CHAPTER 3

RESULTS

3.1 Aim 1 To confirm VNS effects on the heart and determine the effects of VNS frequency and duration on normal sinus rhythm (NSR) using ECG morphology (R-R interval, P-R interval, QRS complex and Q-T interval).

Protocol 1 (n=7): The effect of VNS on ECG parameters during NSR

The 10 mA with 5 Hz of VNS significantly prolong P-R and R-R intervals in all durations when compared with baseline. The P-R interval was prolonged for 19.59%, 20.65% and 16.51% when applied 5 Hz VNS for 10, 15 and 20 s, respectively. For the R-R interval prolongation, 17.9%, 19.1% and 18% prolonged occurred while applied 5 Hz VNS for 10, 15 and 20 s respectively. Both P-R and R-R intervals were changed less than 21% in all VNS duration. On the other hand, VNS did not alter the QRS complex and Q-T intervals as shown in Table 3-1. When a VNS frequency was changed from 5 Hz to 20 Hz, it induced severe heart block in all VNS duration as shown in Figure 3-1. Because of the severe heart block condition, the ECG parameters of 20 Hz VNS could not be measured. The electrical artifacts in the ECG recording windows occurred when we applied VNS and the artifacts were vanished when VNS stopped.

Table 3-1: ECG parameters at baseline, and at the VNS period with 10 mA, 5 Hz of VNS for 10, 15 and 20 s (n=7)

Parameters	VNS 5 Hz					
	10 s		15 s		20 s	
	BL	Stim.	BL	Stim.	BL	Stim.
P-R interval (ms)	127±6	152±4*	135±10	163±11*	135±11	157±10*
R-R interval (ms)	663±43	782±64*	706±45	841±58*	699±47	824 ±53*
QRS complex (ms)	33±7	34±6	37±6	35±6	40±7	41±7
Q-T interval (ms)	363±18	360±18	376±20	390±15	371±20	384±17

Values are expressed as mean ± SE. *P< 0.05 vs. baseline.

VNS= vagal nerve stimulation; BL=baseline; Stim.=stimulation

Baseline

5 Hz of VNS

20 Hz of VNS

Figure 3-1: ECG recording windows compared between baseline, 5Hz of VNS and 20 Hz of VNS. The electrical artifacts occurred when applying VNS and its frequency depended on VNS frequency. At 20 Hz of VNS, the severe heart block conditions were occurred.

3.2 Aim 2 To determine the effect of VNS frequency and duration on the DFT

Protocol 2 (n=7): The effect of VNS on DFT

VNS caused the decreasing of DFT as shown in Figure 3-2. The DFT decreased when we performed VNS. However, the DFT significantly decreased in some conditions. For the 5 Hz VNS, delivered voltage and energy significantly decreased at 15 and 20 s of VNS duration. The lowest averaged of DFT for this frequency was 355.29 V and 11.17 J at 20 s of VNS duration. For 20 Hz VNS, delivered voltage and energy significantly decreased only at 10 s of VNS duration. The lowest averaged of DFT for this frequency was 332.5 V and 9.51 J at 10 s of VNS duration. For other DFT parameters, pulse width (ms) and impedance (Ω), have shown in Table 3-2. In the VF induction period, some of our models could not induced VF by the same amount of AC current after applied VNS for a while. Thus, we increased VF induction period from 2 s to be 3 or 4 s for completely VF induction. Although VNS (20 Hz, 10 s) caused the lowest DFT, in the 1st protocol its caused severe heart block. We could not measured the changed of ECG parameters in 20 Hz of VNS frequency. The VNS parameter that conducted to the 3rd protocol, should be the most effective and suitable in both 1st and 2nd protocols. Thus, suitable VNS parameters should be 10 mA, 5 Hz. The VNS duration that provided the lowest DFT of 5 Hz VNS is 20 s. So, the most effective VNS parameters for the 3rd protocol is 10 mA, 5 Hz for 20 s.

