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ORIGINAL CONTRIBUTION

The Human Heart Rate Response Profiles to Five Vagal Maneuvers

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Healthy teens and adults performed four vagotonic maneuvers. A large series of strabismus surgery patients had deliberately quantified tension on extraocular rectus muscles during general anesthesia. The mean bradycardia was greatest for diving response (apneic facial exposure to cold) and Valsalva maneuver and least for pressure on the globe and carotid sinus massage. Bradycardia occurred for every subject for the non-surgical maneuvers, however, extraocular muscle tension frequently caused no change in heart rate or even tachycardia. The inter-subject variance in percent heart rate change was greatest for surgical oculocardiac reflex. Of the rectus muscles, the inferior caused the most bradycardia while the lateral caused the least. The percent oculocardiac reflex was not age dependent. Occasional patients demonstrated profound bradycardia with strabismus surgery.

Of these maneuvers, diving response has theoretical advantage in treating paroxysmal atrial tachycardia.

The human cardiac vagal efferent was stimulated by several carefully controlled maneuvers resulting in wide inter-maneuver differences in bradycardia magnitude. The greatest intra-maneuver variability occurred with surgical oculocardiac reflex.

INTRODUCTION

Several non-invasive maneuvers have the capacity to elicit a profound vagal cardiac inhibition in some humans [1, 2]. Vagal maneuvers can produce well-tolerated heart rates much lower than the normal inherent automaticity of adult cardiac conduction tissue (denervated ventricular rates of 30 bpm) [3-5]. However, the degree of heart rate slowing varies from person to person. Some animals have much less intra-species variability for some maneuvers such as the diving response in marine mammals [6]. For a given person, or over groups of subjects, variability exists in the degree of bradycar-

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[b] *Abbreviations:* VM, Valsalva maneuver; CSM, carotid sinus massage; GP, globe pressure; DR-in, diving response with apneic facial immersion; DR-on, diving response with apneic application of icewater bag to the face; OCR, oculocardiac reflex; bpm, beats per minute; MR, medial rectus; LR, lateral rectus; SR, superior rectus; IR, inferior rectus.

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[c] A tribute to Ethan R. Nadel, Ph.D.

dia from one maneuver to another [1, 7-9]. The choice of initial vagal maneuver to treat paroxysmal atrial tachycardia is influenced by the relative propensities to slow the heart [10-11].

Vagal reflexes are well known in visceral and orbitofacial surgery [12]. Of particular interest to pediatric ophthalmologists is the oculocardiac reflex, a trigeminovagal reflex arising from tension on extraocular muscles [13]. Many strabismus surgery patients have minimal change in heart rate with multiple manipulations of the extraocular muscles, while a few similarly stimulated will repeatedly drop heart rate to 20 percent of resting rate [14]. Direct pressure on the eyeball also produces an oculocardiac reflex, which for the purposes of this paper will be called "Globe Pressure" (GP)[b] [15]. This report compiles the cardiac vagal profiles of a relatively large number of healthy adults and teens performing non-invasive vagal maneuvers and compares them to the intraoperative vagal responses of a large series of controlled extraocular muscle tension oculocardiac reflexes from adults and children with strabismus.

METHODS

From 1978 through 1997, with the approval of Institutional Review Committees from the University of Alaska-Fairbanks, Yale University School of Medicine, the Mayo Graduate School of Medicine, Rochester, Indiana University-Purdue University, Indianapolis, and Providence Alaska Medical Center, normal subjects and patients with ocular motility disorders were enrolled in prospective investigations of vagal reflexes.

Electrocardiograph recordings were obtained at least 15 seconds prior to and during the following non-invasive maneuvers in 37 subjects in supine position. Ages ranged from 10 to 71 (mean 32 ± 13 years). Valsalva maneuver (VM) was produced by having the subject inflate a mercury manometer to a pressure of 40 mm Hg for 15 seconds followed by a return to normal ventilation. Carotid sinus massage (CSM) was a 15-second manual depression of the right or left carotid sinus to level of the anterior spinous process during normal, non-Valsalva respiration. Globe Pressure (GP) was a 30-second inflation of a Honan® Balloon to 40 mm Hg over one eye during normal ventilation. The diving response was produced by 30-second apnea and exposure to ice water (1°C) in a 4 ml (0.10 mm thick) plastic bag completely covering the face and forehead (DR supine or DR-on) [16]. Placement of the ice bag on only the forehead reduces the effect [17, 18].

