The Best Choice of Double Burst Stimulation Pattern for Manual Evaluation of Neuromuscular Transmission

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In clinical anesthesia, the degree of neuromuscular blockade should be quantitatively evaluated by mechanical myography (MMG) or electromyography (EMG). Only in a very few departments, however is the neuromuscular function routinely evaluated by such equipment because of economical reasons and difficulty of handling. To establish a simple method of monitoring neuromuscular function during anesthesia, we have been studying how to evaluate the degree of neuromuscular blockade by using only a nerve stimulator.

Previously, Viby-Mogensen and his colleagues showed that the "period of no response to twitch and TOF stimulation" and "surgical relaxation" simply by feeling the posttetanic twitch response (posttetanic count) or the number of responses to the TOF stimulation[1,2]. However, when there was a reaction to all four stimuli on TOF stimulation (recovery phase), especially when the TOF ratio exceeds 0.4, it was extremely difficult to detect the fade[3]. To overcome this difficulty, "double burst stimulation (DBS)" was applied to manual evaluation of neuromuscular transmission[4]. This DBS consists of two very short bursts that are separated by 750 msec. Each burst consists of three supramaximal stimulation, which are separated by an interval of 20 msec. (fig. 1). Our preliminary study revealed that DBS was a little more painful than TOF stimulation but much less than tetanic stimulation (50 Hz, 5 sec.) in the awake volunteers. When DBS was applied during the recovery phase, two evoked responses were observed. The previous pattern of DBS was called "double burst three three ($DBS_{3.3}$)", and the results of clinical study were that, the $DBS_{3.3}$ was significantly better than the TOF stimulation when the TOF ratio was below 0.8[4,5]. In other words, it was easier to detect the fade by using the $DBS_{3.3}$ than with TOF stimulation. However, we were interested in whether or not the adequate recovery from neuromuscular blockade in the end of anesthesia could be determined manually or tactilely. Considering that a TOF ratio of about 0.75 is regarded as reflection of clinically adequate recovery, although the $DBS_{3.3}$ was statistically superior to the TOF stimulation, the result does not match the clinical needs. Because, even the $DBS_{3.3}$ was applied, the investigator could detect the fade in the DBS responses in a very few trials when the TOF ratio was between 0.6 and 0.7[5]. Consequently, we investigated whether, by changing the stimulation pattern in the

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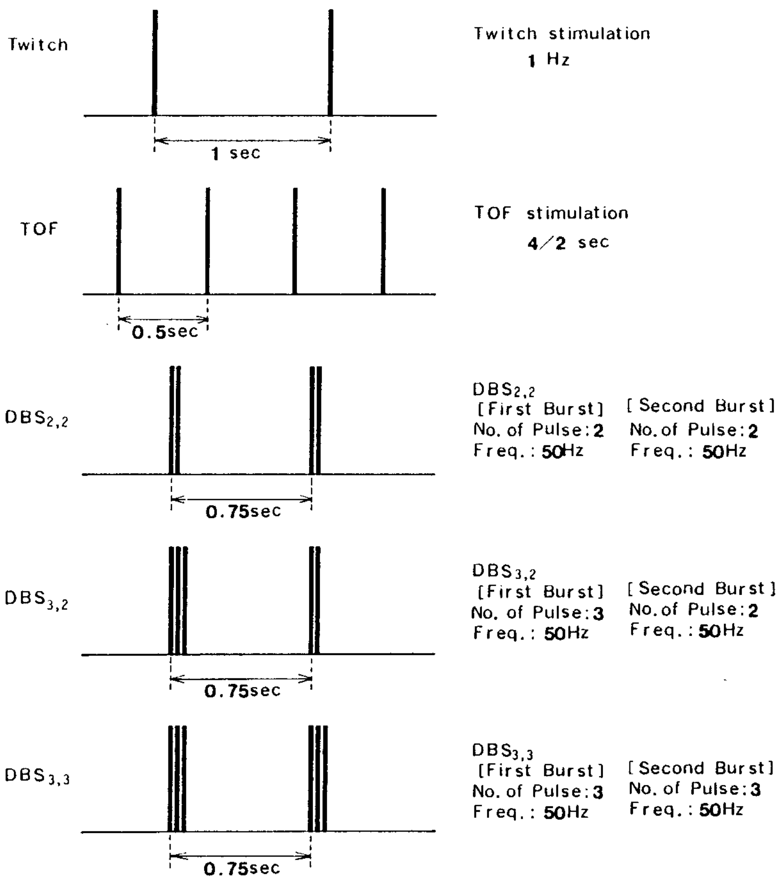

Fig. 1. Illustration of each stimulation pattern twitch, TOF, $DBS_{2.2}$, $DBS_{3.2}$ and $DBS_{3.3}$. A Double Burst Stimulation (DBS) consists of two very short bursts, each separated by 750 msec. Each burst consists of two or three supramaximal stimulation (SS), each separated by an interval of 20 msec (i.e. 50 Hz).

