# The Neuromuscular Effects of Desflurane, Alone and Combined with Pancuronium or Succinylcholine in Humans

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The neuromuscular effects of desflurane administered alone were studied in ten healthy human volunteers aged 20–27 yr. Also, the dose–response relationships of pancuronium and succinylcholine in surgical patients during anesthesia with desflurane (n = 13) were compared to those during isoflurane anesthesia (n = 14). In the volunteers, we measured the mechanical response of the adductor pollicis muscle to stimulation of the ulnar nerve in a train-of-four (TOF) sequence at 2 Hz and at tetanic frequencies of 50, 100, and 200 Hz, each administered for 5 s. Amplitudes of the first response (T1) in each TOF sequence and the ratios of the fourth TOF response (T4) to the first were similar at 3, 6, and 9% desflurane and decreased significantly only at 12% ($P < 0.05$). Desflurane concentrations of 3–12% caused tetanic fade (>10% decrement in amplitude) at 50, 100, and 200 Hz. The addition of $N_2O$ and the duration of anesthetic exposure did not alter desflurane's neuromuscular effects. The only neuromuscular variable influenced by $CO_2$ was T1 amplitude, which decreased as arterial $CO_2$ tension ($Pa_{CO_2}$) increased. The doses of pancuronium that depressed T1 amplitude by 50% ($ED_{50}$) were similar during anesthesia with 1.25 MAC desflurane, $10.5 \pm 2.8$ μg/kg (mean ± SD) and 1.25 MAC isoflurane, $12.3 \pm 5.0$ μg/kg. The $ED_{50}$ doses of succinylcholine were similar during anesthesia with desflurane $132 \pm 76$ μg/kg and isoflurane $123 \pm 36$ μg/kg. We conclude that desflurane significantly depresses neuromuscular function and augments the action of pancuronium and succinylcholine to a degree similar to that of isoflurane. (Key words: Acid–base equilibrium: acidosis, respiratory; alkalosis, respiratory. Anesthetics, gases: $N_2O$. Anesthetics, volatile: desflurane; isoflurane. Neuromuscular transmission: adductor pollicis twitch response. Pharmacology: dose–response curve.)

DESFLURANE is a new volatile anesthetic derived from isoflurane by the substitution of a fluorine atom for a chlorine atom. Its low blood-gas solubility coefficient, 0.42,[1,2] (MAC 7.25%[3]) suggests that it may offer clinical advantages over other potent inhaled anesthetics, including isoflurane.[4] This clinical potential of desflurane has led us to evaluate its propensity to depress neuromuscular

function. To establish the neuromuscular effects of desflurane alone, we studied the effects of different concentrations of desflurane, the presence of $N_2O$, different end-tidal $CO_2$ tensions ($PET_{CO_2}$), and increasing durations of exposure on neuromuscular function in human volunteers. In addition, in patients undergoing surgery, we compared the dose–response relationships of pancuronium and succinylcholine during anesthesia with desflurane or isoflurane.

## Materials and Methods

### DESFLURANE ALONE UNDER VARYING CONDITIONS IN VOLUNTEERS

Following approval from our Committee for Human Research, we obtained informed consent from 10 male volunteers (ASA Physical Status 1) aged 20–27 yr. No preanesthetic medication was given, and anesthesia was induced by inhalation of increasing concentrations of desflurane in oxygen. Tracheal intubation was performed without the aid of neuromuscular blocking drugs during deep desflurane anesthesia (12–15%, end-tidal). Mechanical ventilation was adjusted to maintain $PET_{CO_2}$ at 35–40 mmHg. Esophageal temperature was maintained between 36.5 and 37 °C throughout the study with a Bair Hugger® (Augustine Medical, Eden Prairie, MN) surface warming device. Concentrations of desflurane, $CO_2$, and $N_2O$ were measured by a Puritan Bennett 254 Airway Gas Monitor modified, by the manufacturer, for desflurane analysis.