An additional 19 subjects, aged 18 to 41 years (mean 24 ± 7 years) performed seated 30-second apneic facial immersion in ice water (DR seated or DR-in).

The measurements were carried out in early to late afternoon. The subjects were healthy; specifically, none had cardiac disease or symptomatology. Heart rate was allowed to return to baseline (at least two minutes) between maneuvers. Other than the 19 seated diving response subjects, all subjects performed the four maneuvers, however the order was randomized.

From August 1982 through November 1987, 887 patients aged three months to 90 years (mean 18.5 ± 16, median 6.6 years) underwent strabismus, enucleation or pediatric glaucoma surgery. Some cases were excluded from the current analysis: five for incomplete data recording, 108 who, at the preference of the anesthesiologist, received anticholinergic medication, four who had topical anesthesia, and 67 reoperations yielding 703 primary cases for which the induction and inhalational general anesthesia were deliberately monitored. The oculocardiac reflex was elicited by sterile, gentle isolation of the first rectus muscle of the case and then deliberate, 200 gm (0.2 kilogram-force = 1.9 Newton) square-wave traction delivered for 10 seconds using a modified Jameson hook and a sterile spring-in-tube gauge (Ortho Tract-a-Tube®, Barnhart, Missouri) [19]. Less than 2 percent of these muscles were compromised by thyroid ophthalmopathy. The oculocardiac reflex (OCR) was determined as the percent maximal electrocardiograph change from pre-tension to that produced by the 10-second tension. The first muscle pulled was based on the type of strabismus: 221 had initial tension on the inferior rectus (IR), 162 on the lateral rectus (LR), 266 on the medial rectus (MR) and 54 on the superior rectus (SR).

RESULTS

All subjects tolerated the conscious maneuvers or the surgical observations without symptomatic hypotension or oxygen desaturation. In three young surgical cases, the anesthesiologist chose to administer intravenous atropine following significant initial bradycardia, even though no oxygen desaturation or prolonged dysrrhythmia was encountered. After all maneuvers and after each surgical case, heart rates returned to or exceeded the pre-maneuver rates after 1 to 2 minutes.

Descriptive statistics for percent heart rate change for the vagal maneuvers and the intraoperative oculocardiac reflex split by initial extraocular muscle are given in Table 1. There was a significant difference in heart rate change for these ($F_{(5,864)}$ = 11.6, p < .0001) as shown as box-plots (Figure 1) and as cumulative frequencies (Figure 2). By un-paired analysis, the means of heart rate change for each maneuver are compared in Table 2 and the variances are compared in Table 3. There was a significant difference in oculocardiac reflex due to different initial extraocular muscle ($F_{3,699}$ = 5.7, p = .0007) as shown in Figure 3.

Figure 4 shows no significant age-related effect on percent heart rate change for the surgical oculocardiac reflex (r^2 = .0014, $F_{(1,701)}$ = 1.0, p = .32). To aid in comparison with the teenage and adult

