Functionally Adapted Stimulation Patterns for a Dynamic Training of Skeletal Muscle Ventricles in Adult Goats

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Abstract

When skeletal muscle is inadequately stimulated for cardiac assistance, the result is often a loss of muscular function accompanied by atrophy, fatty degeneration and fibrosis. It was consequently of interest to find the stimulation patterns required to train skeletal muscle ventricles against a load in order to minimise damage and failure. The stimulation patterns during the dynamic training of SMVs in 24 Boor goats were evaluated by measuring their hydrodynamic response in an intrathoracic training device. The patterns consisted of an increasing number of bursts per minute and differed in burst frequency and pulse application. In group I, eight goats were stimulated with pulses of 33 Hz burst frequency and a constant burst length of 500 milliseconds. Six of the SMVs failed (75%). In the second group (IIa) an increasing number of pulses per burst of 85 Hz were used, but three of the four SMVs failed. However, in group IIb with the pulse stimulation of 50 Hz and increasing from 2 to 20 pulses during the first period and followed by a frequency training from 3 to 30 burst per minute, no SMV failed. The stroke volume per minute improved as a result of the increase in beat frequency. Nevertheless, the stroke volume of a single contraction decreased by more than 50% by the end of the training program. The study showed that functionally adapted stimulation patterns for dynamically training skeletal muscle ventricles produced effective autologous pumps for cardiac assistance.

Key words: muscle contraction, electrical stimulation, dynamic training, cardiac assistance.

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About 25 years ago it was found that fatigable fast-twitching muscular fibers of the skeletal muscle could be transformed into fatigue-resistant slow-twitching fibers by slow rate electrical stimulation of 2 to 10 Hz [19, 22, 23]. This muscle plasticity was achieved by the capacity of gene expression for various myosin isoforms. The transformation of slow rate electrical stimulation into heart syncronized burst stimulation occurred during the conditioning of cardiomyoplasty in patients [5, 6, 7]. The bursts per minute were increased. Even a stimulation protocol with a fixed rate of 50 bursts per minute and an increasing number of pulses per burst from two to six was shown to be effective at avoiding muscle fatigue [15,16]. An electrically conditioned SMV wrapped around a stiff mandril and stimulated with an increasing number of bursts with 30-55 Hz was not fatigued but had a low potential for cardiac assistance [1, 3, 4, 14, 18, 20, 21, 24]. Unlike earlier electrical conditioning studies, it was decided to test the electrical stimulation patterns in SMVs during chronic animal experiments by evaluating the hydrodynamic energy of each contraction. Stimulation patterns were adapted to the stroke work and load used later in circulation.

Methods

Experimental investigations were carried out on 24 Boor goats aged between 3 and 7 years and weighing between 46 and 67 kg. They were supervised by a representative of the Society for Prevention of Cruelty to Animals of the District President of Kiel.

The operation took place under insufflation anaesthesia with a mixture of halothane-nitrogene monoxide. The latissimus dorsi muscle (LDM) was dissected free and wrapped as a double layered muscular tube round the central chamber of an elastic training device (Fig. 1), as described in earlier studies [8-12].

A myostimulator (Fig. 1) produced pulse trains along two myoelectrodes, which were woven round the branches of