Neuromuscular function was assessed by measuring the mechanical evoked response of the adductor pollicis muscle to supramaximal stimuli applied to the ulnar nerve at the wrist, *via* subcutaneous needle electrodes. The stimulation patterns used were train-of-four (TOF) at 2 Hz and tetanus for 5 s at 50, 100, and 200 Hz. During the period of recording, each stimulation sequence was delivered consecutively, at intervals of 15 s. We measured the amplitude of the first response (T1) in each TOF sequence, calculated the ratio of the amplitude of the fourth TOF response in each train to that of the first (TOF ratio), and measured the percentage decrement in the amplitude of each tetanic response over 5 s (tetanic fade).

Each volunteer was studied during several different experimental states during the study period, which lasted several hours. Neuromuscular function was measured during desflurane concentrations of 6, 9, and 12% without

$N_2O$, and at 3, 6, 9, and 12% with $N_2O$. The lower concentrations were administered in random order, and the highest was always administered last. In the first five volunteers, desflurane was administered initially with $N_2O$, which was subsequently discontinued. In the remaining five, desflurane was initially administered without $N_2O$, this being commenced later. Subsequently, neuromuscular function was studied during spontaneous breathing (hypercapnia) at 6, 9, and 12% desflurane and then during mechanical hyperventilation to an $PET_{CO_2}$ of 25 mmHg (hypocapnia) at one of the desflurane concentrations used during hypercapnia. Neuromuscular variables compared at different arterial $CO_2$ tensions ($Pa_{CO_2}$) were matched for desflurane concentration and $N_2O$ status; e.g., results for 9% desflurane plus $N_2O$ during normocapnia were compared with those at 9% desflurane plus $N_2O$ during hypercapnia and hypocapnia. At the conclusion of the study, to rule out time-dependent effects, two of the normocapnic states from the second of the two initial series were repeated. After any change, end-tidal desflurane concentrations were maintained within 0.3% of the targeted value for at least 15 min before measurement of neuromuscular function was made. When moving from one experimental state to another (i.e., any change in desflurane, $N_2O$, or $CO_2$), no nerve stimuli were applied during the interval (minimum 20 min) between experimental states.

The control amplitude for T1 was intended to be that obtained in the awake state. However, none of the volunteers tolerated a supramaximal stimulus while awake. Therefore, control T1 was taken as the amplitude observed at a desflurane concentration of 6%, without $N_2O$, during the initial phase of the experiment. We chose this as the control state because it was the lowest desflurane concentration at which the effect of the addition of $N_2O$ could be studied (at 3% desflurane, $N_2O$ was always administered to ensure an adequate level of anesthesia). The other variables measured (TOF ratio and tetanic fade) do not require control responses.

Values of each neuromuscular variable at different concentrations of desflurane were compared by repeated-measures analysis of variance (ANOVA) with Scheffe's F-test for multiple comparisons. Results obtained for each subject with and without $N_2O$, and early and late in the experiment were compared by paired $t$ test. The magnitude of each variable at the same concentration of desflurane but during hypocapnia, normocapnia, and hypercapnia were compared by repeated-measures ANOVA with Scheffe's F-test for multiple comparisons.

Statistical significance was inferred at $P < 0.05$.

## DESFLURANE WITH PANCURONIUM OR SUCCINYLCHOLINE IN PATIENTS

Our Committee on Human Research gave approval for the study, and 27 adult surgical patients, ASA Physical Status 1 or 2, gave written informed consent. Preanesthetic medication was midazolam 0.02–0.08 mg/kg iv. Anesthesia was induced with sodium thiopental (maximum dose 5 mg/kg iv) $N_2O$ 60–70% (inspired concentration) and gradually increasing concentrations of either desflurane or isoflurane. The assignment of anesthetic vapor to each patient received was made randomly. Tracheal intubation was performed during deep vapor anesthesia, without the aid of neuromuscular blocking drugs or topical anesthesia of the larynx. Mechanical ventilation was commenced and adjusted to maintain $PET_{CO_2}$ at 30–35 mmHg. After induction of anesthesia, $N_2O$ was discontinued, and anesthesia was maintained with 1.25 MAC desflurane (8.5–9.5%)[3] or isoflurane (1.5–1.7%). Gas and vapor concentrations were measured by a Puritan Bennett 254 Airway Gas Monitor modified by the manufacturer to allow desflurane analysis.

