	19·7
Group 1 n = 5		mN	1·2	1·2	1·2	1·5
5·0 ± 2·7	−74·2 ± 8·9	mV	20·1	24·3	32·1	33·1
Group 2 n = 5		mN	5·1	5·9	11·3	13·1
6·3 ± 1·0	−67·8 ± 10·1	mV	28·4	36·2	37·4	38·2
Group 3 n = 9		mN	21·2	2·6	3·3	3·7
20·0 ± 9·7	−65·2 ± 9·6	mV	27·2	34·7	35·9	38·6
Group 4 n = 12		mN	30·5	12·5	8·3	9·7
31·5 ± 4·9	−64·6 ± 14·6	mV	39·4	46·2	45·8	46·4
Group 5 n = 5		mN	55·5	3·1	–	–

SMC on EDL muscles. Membrane depolarization and contracture tension were recorded at 7 and 14 days after denervation (Fig. 3). Records showed that SCh- and SMC-induced contracture tension and membrane depolarization were similar, namely 23 mN cf. 20 mN/17 mV cf. 15 mV, and 32 mN cf. 33 mN/20 mV cf. 19 mV, respectively. Membrane depolarization in normal EDL muscles also corresponded with previous records (Table 3). Results of these experiments showed that SMC acted as a depolarizing agent in normal EDL muscles and that depolarization increased after denervation, therefore the mode of action of SMC was similar to that of SCh.

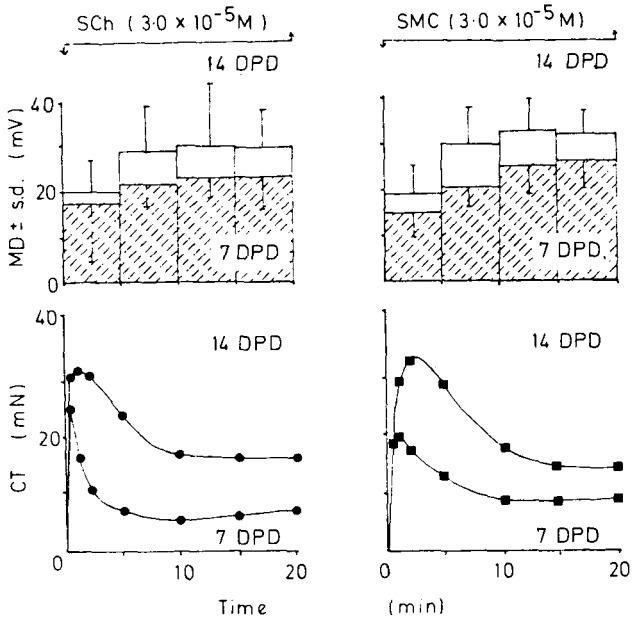

FIG. 3. Comparison of simultaneous measurements of mean membrane depolarization (MD) and mean contracture tension (CT) in isolated rat EDL muscle in response to succinylcholine (SCh) or succinylmonocholine (SMC) at 7 (n = 5), and 14 (n = 4) days after denervation at 20 °C. DPD ≡ days post denervation.

DISCUSSION

Estimation of SCh-induced K^+ efflux from rat EDL muscles recorded in this investigation showed that at 1–7 days after denervation the level was above normal, increased rapidly at 8–14 days, continued to increase up to 50–56 days after denervation, and remained above normal levels even at 147 days after denervation. Results of this investigation showed an increase in K^+ efflux comparable with the increase in serum K^+ recorded in the rat after spinal cord transection during the onset of SCh hypersensitivity by Carter et al (1981).

Previous experimental evidence indicates that there is a species difference in the onset and duration of SCh hypersensitivity following peripheral denervation (Stone et al 1970; John et al 1974; Gronert et al 1973: Gronert & Theye 1975). In the baboon, hyperkalaemia was measured after 4 days following femoral and sciatic nerve section; it reached a peak 8 days later, and subsequently remained constant from then until the end of the period studied at 30 days after denervation (John et al 1974). In the dog the onset of hyperkalaemia was observed at 7 days after sciatic nerve section, reached a peak at 28 days and remained constant until 35 days following denervation, after which it declined (Stone et al 1970). In man, sequential measurements in response to SCh and SMC have not been made because there would be a risk of cardiac arrest (Tobey 1970). However, hyperkalaemia has been reported at 21 days after peripheral nerve injury by Tobey et al (1972), and at 7 days after spinal cord trauma (John et al 1974). If comparisons between rat, dog, baboon and man are acceptable, it would appear that the onset of SCh hypersensitivity is similar and that the development of hyperkalaemia in man may be earlier than previous records indicate (Weintraub et al 1969; Tobey et al 1972; John et al 1974).