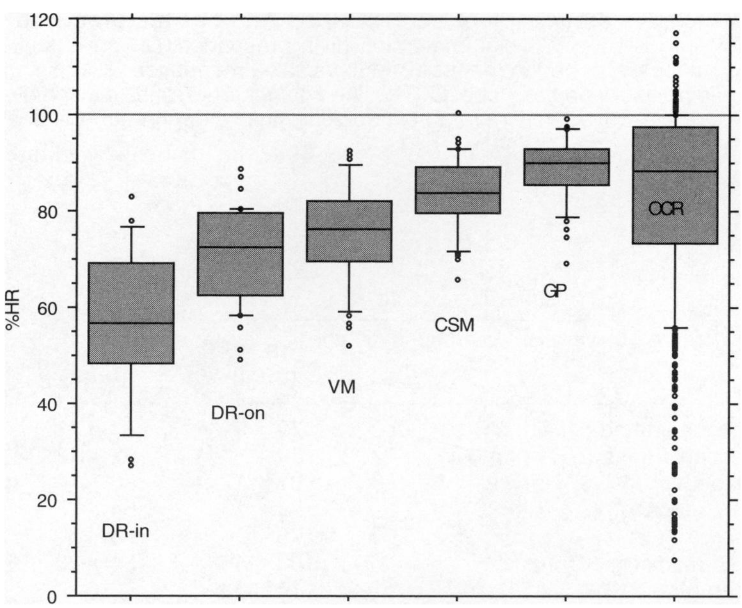

Figure 1. Box Plots of the heart rate percent changes produced by vagal maneuvers. DR-in is seated, facial immersion diving response. DR-on is supine apneic application of an ice-water bag to the face. VM is Valsalva maneuver. CSM is carotid sinus massage. GP is pressure on the globe. OCR is the oculocardiac reflex elicited by a 10-second, 200 gram, square-wave tension on an extraocular muscle during general anesthesia.

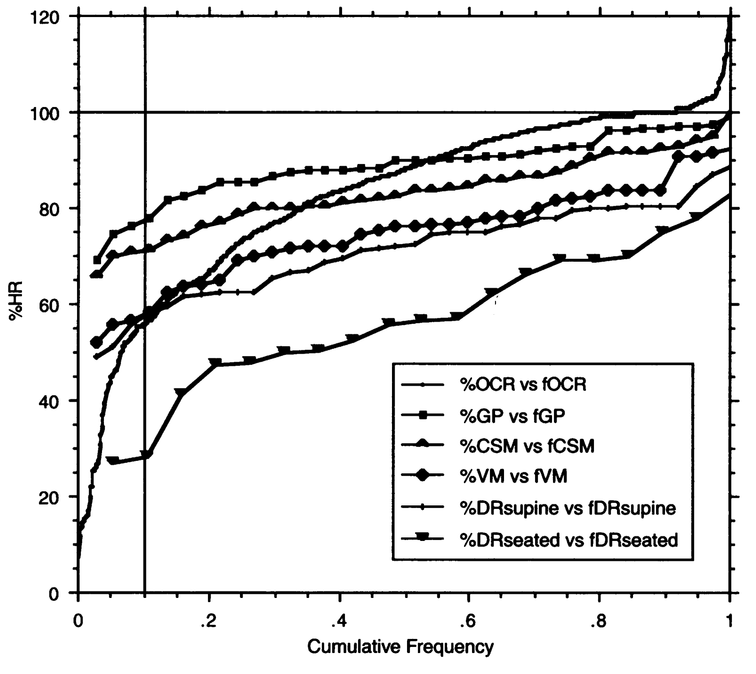

Figure 2. Cumulative Frequency of percent heart rate change produced by vagal maneuvers. DR-in is seated, facial immersion diving response. DR-on is supine apneic application of an ice-water bag to the face. VM is Valsalva maneuver. CSM is carotid sinus massage. GP is pressure on the globe. OCR is the oculocardiac reflex elicited by a 10-second, 200 gm, square-wave tension on an extraocular muscle during general anesthesia.

Table 1.

Maneuver	Pre-HR (bpm)	HR_{min} (bpm)	%Δ HR
Diving response seated (DR-in; n = 19)	72 ± 9	41 ± 12	-43%
Diving response supine (DR-on; n = 37)	80 + 17	57 ± 12	-29%
Valsalva maneuver (n = 37)	81 ± 17	60 ± 10	-25%
Carotid sinus massage (n = 37)	77 ± 16	64 ± 15	-17%
Globe pressure (n = 37)	76 ± 16	68 ± 7	-11%
Oculocardiac reflex (n = 703)	103 ± 46	84 ± 28	-17%
OCR children (age <10, n = 457)	114 ± 52	92 ± 27	-19%
OCR adults (age >10, n = 246)	83 ± 18	70 ± 26	-16%