To measure neuromuscular responses, subcutaneous needle electrodes were inserted adjacent to the ulnar nerve at the wrist, and supramaximal impulses in a TOF pattern (2 Hz) were delivered at intervals of 12 s. The evoked twitch tension of the adductor pollicis was measured by a mechanical force transducer and recorded on a polygraph. The amplitude of the first twitch response of each train (T1) was allowed to reach a plateau and stabilize. The T1 response immediately preceding the first administration of pancuronium or succinylcholine became the control to which all subsequent T1 responses were compared.

In the pancuronium group, patients received a bolus of 5 μg/kg iv. When the maximal depression of T1 (i.e., three successive responses without further decrease in amplitude) had been obtained, or when 7 min had passed with no decrease of the twitch tension from control, a second bolus of 5 μg/kg was administered. Subsequent doses were administered, in a similar fashion, until T1 depression was >90%. A dose–response curve was constructed by linear regression of the logarithm of the cumulative dose versus the probit transform of the depression of T1 response.

In the succinylcholine group, each patient received, in order, iv boluses of 40, 80, 160, 200, 300, or 400 μg/kg. After administration of each dose, the maximum depression of T1 was recorded and the twitch tension allowed to recover. When the level of recovery had been stable (i.e., no change in T1 amplitude) for 10 min at ±5% of the original baseline, the next dose was administered, and this sequence was continued until the T1 depression exceeded 90%. The dose–response relationship was determined by linear regression of the logarithm of each dose versus the probit transform of the T1 depression which it produced.

The slopes of the dose–response curves and estimated doses producing 50 and 90% depression of T1 ($ED_{50}$ and $ED_{90}$, respectively) obtained during desflurane or isoflu-

TABLE 1. Neuromuscular Responses during Desflurane Anesthesia

| Desflurane Concentration | n | T1 Amplitude (% of control) | TOF Ratio (%) | Fade (%) | | |
|---|---|---|---|---|---|---|
| | | | | 50 Hz | 100 Hz | 200 Hz |
| 3% + N$_2$O | 10 | 101 ± 37 (37–166) | 100 ± 2 (96–103) | 18 ± 12 (0–38) | 26 ± 14 (6–50) | 55 ± 27 (7–96) |
| 6%, no N$_2$O | 10 | 100 (control) | 97 ± 5 (83–102) | 16 ± 12 (3–33) | 36 ± 12 (10–47) | 71 ± 35 (8–96) |
| 6% + N$_2$O | 9 | 111 ± 26 (76–155) | 97 ± 6 (83–100) | 19 ± 13 (7–47) | 33 ± 17 (13–56) | 71 ± 33 (10–100) |
| 9%, no N$_2$O | 9 | 93 ± 17 (58–118) | 95 ± 9 (72–105) | 24 ± 13 (7–43) | 75 ± 10 (58–88) | 96 ± 5 (86–100) |
| 9% + N$_2$O | 10 | 109 ± 41 (38–191) | 96 ± 8 (73–100) | 31 ± 14 (11–48) | 69 ± 22 (19–100) | 78 ± 31 (22–100) |
| 12%, no N$_2$O | 9 | 81 ± 21 (35–104) | 84 ± 11 (65–96) | 60 ± 26 (3–92) | 88 ± 21 (32–100) | 95 ± 14 (59–100) |
| 12% + N$_2$O | 4 | 70 ± 40 (41–127) | 70 ± 36 (17–100) | 57 ± 26 (18–71) | 75 ± 26 (44–100) | 91 ± 9 (79–100) |

Mean ± SD. (Range in parentheses.)

rane anesthesia were compared by Student's *t* test. Statistical significance was inferred at $P < 0.05$.