DBS, it is possible to manually evaluate the neuromuscular function, when the TOF ratio climbs above 0.6 with reasonable certainty.

Materials and Methods

Fifty adult patients (ASA: class 1–2, Age: 42 ± 11.3 years, BW: 57.8 ± 9.1 kg) undergoing gastroenterologic operation were studied. No patient had neuromuscular disease nor recieved any drugs that would alter neuromuscular function. One hour after giving 0.01 mg/kg atropine (i.m.), anesthesia was induced with 3–5 mg/kg thiopental (i.v.) and maintained with enflurane 1.5–2.0% inspired concentration with 50% nitrous oxide in oxygen. Tracheal intubation was carried out following intravenous administration of 1.0 mg/kg succinylcholine. For further paralysis, pancuronium (0.1 mg/kg, i.v.) was used. Following induction of anesthesia, the ulnar nerve was stimulated at the wrist through percutaneous electrodes connected to a nerve stimulator (MyotestDBS®) of the Myograph 2000®(mechanical myograph, Biometer International). This nerve stimulator can supply twitch, tetanic, TOF and DBS. To evaluate the degree of relaxation, the adduction force of the resultant thumb twitch was measured with the force transducer and recorded on a polygraph. Temporarily removing the

Table 1. Comparison of the palpability of fade between the evoked $DBS_{2.2}$ and $DBS_{3.3}$ responses. When TOF ratio was between 0.51 and 0.6, the $DBS_{3.3}$ method was significantly better than the $DBS_{2.2}$. However, in the other range of the TOF ratio, there was no significant difference between the two method.

True TOF ratio	$DBS_{2.2}$		$DBS_{3.3}$		
	n fade/total	% fade	n fade/total	% fade	
≧ 0.40	48/48	100	48/48	100	n.s.
0.41 ~ 0.50	47/49	95.9	49/49	100	n.s.
0.51 ~ 0.60	32/47	68.1	38/47	80.9	*
0.61 ~ 0.70	12/47	25.5	16/47	34.0	n.s.
0.71 ~ 0.80	1/48	2.1	5/48	10.4	n.s.
0.81 ~ 0.90	0/47	0	0/47	0	n.s.
0.91 >	0/44	0	0/43	0	n.s.

* P <0.05 n.s. = not significant

Table 2. Comparison of the palpability of fade between the evoked $DBS_{3.3}$ and $DBS_{3.2}$ responses. The $DBS_{3.2}$ is shown to be significantly better than the $DBS_{3.3}$ when the TOF ratio is between 0.51 and 0.8.

True TOF ratio	$DBS_{3.3}$		$DBS_{3.2}$		
	n fade/total	% fade	n fade/total	% fade	
≧ 0.40	48/48	100	48/48	100	n.s.
0.41 ~ 0.50	49/49	100	47/47	100	n.s.
0.51 ~ 0.60	38/47	80.9	47/47	·100	*
0.61 ~ 0.70	16/47	34.0	42/47	89.4	*
0.71 ~ 0.80	5/48	10.4	29/46	63.0	*
0.81 ~ 0.90	0/47	0	3/47	6.4	n.s.
0.91 >	0/43	0	0/44	0	n.s.

* P <0.05 n.s. = not significant

transducer from the patient's thumb, the observer evaluated tactilely the response to nerve stimulation. The observer's task was to determine whether or not he felt the fade in $DBS_{2.2}$, $DBS_{3.2}$, or $DBS_{3.3}$ responses in random order. The TOF ratio for each trial was recorded. In order to compare the DBS response ratio with the TOF ratio, the response to $DBS_{2.2}$, $DBS_{3.2}$, $DBS_{3.3}$, and TOF response were recorded mechanically. The ratios of responses to DBS were calculated in the ranging of TOF ratio from 0.2 to 0.9. The DBS ratio compares the height of the second response to that of the first. The average values (mean ± SD) of DBS response were also calculated in the 20 patients. The chi-square test was applied for statistical comparison.