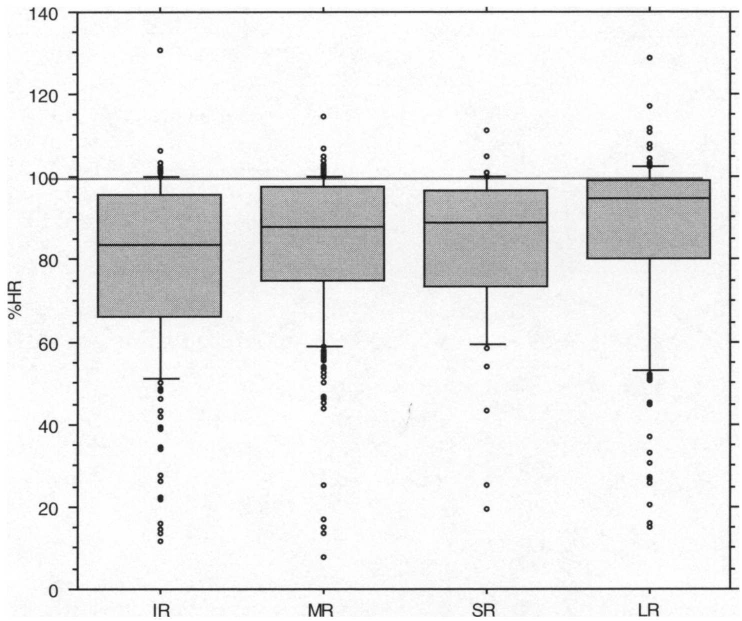

Figure 3. Box Plots of percent heart rate change produced by surgical oculocardiac reflex on each rectus muscle. IR is the inferior rectus, MR is the medial rectus, SR is the superior rectus, and LR is the lateral rectus.

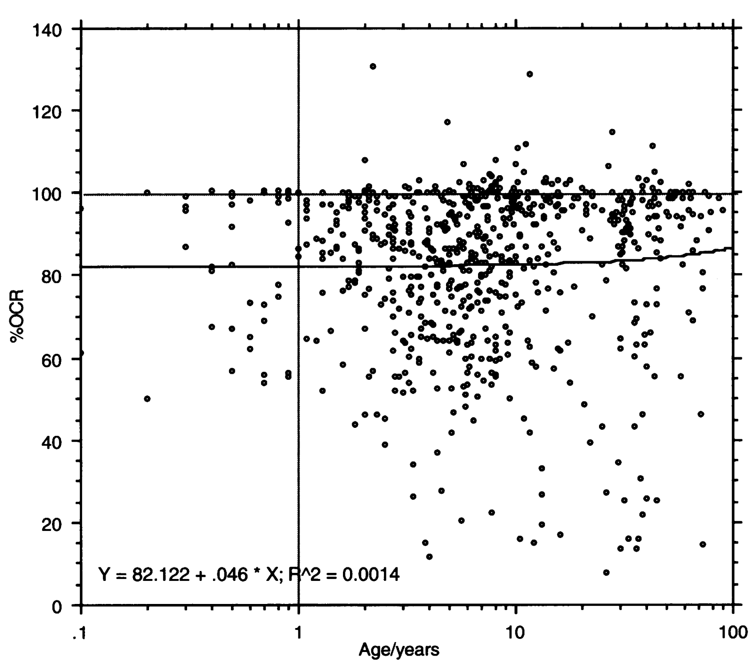

Figure 4. Regression of percent heart rate change (ordinate) due to surgical oculocardiac reflex versus age of the patient (abscissa).

Table 2. Compared heart rate means (unpaired t-Test) for human vagal maneuvers.

T-value (p)	Mean %Δ	Dr-on	VM	OCR	CSM	GP
DR-in	-43%	-4.2 (<.0001)	-5.2 (<.0001)	-5.5 (<.0001)	-8.5 (<.0001)	-11 (<.0001)
DR-on	-29%		-1.5 (.13)	-3.4 (.0006)	-5.8 (<.0001)	-8.9 (<.0001)
VM	-25%			-2.4 (.02)	-4.0 (<.0001)	-6.9 (<.0001)
OCR	-17%				0.19 (.85)	1.8 (.07)
CSM	-17%					-3.2 (.002)
GP	-11%					

Table 3. Compared heart rate variances for human vagal maneuvers.

F-value (p)	Variance	Dr-in	VM	DR-on	CSM	GP
OCR	398 $(\%HR)^2$	59 (.13)	0.26 (<.0001)	-24 (<.0001)	0.16 (<.0001)	0.12 (<.0001)
DR-in	236		2.3 (.05)	2.5 (.03)	3.8 (.002)	5.1 (.0003)
VM	103			0.91 (.78)	-1.7 (.12)	2.2 (.02)
DR-on	95				1.5 (.20)	2.1 (.03)
CSM	62					1.3 (.39)
GP	46					

normal subjects, the surgical oculocardiac reflex patients were divided into 246 older than 10 years and 457 less than 10 years of age. The actual heart rates before and due to the vagal maneuvers are given in Table 1.