## Results

### DESFLURANE ALONE UNDER VARYING CONDITIONS

Values for T1 and the TOF ratio were similar at 3, 6, and 9% desflurane and decreased significantly only at 12% (table 1 and fig. 1). All concentrations of desflurane produced significant tetanic fade, >10%, at all three frequencies (table 1 and fig. 2). Values obtained at a given concentration of desflurane with and without N$_2$O did not differ. Therefore, the data for each variable with and without N$_2$O were pooled to generate figures 1 and 2.

The effect of Pa$_{CO_2}$ was studied in only eight volunteers because of technical problems in achieving appropriately

matched states (*i.e.*, matched for desflurane concentration and for the presence or absence of N$_2$O) in two volunteers. T1 amplitude was greater during hypocapnia than during hypercapnia (fig. 3). Changes in Pa$_{CO_2}$ did not affect the other neuromuscular variables studied.

When neuromuscular function during the initial period of the study was compared to that during equivalent experimental states in the final period, no differences were found (*i.e.*, the duration of exposure to desflurane had no effect).

### DESFLURANE WITH PANCURONIUM OR SUCCINYLCHOLINE

Patients receiving desflurane or isoflurane did not differ in age, weight, or gender distribution (table 2). The interval between the induction of anesthesia and adminis-
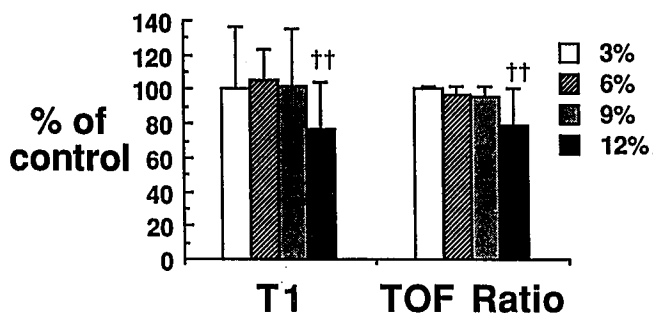


FIG. 1. Train-of-four responses were not depressed except at 12% desflurane. T1 = the amplitude of the first response in each train; TOF ratio = the amplitude of the fourth response divided by that of the first. The control response was the amplitude of the response observed at a desflurane concentration of 6%, without nitrous oxide. Data with and without nitrous oxide are combined. Columns are mean values, and error bars are standard deviations. ††$P < 0.05$: 12% versus 3, 6, and 9%.
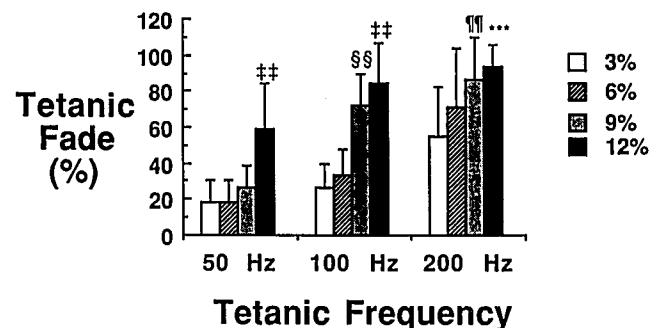