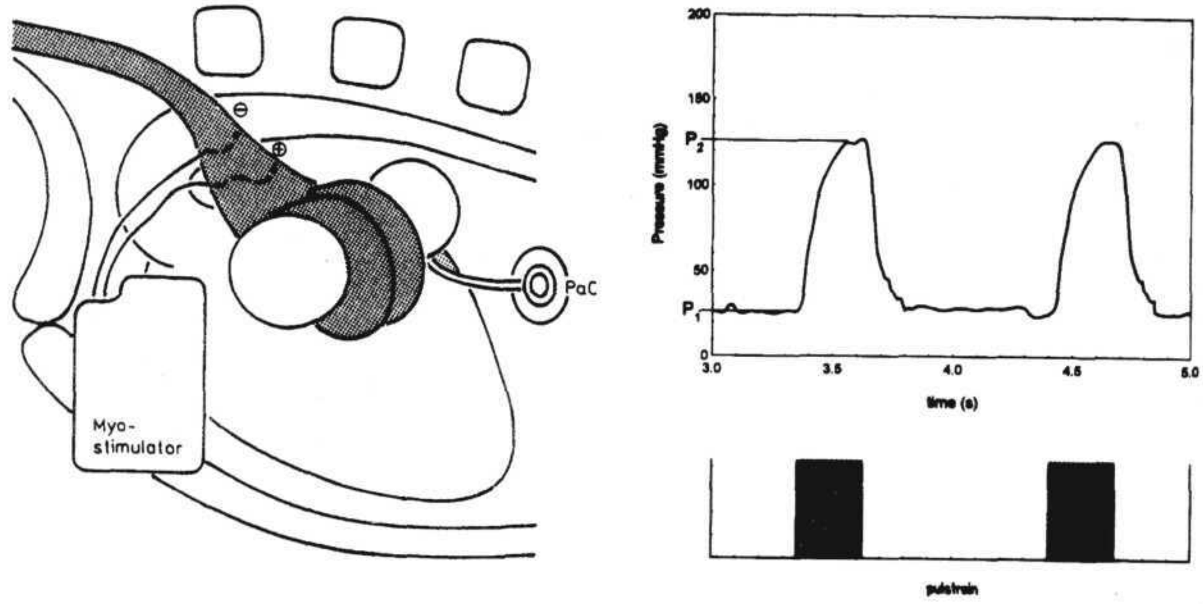

Figure 1. An intrathoracic SMV which is stimulated by a myostimulator is placed around an elastic training device. It's inner cavity isfilled with saline solution and connected to a subcutaneously implanted Port-a-Cat, a small chamber where pressure measurements were to be performed by punction. Burst stimulation was followed by muscle contraction, producing a characteristic pressure curve.

the nervus thoracodorsalis of the SMV. When the SMV contracted, volume was shifted into the elastic side bladders of a training device. The pressure increase in the device was recorded using a port-a-cat. As described earlier [8], the stroke volume was calculated from the dynamic pressure difference, related to a static compliance curve of the frogger. Pressure and stroke volume were used to calculate stroke work.

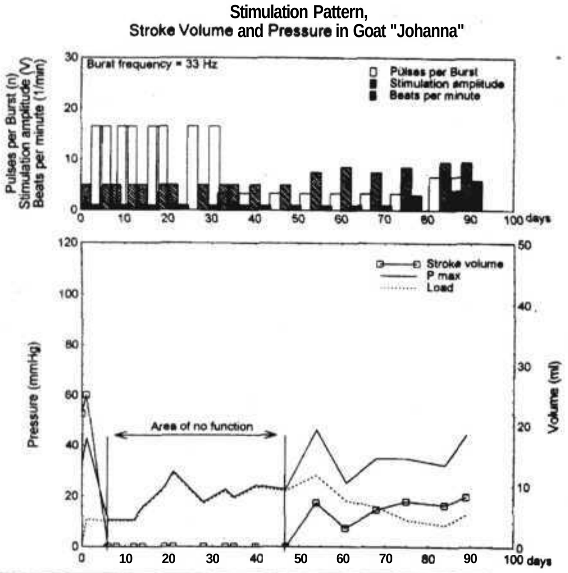

Figure 2. A failing SMV overstressed bystimulation shows a moderate recovery after the reduction of burstlength from 500 milliseconds and 16 pulses to a burstlength of 100 milliseconds and 4 pulses.

In group I, the SMVs were stimulated using Itrels 7420 from Medtronic, with bursts of 500 milliseconds length with a 33 Hz burst frequency and a pulse width of 210 microseconds. In group IIa, a stimulation with a burst frequency of 85 Hz and a pulse width between 100-120 microseconds was used. In twelve goats of group IIb, Telectronic myostimulators model 7220 started the stimulation at three bursts per minute, the number of pulses per burst ranging from 2 to 20. Thereafter the bursts per minute were increased. During stimulation an output of 5 Volts was delivered by all myostimulators.

