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Self-learning fuzzy logic control of neuromuscular block

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Summary

We have assessed the performance of a "self-learning" fuzzy logic controller to administer atracurium to a required depth of neuromuscular block. We studied 20 ASA I and II patients undergoing surgery anticipated to last longer than 90 min. A Datex Relaxograph was used to measure the degree of neuromuscular block, and control to a T1 twitch height set point of 10% of baseline neuromuscular function was selected. The controller commenced with a blank rule-base and instructed a Graseby 3400 infusion pump to administer an atracurium infusion to maintain this level of block. The system achieved stable control of neuromuscular block with a mean T1 error of −0.52% (SD 0.55%) accommodating a range in mean atracurium infusion rate of 0.25–0.44 mg kg^{-1} h^{-1}. These results compare favourably with the more computationally intensive and unwieldy adaptive control strategies for atracurium infusion used previously. There was less variation in infusion rates than in our previously studied fixed rules fuzzy controller. (*Br. J. Anaesth.* 1997; **78**: 412–415).

Key words
Neuromuscular block, atracurium. Computers, fuzzy logic.

Provision of reliable neuromuscular block is an important part of modern anaesthetic practice. Newer agents provide rapid onset of dense yet short-acting block providing good conditions for surgery. However, these agents require careful monitoring to reduce the incidence of clinically significant fluctuations in the density of block, and allow rapid offset at the end of surgery. In longer operations multiple incremental doses of neuromuscular blocking agents may be required. Neuromuscular block therefore lends itself to control by continuous drug infusion, but pharmacokinetic and pharmacodynamic differences between patients makes selection of an appropriate infusion rate to maintain the desired level of block difficult.[1]

Closed-loop control provides the ability to maintain stable neuromuscular block while allowing for variation in the individual's response to the drug. This benefits the patient in that the minimum quantity of drug is administered and the clinical workload is reduced, allowing more time to be spent on other aspects of anaesthesia. The reliability of neuromuscular block monitoring with electromyography permits a precise control strategy to be implemented. Various controllers have been demonstrated in the past, from simple on–off type to complex model-based controllers.[2–11] We have demonstrated previously the use of fuzzy logic in the control of neuromuscular block with a fixed rule-base. While this controller provided accurate control of neuromuscular block, we noted considerable variation in blocker infusion rate.[12 13] In addition, such a controller is not adaptive and it is difficult to deduce a general fixed rule to accommodate individual variations between patients. These problems may be overcome by adding a self-learning facility to the controller. Such a controller has been demonstrated previously only in computer simulation.[14 15] This is the first study investigating the clinical use of self-learning fuzzy logic control.

Patients and methods

The study was approved by the local Ethics Committee and 20 adult ASA I or II patients undergoing surgery anticipated to last longer than 90 min gave written informed consent.

The closed-loop system comprised a general purpose IBM compatible computer (PC) interfaced to a Datex Relaxograph and a Graseby Medical 3400 infusion pump. The PC was programmed to use the "self-learning" fuzzy logic control strategy and coordinate communication via serial links. The system was tested actively by computer simulation in "worst-case" and "noisy-signal" scenarios, and a further check on the adequacy of patient response was implemented to eliminate the possibility of erroneous controller outputs arising should the patient not receive atracurium, for example the infusion catheter became blocked or disconnected. A hierarchical alarm structure was used to deal with alarm conditions appropriately. System hardware and software integrity were tested in real-time using a simulation device attached to the Relaxograph.[16]

Patients received a standard anaesthetic. Anaesthesia was induced with alfentanil 10 μg kg^{-1} and a sleep dose of propofol, followed by an infusion of 10 mg kg^{-1} h^{-1}. The patient's lungs were ventilated

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manually with 67% nitrous oxide in oxygen while the automated atracurium delivery system was set up. One arm was placed supine on an extension board and secured with tape. MSB unilect silver–silver chloride electrodes were placed on skin previously cleansed with alcohol solution. The two stimulating electrodes were placed over the ulnar nerve distribution in the forearm, the recording electrodes were placed one on the hypothenar eminence and one at the base of the fifth metacarpal, and the ground electrode was placed on the radial side of the forearm at the wrist. The Relaxograph was then calibrated and set to deliver a train-of-four supramaximal stimulus every 20 s. The Relaxograph was observed for at least 3 min before neuromuscular block was commenced to ensure a stable baseline. We used the first response to train-of-four (T1) as the end-point for monitoring and control. A T1 set point at 10% of baseline was chosen. A filename was entered for data storage and the concentration of atracurium (2 mg ml^{-1}) entered so that the computer could convert the controller output from a mass rate to a flow rate, that is ml h^{-1}. The patient's weight was entered to enable the loading dose of 0.33 mg kg^{-1} to be calculated, which it then delivered at 1200 ml h^{-1} to facilitate tracheal intubation. Anaesthesia was maintained with propofol 8–10 mg kg^{-1} h^{-1}, the patient's lungs ventilated mechanically with oxygen and nitrous oxide, and morphine was administered as appropriate. The fuzzy logic controller maintained neuromuscular block throughout. Recovery of T1 was monitored every 20 s, giving an indication of patient sensitivity to the drug, allowing the controller to create its first control rule. Thus, for instance, if recovery was rapid, a high initial infusion rate was selected as T1 approached 10%, to a maximum rate of 100 mg h^{-1}. If T1 failed to decrease below the 10% set point, the computer was programmed to deliver an additional 5-mg bolus and repeat as necessary until T1 was less than 10%. The fuzzy controller commenced operation when T1 had recovered to between 5% and 10%. To reduce spurious data from noisy signals the median of the previous three readings was used. This median T1 value, calculated each 60 s, was then used for action by the controller. In addition, the supervising anaesthetist could administer an atracurium bolus should neuromuscular block be inadequate, alter the T1 set point or quit the programme as required.