FIG. 2. Tetanic responses were depressed at all concentrations of desflurane, and the magnitude of this depression was increased at greater concentrations and higher frequencies. Fade is the percent decrement in amplitude of the response over 5 s. Data with and without nitrous oxide are combined. Columns are mean values, and error bars are standard deviations. ‡‡$P < 0.05$: 12% versus 3, 6, and 9%. §§$P < 0.05$: 9% versus 3 and 6%. ¶¶$P < 0.05$: 9% versus 3%. ***$P < 0.05$: 12% versus 3 and 6%.
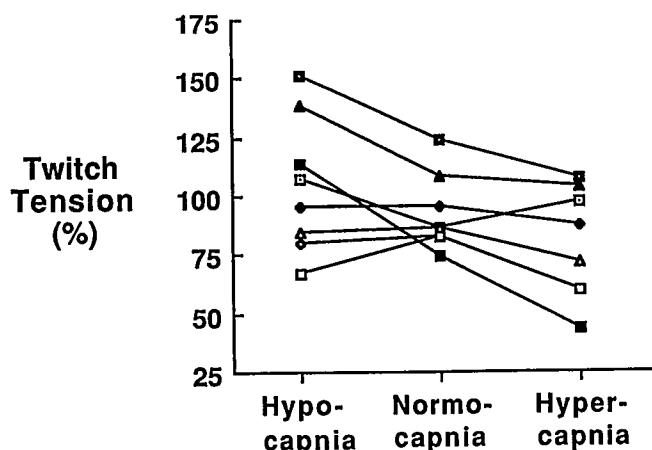
FIG. 3. Twitch tension during hypocapnia ($Pa_{CO_2}$ 24–27 mmHg), normocapnia ($Pa_{CO_2}$ 34–44 mmHg), and hypercapnia ($Pa_{CO_2}$ 42–68 mmHg) for individual volunteers. Twitch tension was significantly greater during hypocapnia than during hypercapnia ($P < 0.05$; repeated-measures ANOVA). The effect of $Pa_{CO_2}$ was studied in only eight volunteers because of technical problems in achieving appropriately matched states (i.e., matched for desflurane concentration and for the presence or absence of nitrous oxide) in two volunteers.

tration of the first dose of neuromuscular blocking drug varied from 24–59 min in the pancuronium group and 34–69 min in the succinylcholine group. In both groups this interval was similar for patients receiving desflurane or isoflurane. When the slopes of the dose–response curves during desflurane and isoflurane were compared, no significant differences were found, either for pancuronium or for succinylcholine (table 3, figs. 4 and 5). The $ED_{50}$ and $ED_{90}$ values for pancuronium obtained during desflurane anesthesia (10.5 ± 2.8 and 22.6 ± 6.9 μg/kg, respectively [mean ± SD]) were not different from those obtained during isoflurane anesthesia (12.3 ± 5.0 and 22.4 = 8.7 μg/kg, respectively). The same was true for the $ED_{50}$ and $ED_{90}$ values for succinylcholine obtained during desflurane (132 ± 76 and 233 ± 100 μg/kg, respectively) and isoflurane (123 ± 36 and 210 ± 78 μg/kg, respectively) anesthesia.

## Discussion

Because of the many experimental states tested in part 1, the duration of the anesthesia was up to 8 h. Throughout this time, in addition to the neuromuscular study, cardiovascular responses to desflurane were investigated. The cardiovascular studies involved insertion of radial and pulmonary artery catheters. Because of the duration of anesthesia and the invasive monitoring employed, we could not justify repeating the study in a second group of volunteers purely to have a control group with a known anesthetic, such as isoflurane. Our results for desflurane, therefore, are compared with those for other volatile anesthetics from earlier studies.

Our results indicate that desflurane depresses neuromuscular function. Desflurane decreased the T1 amplitude only at high concentration, an effect already demonstrated with diethyl ether and enflurane.[5,6] Miller et al. were unable to demonstrate an effect of isoflurane concentration on T1 amplitude.[7] However, they studied isoflurane concentrations of 0.6–1.9%, i.e., of a maximum of only 1.5 MAC. We found a significant decrease in T1 amplitude only at 12%, i.e., at 1.67 MAC.[3] Possibly an effect on T1 amplitude would have become apparent in the study by Miller et al. if they had studied a higher isoflurane concentration. In both their study and ours, neuromuscular responses were measured after end-tidal concentrations of anesthetic had been stable for 15 min. However, the blood/muscle partition coefficient of desflurane is 2.02, and that of isoflurane is 2.92.[2] Therefore, equilibration between muscle and end-tidal concentrations may have been more complete for desflurane than for isoflurane. This might have increased the comparative difference between the muscle partial pressures of anesthetic used in the two studies.