DISCUSSION

The human response to the four awake non-invasive vagal maneuvers and to the general anesthetic, surgical extraocular muscle tension oculocardiac reflex was widely variable. The mean change in heart rate could be ranked: DR-in > DRon > VM > OCR = CSM > GP. This is similar to the results of Berk [20]. The variance of these responses could be ranked: OCR > DR-in > VM = DR-on > CSM = GP. For the surgical oculocardiac reflex, the degree of heart rate slowing could be ranked: IR > MR = SR > LR. Newer studies employing controlled extraocular muscle tension and real (non-ordinal) data find similar OCR dependence on rectus muscles [14, 21, 22]. Children had slightly more oculocardiac reflex, but this was not statistically age dependent. Though the mean bradycardia due to oculocardiac reflex was only moderate, the wide variance indicated that the more profound 10 percent had heart rate slowing, which equaled or exceeded facial immersion diving response (Figure 2). In addition, nearly 10 percent of patients demonstrated tachycardia in response to a 10 second, 200 gm pull on their first rectus muscle, while none of the vagal maneuver subjects had a progressive rise in heart rate.

Variable heart rate could result from variability in afferent stimulus. These maneuvers were carefully and reproducibly quantified with few exceptions: exact facial area of cooling, exact lung volume with breath hold and degree of digital pressure with carotid sinus massage. These maneuvers and surgical manipulations were designed to safely produce a sufficient heart rate impact as one might desire when treating paroxysmal atrial tachycardia. It might be possible to intensify the vagotonic effect by increasing the intensity and/or duration of the stimuli. The diving response is temperature dependent and usually reaches maximal bradycardia within 30 seconds of apnea [18]. Valsalva might be increased by increasing breath-hold time or pressure. One could increase the duration and pressure for carotid sinus massage or Honan® Balloon application, although these were on the upper limit of comfort and/or perfusion considerations. The oculocardiac reflex is influenced by the degree and wave-type of extraocular muscle tension [21], however more prolonged, higher tension pulls can be associated with a rebound tachycardia [23].

Profound bradycardia below the ventricular inherent rhythm can occur with all these maneuvers. Even the maneuver we found to be weakest, bilateral globe pressure, can cause asystole of 12 seconds [15]. In a study of oculocardiac reflex in 810 patients undergoing various types of anesthesia, one woman developed bradycardia equivalent to 3.8 bpm. [24]. In the absence of anticholinergic prophylaxis, approximately 4 percent of strabismus patients will experience a 50 percent or greater bradycardia due to routine extraocular muscle tension [25]. Cardiac arrest longer than 10 seconds may occur in up to 15 percent of retinal detachment patients [26].

In general, these oculocardiac reflex-prone patients are not prone to exaggerated vagal responses to other maneuvers [27]. The diving response is also associated with profound heart rate slowing; an 11-second, ice water apneic facial immersion asystole was not associated with syncope due to intense, concomitant peripheral vasoconstriction [3]. Though oculocardiac reflex and diving response share the same trigeminal afferent nerve, it is not yet clear whether oculocardiac reflex has the intense, concomitant peripheral vasoconstriction. In general, the brain stem processing of these vagal reflexes has been mapped [1] but may be altered by variable afferent nerve impulses, combined afferent impulses, the effects of baroreceptors [28, 29] or micro-differences in the human vagus efferent nuclei. I hope this report stimulates neurophysiologists to elucidate mechanisms for the inter-maneuver and intra-maneuver variability in humans.

This report of a large number of subjects and patients emphasizes two clinical points. The first concerns which vagal maneuver is the favored initial treatment of supraventicular tachyarrhythmia since this is not uniformly known [11]. Mehta found Valsalva superior to, and carotid sinus massage inferior to face immersion in 50°C water, but the breath hold duration was too short [10]. Diving response with ice water face immersion and breath hold for over 20 seconds may be the best initial vagal maneuver since it has more average vagal effect and has maintained central mean arterial pressure [30, 31] and cerebral blood flow [32]. The second clinical point warns that relatively uncommon, significant bradycardia can accompany extraocular muscle tension, and, therefore, post-operative strabismus surgery adjustments should be done with the patient supine [33, 34]. This is particularly important when tension is applied to the inferior rectus muscle.

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