The performance of the fuzzy controller was analysed by raw T1 values. T1 errors (measured T1 value–the set point T1 value) were analysed for mean and root mean square deviation (RMSD) for the entire duration of control. In addition, these values were determined for the initial 30 min of control to allow comparison with our previous controller[12]. Mean (SD) atracurium infusion rates delivered every 1 min during control in each individual case were also calculated and then summarized for all 20 patients as mean (SD) and range.

Results

We studied 20 patients, mean age 43 (range 25–73) yr and mean weight 67 (48–85) kg. Mean duration of control was 75 (46–143) min. Tables 1 and 2 show the control performance indices for both total duration of control and for the first 30 min of control. The mean T1 error from set point was −0.52% (SD 0.55%; range −1.94 to +0.37%) for the total duration of control, and −0.74% (0.73%; −1.80 to +0.90%) for the first 30 min of control. The variation about this mean was low, with a mean SD of 2.3% (0.62%; 1.00−3.61%) for the total duration of

Table 1 Control performance indices for the total duration of control

Patient No.	Duration of control (min)	Error from set point (%)			Atracurium infusion rate (mg kg^{-1} h^{-1})	
		Mean	SD	RMSD	Mean	SD
1	53	−0.45	1.00	1.10	0.25	0.11
2	56	0.28	2.99	3.00	0.32	0.15
3	79	0.37	1.67	1.71	0.36	0.10
4	61	−0.43	1.46	1.52	0.36	0.04
5	86	−0.46	2.37	2.42	0.29	0.17
6	64	−0.97	1.97	2.20	0.35	0.23
7	76	−0.21	3.61	3.62	0.31	0.14
8	112	−0.36	3.14	3.16	0.31	0.13
9	57	−0.08	2.13	1.87	0.36	0.16
10	134	−0.48	2.22	2.27	0.38	0.22
11	143	0.33	1.97	2.00	0.27	0.08
12	65	−0.82	1.90	2.07	0.30	0.12
13	36	−1.24	2.35	2.65	0.28	0.10
14	53	−0.34	2.20	2.23	0.32	0.08
15	39	−1.04	2.60	2.80	0.42	0.22
16	63	−0.52	1.91	1.98	0.44	0.12
17	65	−0.50	2.15	2.21	0.30	0.12
18	112	−1.94	3.15	3.69	0.35	0.32
19	63	−0.47	2.49	2.53	0.38	0.15
20	86	−0.97	2.62	2.80	0.35	0.13
Mean	75.15	−0.52	2.30	2.39	0.34	0.14
SD	29.36	0.55	0.62	0.66	0.05	0.06
Range	36–143	−1.94–0.37	1.00–3.61	1.10–3.69	0.25–0.44	0.04–0.32

Table 2 Control performance indices for the first 30 min of control

Patient No.	Error from set point (%)			Atracurium infusion rate (mg kg^{-1} h^{-1})	
	Mean	SD	RMSD	Mean	SD
1	−0.67	1.23	1.40	0.27	0.14
2	−1.49	3.11	3.45	0.33	0.21
3	0.89	2.20	2.38	0.38	0.13
4	−1.05	1.75	2.04	0.37	0.04
5	0.14	2.76	2.76	0.29	0.15
6	−1.29	2.26	2.60	0.37	0.24
7	−0.51	2.36	2.41	0.41	0.10
8	−1.38	2.83	3.15	0.38	0.12
9	−0.36	2.35	1.83	0.35	0.18
10	−0.66	2.80	2.88	0.48	0.22
11	0.63	2.59	2.67	0.24	0.11
12	−1.59	1.79	2.39	0.32	0.14
13	−0.78	2.27	2.40	0.30	0.10
14	−0.67	2.24	2.33	0.31	0.10
15	−1.73	2.47	3.00	0.42	0.22
16	−1.75	1.90	2.57	0.46	0.15
17	−0.28	2.61	2.62	0.31	0.16
18	−0.70	5.02	5.07	0.44	0.44
19	−0.44	2.78	2.81	0.39	0.17
20	−1.04	2.89	3.04	0.30	0.08
Mean	−0.74	2.51	2.69	0.36	0.16
SD	0.73	0.75	0.73	0.07	0.08
Range	−1.80–0.90	1.20–5.0	1.40–5.10	0.27–0.48	0.04–0.44