The progressive decline in muscle mass measured in this investigation would indicate a loss of intracellular protein, a lower concentration of negative ions and a consequent reduction in $[K^+]_i$ according to the Gibbs-Donnan equilibrium. However an increase in $[K^+]_i$ concomitant with a greater rate of intramuscular protein synthesis has been reported within 48 h after denervation in rat diaphragm muscle by Harris & Manchester (1966). Also Kernan (1965) found that $[K^+]_i$ was 23·5 $mmolL^{-1}$ greater than normal in acutely denervated rat EDL muscle.

A reduction in $[K^+]_i$ or increase in $[Na^+]_i$ was indicated in chronically denervated muscles by the reduction in the resting membrane potential according to the principles identified by Hodgkin & Horowicz (1959) in which the ratio $[K^+]_i/[K^+]_o$ determined the resting potential, when $[K^+]_o$ was greater than 5 mM and the Na^+ pump activity was normal. The decrease in the resting membrane potential measured in this investigation was also observed in rat EDL muscle by Redfern & Thesleff (1971), Kendig et al (1972), and Albuquerque & McIsaac (1970) who considered that the inability of the sodium pump to maintain intracellular sodium ion concentrations at a low level would contribute to a change in the ratio of the potassium ion $[K^+]_i/[K^+]_o$. A change in the properties of the membrane would involve a greater potassium conductance during depolarization, or a greater quantity of depolarization at extrajunctional acetylcholine (ACh) receptor sites. This proposition would be supported by the increase in the duration of the outward current during depolarization in denervated skeletal muscle recorded by Klaus et al (1960) and Thesleff (1963).

Results of this investigation showed that there was significant correlation between K^+ efflux and muscle atrophy ($r = 0·72$) which indicated that the increase in K^+ efflux was concomitant with a progressive increase in muscle atrophy after denervation and that intracellular changes may affect the levels of $[K^+]_i$ available for ionic flux.

This proposition would be supported by the increase in maximum contracture tension, recorded in this study in conjunction with K^+ efflux, on the assumption that SCh-induced contracture tension is present after denervation as a result of the depolarizing action of SCh at many extrajunctional ACh receptor sites in addition to the neuromuscular junction receptors. The time course for the development of SCh hypersensitivity is similar to that established for the proliferation of extrajunctional acetylcholine receptors (Albuquerque & McIsaac 1970). Development of extrajunctional receptors after denervation has been extensively reviewed (Fambrough 1970; Dreyer et al 1976; Fulpius 1976) and the increase in extrajunctional ACh receptors in denervated muscle membrane is well established (Frank et al 1975; Dolly & Barnard 1977).

Comparative records of SCh-induced K^+ efflux from immobilized and denervated canine gastrocnemius muscle, in which 30% weight loss was recorded, showed that immobilized muscle produced a threefold increase in K^+ efflux compared with a twentyfold increase at 24 days after sciatic nerve section (Gronert et al 1973; Gronert & Theye 1974). Results of experiments in that investigation showed that K^+ efflux was ten times greater than normal

from rat EDL muscle at 21·9 (s.d. ± 9·6) days after denervation, in which muscle atrophy was 40%. Variability in the magnitude of the K^+ efflux between the rat and dog may be due to a species difference. The difference between K^+ efflux from immobilized and denervated canine muscle indicates that muscle atrophy causes intracellular changes which alter the response to SCh at the neuromuscular junction in normal immobilized muscle and that after denervation the response is excessive because membrane changes accompany intracellular changes and potentiate SCh hypersensitivity.

Results obtained in the present investigation showed that there was a significant relationship between K^+ efflux and maximum contracture tension produced in response to SCh, and that SCh and SMC produced similar K^+ efflux and contracture tension. Therefore both cholinergic agents were equally potent in the mode of action on denervated rat EDL muscle.

These results indicated that SMC would cause levels of hyperkalaemia similar to those observed clinically after intravenous injection of SCh and it would not be a suitable substitute for SCh after peripheral nerve section. Moreover in this investigation the main actions of SMC and SCh on skeletal muscle membrane in both isolated normal and denervated muscle preparations have been shown to be similar. Both agents have similar actions, namely depolarizing, which further contravenes the clinical use of SMC after peripheral nerve section.

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