Results

$DBS_{2.2}$ was applied to a total of 330 times, $DBS_{3.2}$ was carried out in 326 times, and $DBS_{3.3}$ 329 times at different TOF ratios. The results of these investigations on three DBS patterns are compared in table 1 ($DBS_{2.2}$ vs $DBS_{3.3}$) and table 2 ($DBS_{3.3}$

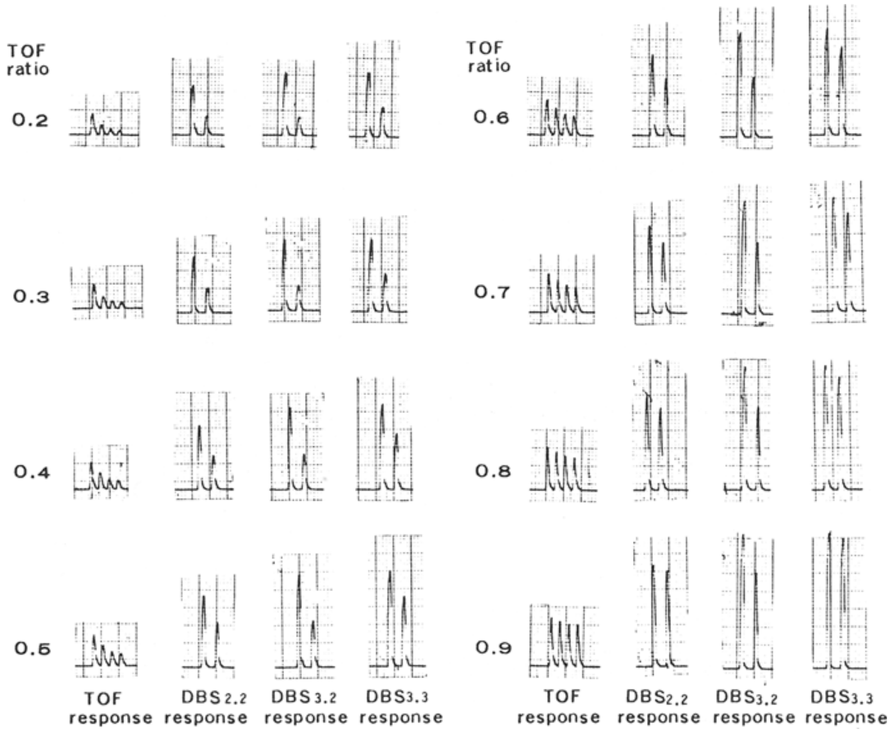

Fig. 2. Illustration of the evoked responses to TOF, $DBS_{2.2}$, $DBS_{3.2}$ and $DBS_{3.3}$. The degree of fade in $DBS_{3.2}$ responses are larger than in the $DBS_{2.2}$ and $DBS_{3.3}$ responses.

Table 3. Comparison of the ratios of response to $DBS_{3.3}$, $DBS_{2.2}$ and DBS3.2 measured mechanically in the TOF ratios ranging from 0.2 to 0.9

TOF ratio	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
$DBS_{3.3}$ (±SD)	0.36 (±0.056)	0.40 (±0.056)	0.51 (±0.043)	0.62 (±0.06)	0.70 (±0.054)	0.79 (±0.05)	0.89 (±0.029)	0.96 (±0.016)
$DBS_{2.2}$ (±SD)	0.31 (±0.045)	0.39 (±0.048)	0.48 (±0.043)	0.60 (±0.043)	0.68 (±0.042)	0.68 (±0.04)	0.88 (±0.026)	0.94 (±0.012)
$DBS_{3.2}$ (±SD)	0.23 (±0.03)	0.29 (±0.035)	0.36 (±0.04)	0.44 (±0.036)	0.52 (±0.042)	0.60 (±0.045)	0.70 (±0.033)	0.73 (±0.02)

n = 20

vs $DBS_{3.2}$). There are two features in the table 1, one is the $DBS_{2.2}$ response, the other the $DBS_{3.3}$ response. When the TOF ratio was between 0.51 and 0.6, the $DBS_{3.3}$ method was significantly better than the $DBS_{2.2}$. However, in the other range of the TOF ratio, there was no significant difference between the two methods. The results of the investigation on the use of $DBS_{3.2}$ as compared with that of $DBS_{3.3}$ are summarized in table 2. When the TOF ratio was below 0.5 and above 0.8, there was no significant difference between the two. However the $DBS_{3.2}$ was significantly better than the $DBS_{3.3}$ when the TOF ratio was between 0.51 and 0.8. A typical recording of the TOF