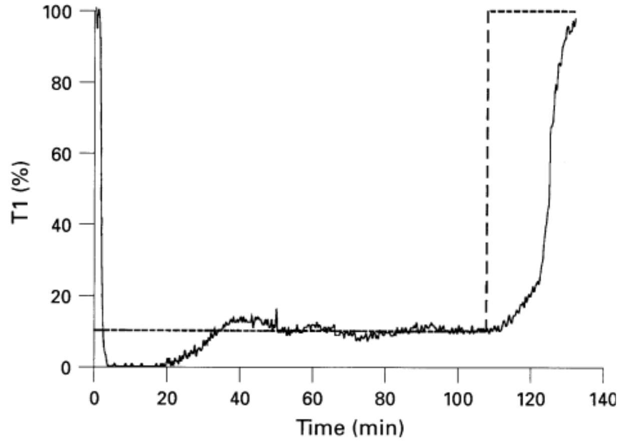

Figure 1 Sample clinical trace obtained with self-learning fuzzy controller showing stable neuromuscular block at the 10% level over 75 min. ------ = Desired T1 value, ——— = raw T1 values.

control and 2.51% (0.75%; 1.20–5.00%) for the first 30 min. Mean RMSD values were similar to the mean SD, being 2.39% (0.66%; 1.10–3.69%) for the total duration of control, and 2.69% (0.73%; 1.40–5.10%) for the first 30 min, confirming that mean error was close to zero. Figure 1 shows a sample clinical trace.

Mean atracurium requirements varied from 0.25 to 0.44 mg kg^{-1} h^{-1} for the total duration of control and from 0.27 to 0.48 mg kg^{-1} h^{-1} for the first 30 min. The SD of the infusion rates of atracurium delivered over the period of control gives an indication of the variation in infusion rate for that period in each patient. The mean SD atracurium infusion rate was 0.14 mg kg^{-1} h^{-1} for the total duration of control and 0.16 mg kg^{-1} h^{-1} for the first 30 min. In all cases good operating conditions prevailed throughout and all neuromuscular block was antagonized easily at the end of surgery. No patient required a bolus dose of atracurium to maintain adequate neuromuscular block.

Discussion

Fuzzy logic is an appropriate, simple and effective technique for controlling non-linear and unpredictable processes, dealing in imprecise, qualitative (i.e. "fuzzy") terms such as "low", "medium" or "high" rather than precise measurements.[17 18] This imprecision permits very simple but effective control rules to be generated which are easy to modify and update rapidly in real-time. Fuzzy logic control is intrinsically suited to the control of physiological processes because it requires little hard input data before it can begin functioning, unlike other strategies such as "neural networks".

For closed-loop control of neuromuscular block the following features need to be addressed when designing the system: recognition of the onset and, more importantly, the rate of decay of neuromuscular block; recognition of the difference between desired and actual T1 value (error); recognition of the rate of change in error from the desired T1 value; and elimination of drift from the desired T1 value when achieved, that is steady state error.

Using a fixed rule-base, we have demonstrated previously that fuzzy logic control is appropriate for controlling neuromuscular block.[12] However, the development of such a controller required the construction of a hand-crafted rule-base which was time and labour intensive. However, by incorporating a "self-learning" layer to the fuzzy controller, it becomes self-teaching in real-time in the clinical situation and dispensed with the need for a pre-set fixed rule-base. Our self-learning controller starts with a blank rule-base, and this is the first study to investigate the clinical application of such an intelligent control technique.

The "self-learning" strategy implemented in our controller functioned by rapidly and repeatedly measuring T1 twitch height and modifying the atracurium infusion rate. This allowed the controller to recognize the patient's drug requirements and select infusion rates appropriate to maintain 90% neuromuscular block. Initially, the fuzzy rule-base is completely blank as the controller is unaware of its first rule until control begins. This first rule is simple and generated by assessing the return of neuromuscular tone towards the desired T1 height. The effect is then assessed and adapted by generating new rules as control continues. This is achieved by adding a performance index which measures the error from a desired trajectory and modifies recently generated control rules so making the controller self-learning. In addition an ageing process was added to the rules generated so that those recently generated carried more weight, or were considered "more relevant" than older rules. This helps eliminate steady state error and continually improves controller performance.