A SMV failure was defined as a systolic-diastolic pressure difference in the training device of less than 20 mmHg

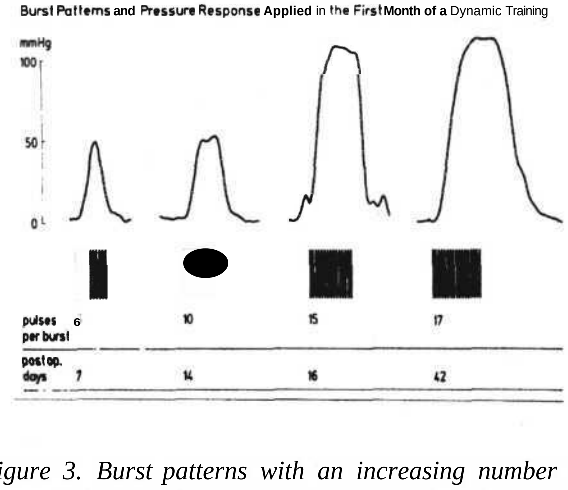

Figure 3. Burst patterns with an increasing number of pulses result in pressure curves with an increasing pressure plateau.

Stimulation patterns for SMVs

Table 1. Peak and endstage data ofSMVs during dynamic training in goats with different stimulation patterns.

Group I. Burst length 500 ms, Burst frequency 33 Hz, Puls width 210 ms.
n = 8 63,4% failure

No	Name	Peak				Endstage			
		Days in training	Pressure/Load [mmHg]	Stroke volume [ml]	Beat frequency [1/min]	Days in training	Pressure/Load [mmHg]	Stroke volume [ml]	Beat frequency [1/min]
1	Biene	119	94/6	29.6	17	162	136/57	12.7	
2	Caren	57	36/3	35.7	4	78	-/0	-	
3	Denise	70	31/5	26.9	6	132	-/0	-	
4	Elisabeth	20	22/0	22	2	69	28/6	17.5	
5	Gabi	15	20/3	12.2	1	17	24/16	5.0	
6	Ihna	2	19/4	10.7	1	7-71	-/0	-	
7	Johanna	6	-/10	-	1	89	30/12	8.0	
8	Luise	38	74/2	45	8	138-193	-/0	-	

Group IIa. Burst length 100-400 ms, Burst frequency 85 HzPuls width 100-120 ms.
n = 4

No	Name	Peak				Endstage			
		Days in training	Pressure/Load [mmHg]	Stroke volume [ml]	Beat frequency [1/min]	Days in training	Pressure/Load [mmHg]	Stroke volume [ml]	Beat frequency [1/min]
1	Katrin	24	57/28	25.4	2	172	34/25	9.0	30
2	Olivia	3	33/10	15	1	11	-/0	-	1
3	Pinky	73	39/10	12.6	6	126	65/33	11.8	30
8	Quincy	13	76/26	51.1	2	25-123	-/0	-	3

Group IIb. Burst length 100-400 ms, Burst frequency 50 HzPuls width 100-150 ms.
n = 12

No	Name	Peak				Endstage				
		Days in training	Pressure/Load [mmHg]	Stroke volume [ml]	Beat frequency [1/min]	Days in training	Pressure/Load [mmHg]	Stroke volume [ml]	Beat frequency [1/min]	
1	Adriane	85	57/24	22.2	18.2	151	54/29	19	24	good
2	Bonni	71	53/18	15.7	13.6	183	67/46	5.0	37.5	good
3	Danni	34	81/24	29.2	3.9	116	73/48	14.5	26.1	good
4	Helga	30	103/41	42.5	3	77	87/58	11.1	20	good
5	Lena	21	87/1	50.4	4	63	105/58	20.8	30	good
6	Mona	13	62/17	31.7	3	83	91/67	7.3	30	good
7	Nina	20	47/22	15.9	4	81	88/62	12.3	30	good
8	Sissi	37	78/11	32.9	5	121	40/13	12.0	30	good
9	Trixi	41	78/9	36.6	4	111	49/9	14	30	good
10	Ulla	35	77/12	16	4	109	63/24	7.0	30	good
1!	Vanessa	76	74/6	34.1	14	104	52/4	18.6	25	good
12	Wanda	16	81/9	24.4	4	132	76/45	9.3	25	good