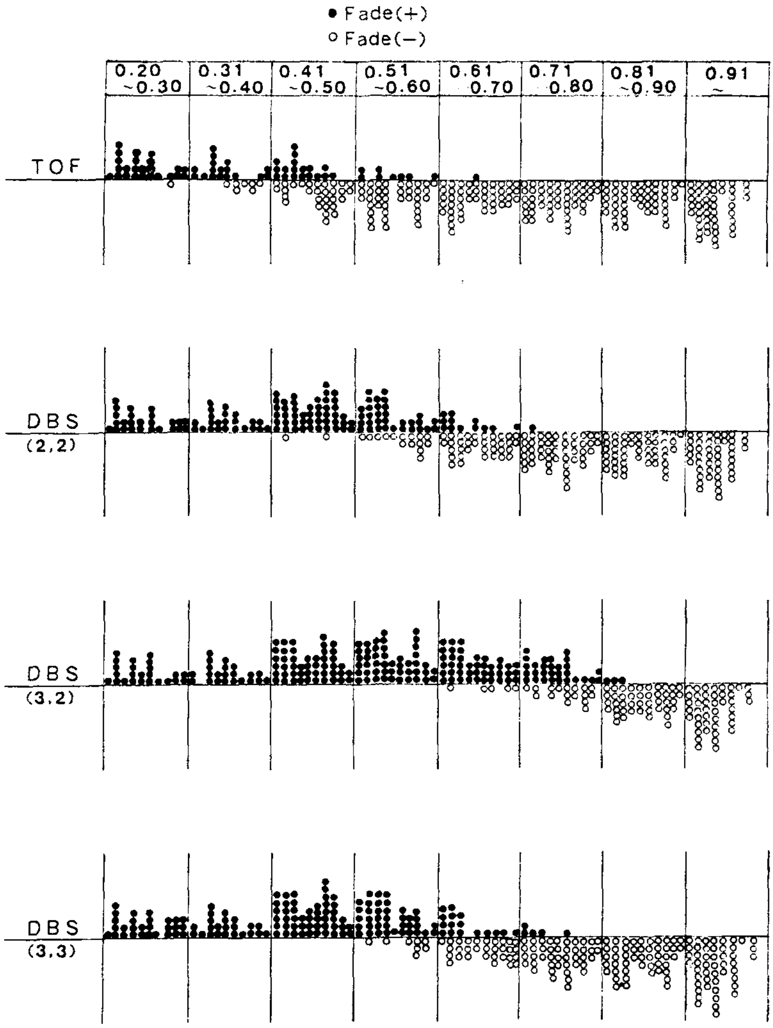

Fig. 3. Illustration of the distribution of all trials, whether or not fade could be felt when the TOF ratio was between 0.2 and 0.95. The black dots indicate a fade which the observer felt and the white circles signify no fade.

and DBS responses measured mechanically is shown in figure 2. The average values of DBS response are shown in table 3.

Discussion

The main purpose of using DBS is to allow the anesthesiologists to manually or tactilely estimate the recovery from the nondepolarizing blockade at the end of anesthesia with adequate recovery being indicated at an TOF ratio of above 0.75. Our results indicate that $DBS_{3.2}$ is the best stimulation pattern among the three for the following reasons. According to the results of $DBS_{2.2}$ and$DBS_{3.3}$, the difficulty of feeling the fade in their responses increased as the TOF ratio approached to 0.6. This means that the border of DBS response ratio (the second response to the first) at which the observer is capable of feeling the fade is around a TOF ratio of 0.6. Because the difficulty of detecting fade tactilely in $DBS_{2.2}$ and $DBS_{3.3}$ increased when the TOF ratio approached 0.6. When the TOF ratio was equal to 0.6, the $DBS_{2.2}$ and $DBS_{3.3}$ responses mechanically measured equaled to about 0.7. Considering this, the border of the DBS response ratio at which the observer is able to detect the fading is around a DBS response ratio of 0.7. On the other hand, as shown in table 3, the $DBS_{3.2}$ has a DBS response ratio of about 0.7 when the TOF ratio is 0.8. Consequently, the $DBS_{3.2}$. is superior to $DBS_{2.2}$ and $DBS_{3.3}$ when the TOF ratio is between 0.51 and 0.8. Figure 3 illustrates the distribution of all trials, whether or not fade could be felt when the TOF ratio was between 0.2 and 0.95. The black dots indicate a fade that the observer felt and the white circles signify no fade. Below a TOF ratio of 0.75, it was easier to detect a fade in the $DBS_{3.2}$ than in the $DBS_{2.2}$, $DBS_{3.3}$, or the TOF stimulation. When the TOF ratio was above 0.8, the observer could detect fade in only a very few trials (3 out of 47 and 0) despite of the use of the $DBS_{3.2}$ pattern. However, these results do not necessarily exclude the possibility of detecting an induced fade by $DBS_{3.2}$ without nondepolarizing muscle blockade. In conclusion, the $DBS_{3.2}$ is a superior stimulation pattern to the $DBS_{2.2}$ or $DBS_{3.3}$ for tactilely evaluating the adequate recovery. In clinical use, however, we recommend the following selection of DBS pattern. After the patient has slept but has not been given any muscle relaxant yet, the anesthesiologist should try to feel the $DBS_{3.2}$ response. If no fade is felt, $DBS_{3.2}$ should be used. If fading is felt (although very rare), $DBS_{3.3}$ should be chosen.

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