While fuzzy logic has been used in other fields in anaesthesia[17–19] this is the first occasion where, by application of a self-learning facility to the fuzzy logic controller, a physiological process during anaesthesia has been controlled entirely by machine alone. The controller determined individual drug requirements and administered atracurium accurately in each case, demonstrating the ability to assess and respond to fluctuating patient conditions during surgery. The success of this self-learning control system should encourage research into the control of other physiological processes.

The results of this study showed improved performance over previous controllers. Control was as good as our previous fixed-rule controller with less erratic infusion rates being demanded; the controller delivered a mean SD atracurium infusion rate of 0.16 mg kg^{-1} h^{-1} for the first 30 min compared with 0.23 mg kg^{-1} h^{-1} in our previous study.[12] Control was implemented with a basic amount of information. At no point did the controller have to administer a bolus in order to regain control of a deteriorating situation and in no case was a diverging or progressively unstable oscillation entered.

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References

1. Beemer GH. Continuous infusion of muscle relaxants—why and how. *Anaesthesia and Intensive Care* 1987; **15**: 83–89.
2. Bradlow HS, Uys PC, Rametti LB, On-line control of atracurium induced muscle relaxation. *Journal of Biomedical Engineering* 1986; **8**: 72–75.
3. Webster NR, Cohen AT. Closed-loop administration of atracurium: steady-state neuromuscular blockade during surgery using a computer controlled closed-loop atracurium infusion. *Anaesthesia* 1987; **42**: 1085–1091.
4. Wait CM, Goat VA, Blogg CE. Feedback control of neuromuscular blockade: a simple system for infusion of atracurium. *Anaesthesia* 1987; **42**: 1212–1217.
5. Uys PC, Morrell DF, Bradlow HS, Rametti LB. Self-tuning, microprocessor-based closed-loop control of atracurium-induced neuromuscular blockade. *British Journal of Anaesthesia* 1988; **61**: 685–692.
6. MacLeod AD, Asbury AJ, Gray WM, Linkens DA. Automatic control of neuromuscular block with atracurium. *British Journal of Anaesthesia* 1989; **63**: 31–35.
7. Denai M, Linkens DA, Asbury AJ, MacLeod AD, Gray WM. Self-tuning PID control of atracurium-induced muscle relaxation in surgical patients. *IEEE Proceedings* 1990; **137**: 261–272.
8. O'Hara DA, Derbyshire GJ, Overdyk FJ, Bogen DK, Marshall BE. Closed-loop infusion of atracurium with four different anesthetic techniques. *Anesthesiology* 1991; **74**: 258–263.
9. Schwilden H, Olkkola KT. Use of a pharmacokinetic–dynamic model for the automatic feedback control of atracurium. *European Journal of Pharmacology* 1991; **40**: 293–296.
10. Mahfouf M, Linkens DA, Asbury AJ, Gray WM, Peacock JE. Generalised predictive control (GPC) in the operating-theatre. *IEEE Proceedings* 1992; **139**: 404–420.
11. Assef SJ, Lennon RL, Jones KA, Burke MJ, Behrens TL. A versatile, computer-controlled, closed-loop system for continuous infusion of muscle relaxant. *Mayo Clinic Proceedings* 1993; **68**: 1074–1080.
12. Mason DG, Edwards ND, Linkens DA, Reilly CS. Performance assessment of a fuzzy controlled for atracurium-induced neuromuscular block. *British Journal of Anaesthesia* 1996; **76**: 396–400.
13. Mason DG, Linkens DA, Edwards ND, Reilly CS. Automated delivery of muscle relaxants Using fuzzy-logic control. *IEEE Engineering in Medicine and Biology* 1994; **13**: 678–686.
14. Linkens DA, Hasnain SB. Self-organizing fuzzy logic control and application to muscle relaxant anaesthesia. *IEEE Proceedings* 1991; **138**: 274–284.
15. Linkens DA, Mahfouf M, Abbod M. Self-adaptive and self-organizing control applied to nonlinear multivariable anaesthesia: A comparative model-based study. *IEEE Proceedings* 1992; **139**: 381–394.
16. Mason DG, Linkens DA, Edwards ND, Reilly CS. Development of a portable closed-loop atracurium infusion system: Systems methodology and safety issues. *International Monitoring and Computing* (in press).
17. Asbury AJ, Tzabar Y. Fuzzy logic: new ways of thinking for anaesthesia. *British Journal of Anaesthesia* 1995; **75**: 1–2.
18. Martin JF. Fuzzy control in anaesthesia. *Journal of Clinical Monitoring* 1994; **10**: 77–80.
19. Schaublin J, Derighetti M, Feigenwinter P, Petersen-Felix S, Zbindeh AM. Fuzzy logic control of mechanical ventilation during anaesthesia. *British Journal of Anaesthesia* 1996; 77: 636–641.