Desflurane caused a decrease in the TOF ratio at a concentration of 12% and dose-dependent fade of the response to tetanic stimulation. Similar effects have been reported for halothane, isoflurane, and enflurane.[6–8] Miller et al.[7] studied tetanic responses in patients during anesthesia with either isoflurane or halothane at 1.25 MAC, a concentration equivalent to the 9% desflurane used in our study. Whereas Miller et al.[7] found no significant fade at 120 Hz in patients receiving halothane and fade in 30% of those receiving isoflurane, we found significant fade (58–88%) in 100% of patients under approximately comparable conditions. Also, Fogdall and Miller reported that in patients receiving enflurane at 1.67 MAC, no fade was apparent at a frequency of 50 Hz.[8] In contrast, we found that 12% (1.67 MAC) desflurane produced fade at 50 Hz in 95% of subjects.

There is no consistent definition of tetanic fade. We defined tetanic fade as a decrement greater than 10% in the amplitude of the response. On our equipment this was equivalent to a decrease of greater than 3 mm. Miller et al.[7] defined significant fade as a decrease in amplitude of greater than 2 mm, although they did not translate this figure into a percentage. Our knowledge of their

TABLE 2. Demographic Data

| Muscle Relaxant | Volatile Anesthetic | n | Gender (M/F) | Age (yr) | Weight (kg) |
|---|---|---|---|---|---|
| Pancuronium | Desflurane | 8 | 6/2 | 36 ± 11 | 72 ± 16 |
| | Isoflurane | 8 | 7/1 | 41 ± 15 | 76 ± 6 |
| Succinylcholine | Desflurane | 5 | 5/0 | 48 ± 19 | 78 ± 15 |
| | Isoflurane | 6 | 5/1 | 37 ± 17 | 79 ± 10 |

Mean ± SD.

TABLE 3. Dose–Response Relationships at 1.25 MAC

| Muscle Relaxant | Volatile Anesthetic | Slope of Probit Response vs. Logarithm of Dose | $ED_{50}$ ($\mu$g/kg) | $ED_{90}$ ($\mu$g/kg) |
|---|---|---|---|---|
| Pancuronium | Desflurane | 4.1 ± 0.9 | 10.5 ± 2.8 | 22.6 ± 6.9 |
| | Isoflurane | 5.0 ± 1.0 | 12.3 ± 5.0 | 22.4 ± 8.7 |
| Succinylcholine | Desflurane | 5.3 ± 1.9 | 132 ± 76 | 233 ± 100 |
| | Isoflurane | 6.1 ± 1.7 | 123 ± 36 | 210 ± 78 |

equipment suggests that the amplitude of a full-scale deflection was between 20 and 30 mm. Therefore, their criterion for tetanic fade would have been a decrement in amplitude of 10% or less. Fogdall and Miller[8] did not define their criterion for fade, but since the study was conducted at the same institution as that of Miller *et al.*,[7] we assume that the criterion for fade was the same in both papers. The lack of a consistent definition of significant fade makes comparisons between studies difficult, but our criterion seems to be at least as stringent as that of Miller *et al.*[7] or Fogdall and Miller.[8] Therefore, we conclude that desflurane is at least as potent as isoflurane, halothane, or enflurane in its ability to induce tetanic fade.

Our purpose in testing tetanic fade at these frequencies was to define the pharmacologic effects of desflurane in a specific experimental setting. Therefore, we cannot draw conclusions as to the clinical implications of these results.

The depression of T1 amplitude and the production of tetanic fade suggest that desflurane has a depressant action on at least two sites in the neuromuscular junction.[9] The effect on T1 is consistent with a postjunctional action.[10,11] The tetanic fade we observed may have been due to an effect on the muscle peripheral to the junction[10]

or to a prejunctional action of desflurane.[9] In a previous study, in patients anesthetized with $N_2O$ and opioids (meperidine or fentanyl), no fade occurred at 50-Hz tetanus,[12] whereas in our subjects, at 50 Hz all concentrations of desflurane produced significant fade. Therefore, we conclude that the tetanic fade observed during desflurane anesthesia was due not simply to nonspecific muscle fatigue secondary to the frequency of stimulation. Rather, our results suggest that desflurane has significant depressant actions at sites in addition to the postjunctional membrane.