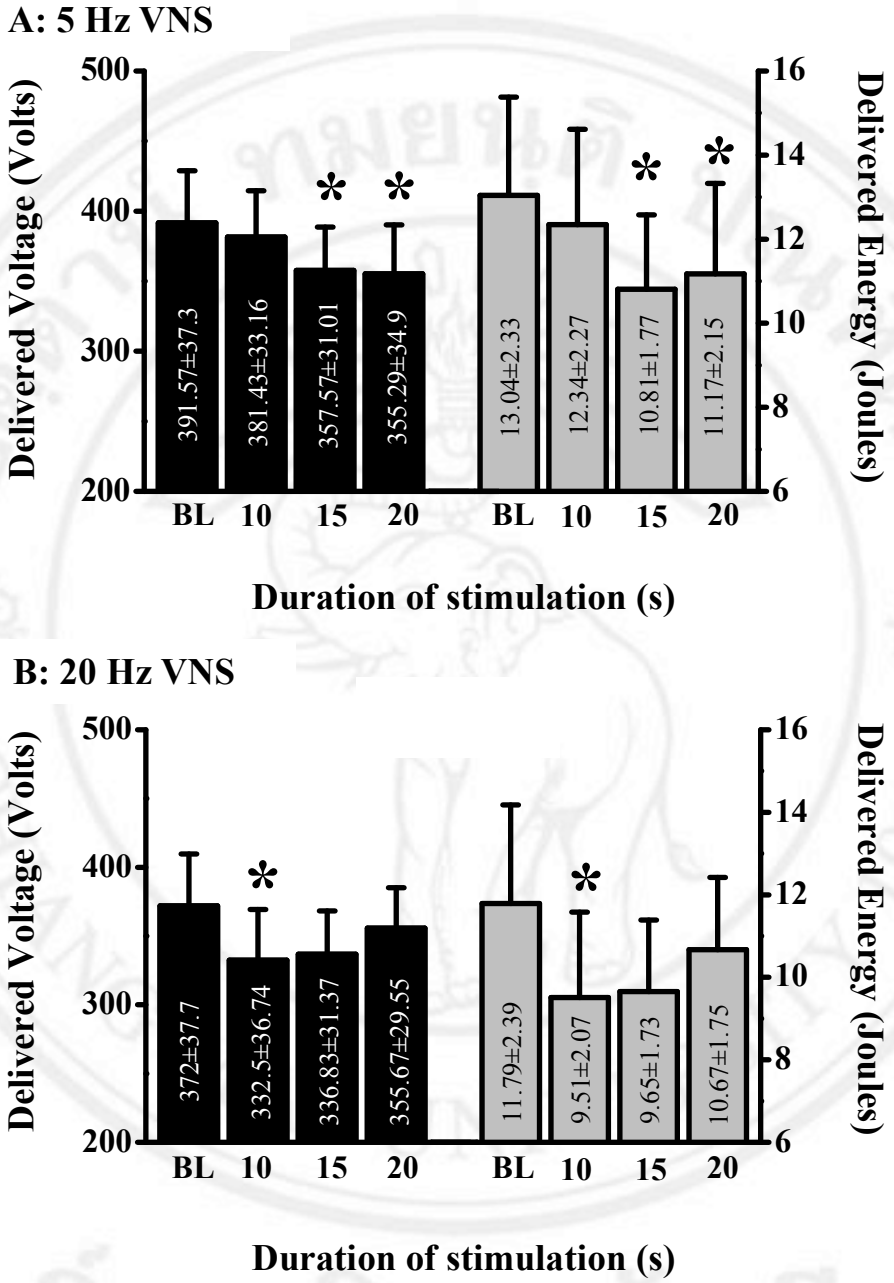

Figure 3-2: Effects of VNS frequencies and durations on delivered voltage and delivered energy of DFT. **A:** DFT comparison between baseline (BL), 10, 15 and 20 s of 5 Hz VNS. The delivered voltage and energy of both 15 and 20 s were significantly reduced. **B:** DFT comparison between BL, 10, 15 and 20 s of 20 Hz VNS. The difference from BL of both delivered voltage and energy was significant only at 10 s of VNS. * $P<0.05$ vs. BL.