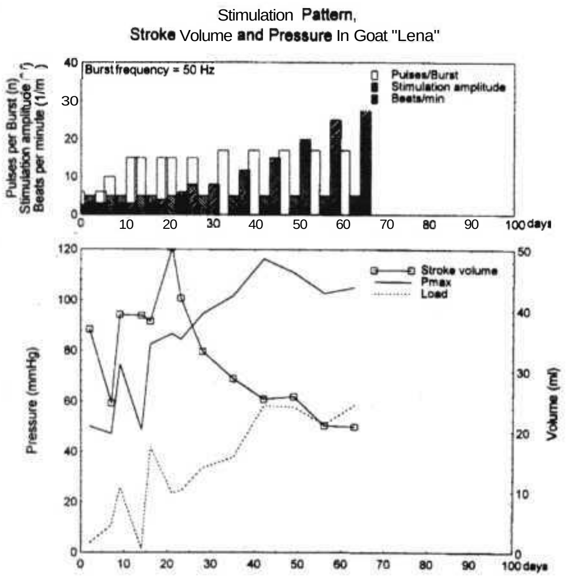

Figure 4. Stroke volume, maximal pressure and load during the dynamic training of a SMV with an increasing number of pulses per burst during the first month and increasing beat frequency in the following stimulation period.

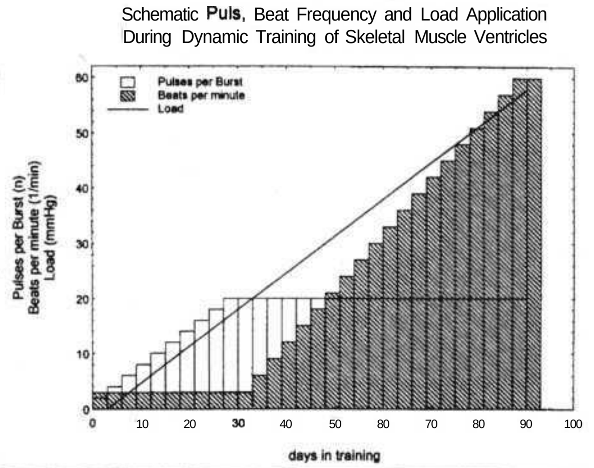

Figure 6. This scheme for puls, beat frequency and load application during a dynamic training of skeletal muscle ventricles has to be used as an orientation and has to become functionally adapted to muscle mass and the continuously increasing daily energy.

in an endstage dynamic training induced by a muscular contraction of an SMV.

Results

The goats tolerated the operative procedure well. Postoperatively they were able to move freely with no apparent physical impairment or discomfort.

Amongst the eight goats of group I six SMVs failed (75%). Three of the four SMVs failed in group IIa, which had a burst frequency of 85 Hz and a burst length of 100-400 milliseconds (Tab. 1). The failures shown in table 1 were usually irreversible. Nevertheless, goat Johanna showed that if the burst length of 500 milliseconds with 16 pulses was reduced to 100 milliseconds with 4 pulses per burst, there was a moderate regeneration of muscular function with a systolic pressure of about 30 mmHg and a stroke volume between 5 and 10 ml. In group IIb a stimulation pattern with a burst frequency of 50 Hz and an increasing number of pulses from 2 to 20 per burst, resulted in