The only variable affected by changes in $Pa_{CO_2}$ was T1. Similar findings have been reported during anesthesia with and without halogenated vapor.[13,14] This change in T1 therefore appears to be intrinsic to alterations in $Pa_{CO_2}$ and not due to desflurane. That alterations in $CO_2$ did not affect tetanic responses suggests a postjunctional mechanism.[9] This is consistent with the results of Wirtavouri *et al.*, who found that altering $CO_2$ affects muscle contractility.[15]

For experiments with desflurane alone, at least 80 min elapsed between induction of anesthesia and the point at which we obtained our control measurements; therefore, we did not evaluate early time-dependent changes in neu-
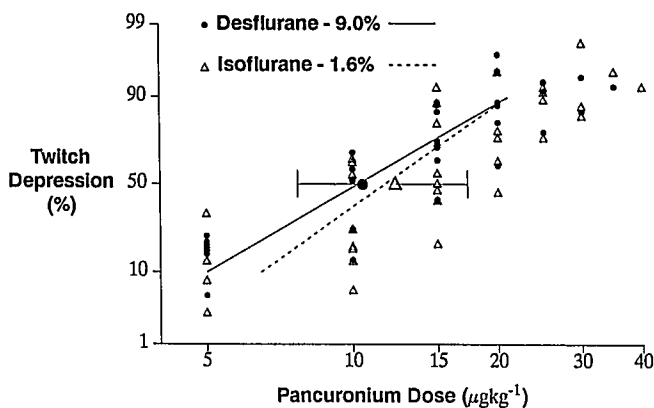


FIG. 4. Logdose–probit plot for pancuronium-induced neuromuscular blockade. Neither the $ED_{50}$ nor the slope of the dose–response relationship differed between desflurane and isoflurane. Points are individual responses for each dose in each patient. Large symbols and error bars represent $ED_{50}$ values (mean and SD, respectively) for that group. Lines are mean slopes for the desflurane 1.25 MAC and isoflurane 1.25 MAC groups.



FIG. 5. Logdose–probit plot for succinylcholine-induced neuromuscular blockade. Neither the $ED_{50}$ nor the slope of the dose–response relationship differed between desflurane and isoflurane. Points are individual responses for each dose in each patient. Large symbols and error bars represent $ED_{50}$ values (mean and SD, respectively) for that group. Lines are mean slopes for the desflurane 1.25 MAC and isoflurane 1.25 MAC groups.
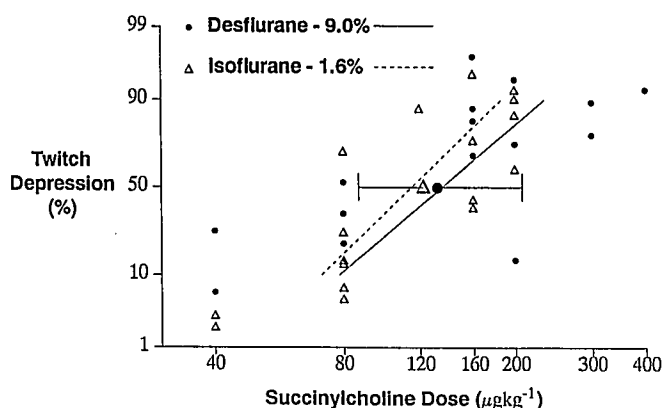
romuscular function. The initial and final measurements of neuromuscular function were separated by an interval of between 2 and 4 h. No neuromuscular variable changed over this time. Similarly, in previous studies, the duration of exposure to isoflurane or halothane did not affect T1 response.[16,17] However, the T1 response is the least sensitive measure of neuromuscular function. Our results show that the more sensitive indices of neuromuscular function—the TOF ratio and tetanic fade—also do not change. Although we cannot anticipate the results of longer exposure, the neuromuscular effects of desflurane do not appear to change over a time period equivalent to the duration of most surgical procedures.