Table 3-2: Defibrillation parameters at baseline, and at the VNS period with 10 mA, 5 and 20 Hz of VNS for 10, 15 and 20 s (n=7)

Parameters	5 Hz VNS			
	BL	**10 s**	**15 s**	**20 s**
Pulse width (ms)	11.6±0.2	11.4±0.2	11.3±0.2	11.2±0.2
Impedance (Ω)	38.1±1.2	37.7±1.1	37.3±1	37.1±0.9
Parameters	**20 Hz VNS**			
	BL	**10 s**	**15 s**	**20 s**
Pulse width (ms)	11.4±0.2	11.1±0.1	11.2±0.1	11.1±0.1
Impedance (Ω)	38±1.1	37±0.8	36.7±0.7	36.3±0.6

Values are expressed as mean ± SE. VNS= vagal nerve stimulation; BL=baseline

3.3 Aim 3 To determine the VNS pathway by local nerve block

Protocol 3 (n=6): The effect of VNS blockade by local anesthetic agent on NSR and DFT

The most effective VNS parameters from 1st and 2nd protocols have been used. The selective parameter of VNS, 10 mA, 5 Hz for 20 s, was performed by using the combination process of 1st and 2nd protocol. ECG was recorded at a NSR condition followed by DFT determination in every episode. During NSR condition, VNS significantly prolonged P-R and R-R intervals but did not alter the P-R and R-R intervals when we performed VNS with mepivacaine as shown in Table 3-3. As well as VNS performed 20 s after VF induction, VNS significantly reduced both of delivered voltage and delivered energy. These effects could be abolished by blocking vagus nerve activity by mepivacaine as shown in Figure 3-3.

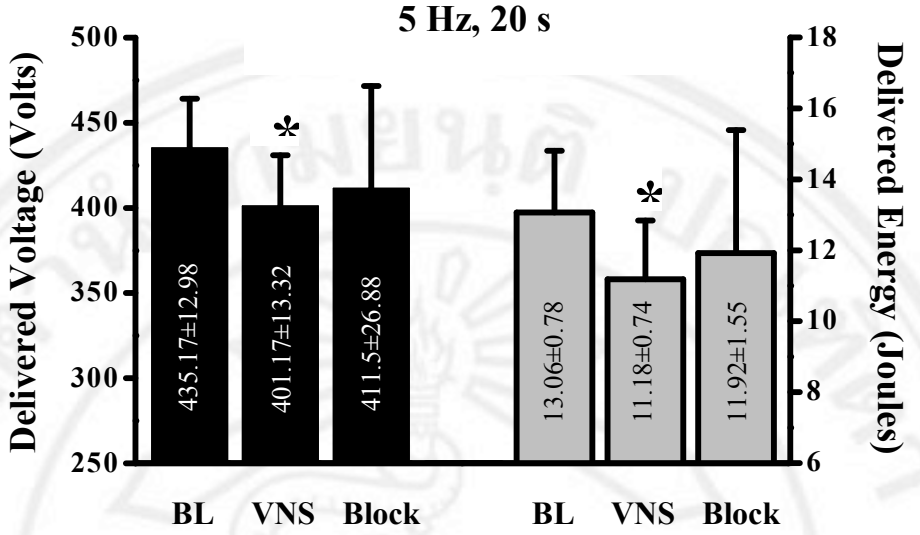

Figure 3-3: Effects of 10 mA, 5 Hz, 20 s of VNS on delivered voltage and delivered energy of DFT, comparison between baseline, VNS and VNS with mepivacaine perfusion. * P<0.05 vs. baseline.

Table 3-3: ECG parameters at baseline, and at the VNS period with 10 mA, 5 Hz of VNS for 20 s (n=6)

Parameters	VNS		VNS Block	
	BL	Stim.	BL	Stim.
P-R interval (ms)	108±3	135±3*	110±4	109±3
R-R interval (ms)	577±39	716±44*	536±28	536±28

Values are expressed as mean ± SE. *P< 0.05 vs baseline. VNS= vagal nerve stimulation; VNS Block= vagal nerve stimulation plus 3% mepivacaine; BL=baseline; Stim.=stimulation