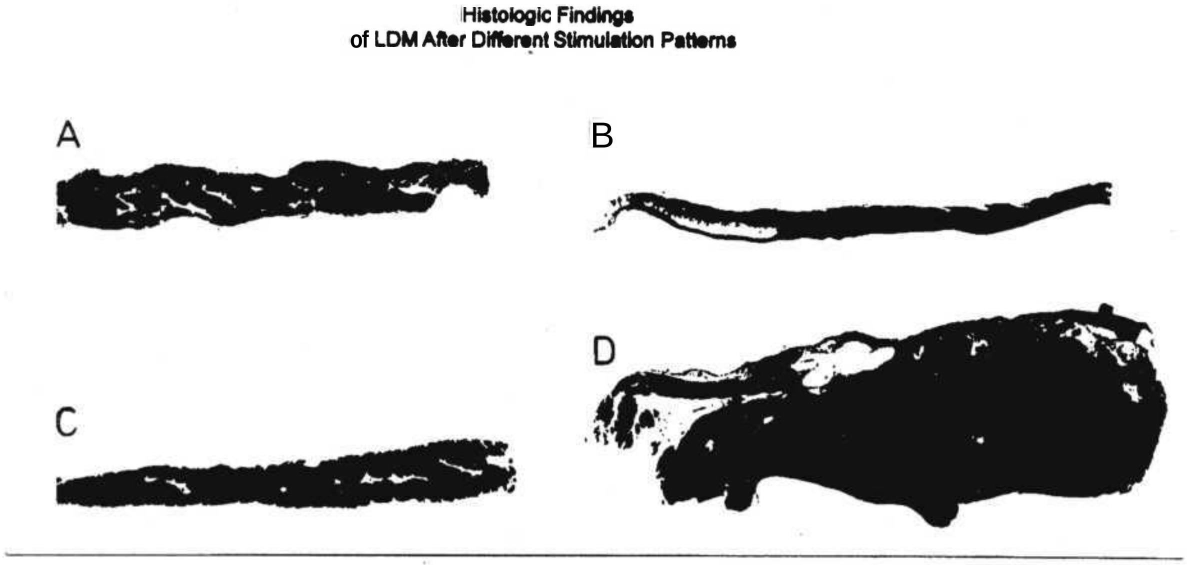

Figure 5. Cross-section of latissimus dorsi muscle in untrained (A) and failed SMV (B) of goat Katrin and from an untrained LDM (C) and of an optimally trained SMV (D) of goat Lena.

effective pumping ventricles. There were no failures in this group.

In Fig. 2 the result of increasing the number of pulses per burst as pressure development is shown. The prolongation of the curve plateau can be seen. Maximal pressure without load ranged between 50 and 80 mmHg.

Pressure and stroke volume (Tab. 1) were mainly dependent on load management. Endstage maximal systolic pressure varied between 28 and 134 mmHg, stroke volume between 5.0 and 20.8 ml. Maximal stroke volume during the first month had decreased by more than 50% by the end of training period (Tab. 1, Fig. 4), although stroke volume per minute increased. A maximal stroke volume per minute was calculated for a beat frequency of 30 bpm of 632 ml.

Histological findings of the SMVs following failure and optimal training are shown in Fig. 5. SMVs with loss of function showed fatty degeneration and fibrosis with little muscular tissue (B). The thickness of untrained LDM was between 4 and 7 mm (A, C), and the optimally trained LMD were 1,5 times as thick as the contralateral untrained (A) one.

Discussion

The stimulation patterns used in group I were transferred from the stimulation management of SMVs in calves used in earlier studies [8, 11]. In calves were two SMV failures amongst nine (22.2%). In Group I and IIa of the adult goats 75% of SMVs failed. If a stimulation pattern is transferred from one animal model to another, the relationship between the stimulation energy and stimulated muscle mass must be considered. The muscle mass of latissimus dorsi muscle in calves ranges between 250-320 g and in goats between 140-160 g. The stimulation energy by the patterns for the goats of group I was apparently higher than was tolerated. The SMVs were overstressed and failed, developing atrophy, fatty degeneration and fibrosis (Fig. 5B). A burst frequency of 50 Hz and reducing the burst length from 500 ms to 100-400 ms appeared suitable for generating a sufficient pressure and did not overstress the SMV.

Vascular delay was not used in any of the goats. It was not considered necessary as in dynamic cardiomyoplasty, where the muscular wrap must grow with the myocardium, or in an extrathoracic SMV used for creating collaterals. Stimulation was started intraoperatively to squeeze the latissimus dorsi muscle in order to prevent muscular swelling as the muscle was fixed relatively tightly around the frogger.

Increasing the pulses per burst during electrical conditioning of skeletal muscle for cardiac assistance was already found to be effective by Lucas [15, 16] for avoiding muscular fatigue and by Jarvis and Salmons for improving the power of each muscular contraction by use of the 'doubled effect' [17]. This is defined as existing in any muscle contraction in which the total mechanical response is greater than the mechanical response to a single, isolated impulse multiplied by the number of impulses in the train [17]. A stimulation pattern with this pulse increasing period followed by a burst and load increasing part, proved to be an excellent stimulation for a dynamic training.

The electrical stimulation pattern for a dynamic training of skeletal muscle by increasing its load and calculating its volume shift had not been evaluated before. Earlier studies done on dog SMVs to calculate stroke energy had no training against an increasing load [2]. Carrying out a load, while increasing the number of bursts per minute, appeared necessary in order to train skeletal muscles to effectively pump blood in circulation later on.

In summary, a stimulation pattern for dynamically training skeletal muscle ventricles was shown to be effective with a pulse increasing period during the first month and followed by a beat frequency increasing one over the following months regarding an increasing load (Fig. 6). Consequently electrically stimulated SMVs with functionally adapted stimulation patterns during dynamic training should become sufficient enough to pump blood for cardiac assistance.

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