For experiments with desflurane and a neuromuscular relaxant, we had to decide whether the anesthesia in the control group should be $N_2O$–narcotic or $N_2O$–isoflurane. Use of a $N_2O$–narcotic control group would have allowed us to determine whether desflurane augmented neuromuscular blockade relative to an opioid anesthetic, and if so, by how much. However, this approach would have left unanswered the important question of whether such augmentation was greater or less than that with other volatile anesthetics under similar circumstances. By using isoflurane in the control group we could define the neuromuscular effects of desflurane in relation to of those of a familiar and widely used anesthetic for which a considerable body of knowledge already exists.

The dose–response relationship of pancuronium during desflurane anesthesia did not differ from that during isoflurane anesthesia. Therefore, it is reasonable to assume that desflurane augments pancuronium-induced neuromuscular blockade in a manner similar to the augmentation caused by isoflurane. This can be illustrated by comparing our results with those determined in previous studies during anesthesia without a volatile anesthetic: the $ED_{50}$ of pancuronium during $N_2O$–fentanyl anesthesia was 32 $\mu g/kg$[18] and during droperidol–fentanyl–piritramide anesthesia, 41 $\mu g/kg$.[19] These are three to four times the value, 10.5 $\mu g/kg$, we determined. This difference is consistent with that found by other investigators for comparisons of volatile versus nonvolatile anesthetics. Our low $ED_{50}$ values are similar to those found by others workers studying anesthesia with a volatile agent.[8,20] Miller et al. derived an $ED_{50}$ for pancuronium of 0.27 $mg/m^2$ during 1.25 MAC isoflurane.[20] Assuming an average body surface area of 1.7 $m^2$ and body weight of 65 kg in their subjects, this $ED_{50}$ converts to 7.1 $\mu g/kg$. By a similar conversion, the $ED_{50}$ for pancuronium during 1.25 MAC enflurane was 7.6 $\mu g/kg$.[8]

We did not study patients who had anesthesia without receiving a volatile anesthetic. However, by examining evidence from earlier studies we may infer that desflurane augments succinylcholine neuromuscular blockade. Two studies by Smith et al. showed that halothane augments

succinylcholine-induced neuromuscular blockade.[21,22] Using the single-dose technique they found that the $ED_{50}$ for succinylcholine was significantly less (0.12 mg/kg) during anesthesia with 0.2–0.4% halothane[21] than during $N_2O$–fentanyl anesthesia (0.19 mg/kg).[22] In addition, Miller et al. have demonstrated that the effect of isoflurane on succinylcholine neuromuscular blockade is even more potent than that of halothane.[20] They found that the $ED_{50}$ of succinylcholine during halothane anesthesia was 1.5 times that during isoflurane anesthesia.[20] Therefore, because the dose–response relationship for succinylcholine with desflurane is similar to that with isoflurane, we can conclude that desflurane augments succinylcholine-induced neuromuscular blockade.

There are several problems associated with constructing dose–response curves for succinylcholine. The single-dose technique is ideal, but it requires a large number of patients, and the results from those who do not respond or who exhibit 100% neuromuscular blockade are difficult to interpret. Cumulative-dose techniques are more efficient but may underestimate the potency of drugs with rapid elimination.[22–24] We administered several doses of succinylcholine to each patient, in a manner similar to that described by Fogdall and Miller[8] and Miller et al.[20] With this technique, each dose of succinylcholine may have influenced the response to subsequent doses. However, because the succinylcholine dosing regimen was consistent throughout the study, and the volatile agent was chosen randomly, any interaction between successive succinylcholine doses would have been similar for both anesthetics. We cannot rule out time-dependent effects of the anesthetic over the period of succinylcholine administration, but we believe that such effects, if any exist, are likely to be minimal. In experiments with desflurane alone we found that over a period of 2–4 h there was no change in the neuromuscular effects of desflurane. Similarly, the neuromuscular effects of isoflurane do not change over time for periods of up to 4 h.[16] Since all of our succinylcholine dose–response studies were completed within 2 h, we consider that our comparison of the results obtained with desflurane and isoflurane is valid.

In conclusion, desflurane, administered in the absence of neuromuscular-blocking drugs, significantly depresses neuromuscular function. In addition, in a manner comparable to that of isoflurane, desflurane significantly augments the action of pancuronium and that of succinylcholine as well.

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