Prolongation of Atrioventricular Conduction Time by Electrical Stimulation of the Carotid Sinus Nerves in Man

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SUMMARY Electrical stimulation of the carotid sinus nerves was applied during diagnostic catheterization of two patients who had coronary artery disease. The immediate reflex prolongation of the atrioventricular (AV) interval was due to prolongation of the AH interval only and was roughly parallel to the reflex RR interval prolongation evoked without atrial pacing. After cholinergic block, the reduced prolongation of both the RR interval and the AV interval caused by reflex inhibition of sympathetic tone followed a time course similar to the arterial pressure decrease. This is the first demonstration in man of the parallel baroreflex effects on the sinoatrial node and the AV node.

THE NEGATIVE chronotropic effect of increased arterial baroreceptor activity has been well documented in animals and in man. Much less information is available on baroreflex control of atrioventricular (AV) conduction. We are not aware of any report on the time course of AV conduction changes in man evoked by the abrupt increase and decrease of baroreceptor afferent activity.

We describe here the reflex effects on AV conduction time evoked by electrical stimulation of the carotid sinus nerves (CSN) during atrial pacing (with His-bundle recording in one case).

Methods

Two patients with coronary heart disease were studied after informed consent during diagnostic cardiac catheterization. Patient 1 was 57 years old and patient 2 was 65 years old. Patient 1 was reexamined 3 years later to exclude the existence of cardiac conduction defects. The techniques for right atrial pacing and for recording His-bundle activity, ECG and brachial artery pressure have been described. The subjects were in stable condition without signs of cardiac failure. No β-blocking drugs were used at the time of the study. In one patient, atropine, 0.04 mg/kg, was administered to block vagal control of the heart. This patient had first-degree AV block.

The studies were performed at least 20 months after implantation of the receiver-electrodes assembly of the CSN stimulator (Angiostat, Medtronic). Therapeutic application of CSN stimulation has been fully described elsewhere.

A modified stimulator produced 0.35-msec pulses for periods of 15–90 seconds. The stimulator was switched on or off by the QRS complex of the ECG. The stimulus frequency was 80–120 Hz and the estimated intensity was ≤ 2.5 V; the exact voltage is unknown due to the nature of the device.

In patients with coronary heart disease, the therapeutically adequate stimulus intensity (used in this study) remains below the threshold for activation of chemoreceptor fibers, as judged from the absence of changes in respiratory rate or minute volume.

All signals were monitored on an instrumentation recorder and analyzed later with the help of a digital computer. AV conduction time was defined as the AV interval between the onset of the pacing stimulus artifact and the peak of the R wave or S wave in the ECG. We determined the mean arterial pressure by electronic low-pass filtering the phasic signal (cutoff frequency 1 Hz). We measured the RR interval and the AV interval accurate to within 2 msec and expressed the response to CSN stimulation as a percent change with respect to the mean of the last 30 prestimulation beats. We constructed average (n = 2–9) plots of the AV interval, mean arterial pressure and (without pacing) the RR interval, using linear interpolation to obtain data points at 0.25-second intervals.

Pre-His and post-His conduction times were measured in patient 1 from a direct recorder (Elema Mingograph, 1 mm = 2.5 msec). The AH interval was defined as the interval between the pacing stimulus artifact and the fast zero-crossing of the biphasic His deflection, the HV interval as the subsequent interval to the onset of ventricular activation. Intervals measured from paper were accurate to within 5 msec.

Statistical Methods

The results are presented as mean ± SEM. The averaging procedure improves the signal-to-noise ratio with the square root of the number of stimulation runs (n), provided the noise is independent of the signal. The latency to onset of a reflex response was estimated by eye from computer-produced graphs with expanded time resolution.
Results

Figure 1 shows a composite plot of the prolongation of both the RR interval and the AV interval, together with the decrease in mean arterial pressure elicited by CSN stimulation in patient 1. The increased AV interval was caused by prolongation of the AH interval (fig. 2); the HV interval remained unchanged (20 ± 1 msec), as did the duration of the QRS complex (78 ± 2 msec). The AH interval increased in 3.5 seconds from 159 ± 1 to 175 ± 1 msec. The strikingly similar time course of the reflex chronotropic and dromotropic changes was confirmed in patient 2 (fig. 3).

The latency to the onset of AV-interval prolongation was estimated to be 0.8–1.4 seconds in patient 1 and 0.9–1.6 seconds in patient 2 (taking into account the atrial pacing interval and the leading effect of interpolation on the AV-interval signal). The time to peak effect was less than 5 seconds, and an overshoot was present in the initial response. The RR-interval prolongation started within the duration of one cardiac cycle (< 1 second), reached a maximum within 5 seconds and also displayed a response overshoot.

After administration of atropine, both the AV interval and the RR interval began to increase only after 2–3 seconds, and reached maximal values after 20 seconds. The delayed and sluggish prolongation of the RR interval and the AV interval caused by reflex inhibition of sympathetic tone was roughly parallel to the time course of the arterial pressure decrease (fig. 3).

Discussion

This study confirms and extends the recent investigation of Mancia et al., who used drug-induced changes of arterial pressure to evaluate baroreflex control of AV conduction in man.

Our principal observations are: (1) CSN stimulation evoked an increase of the AV conduction time that started after a latency of 0.8–1.6 seconds, reached a maximum within about 5 seconds and declined to a steady-state level after 20 seconds (figs. 1 and 3). (2) The AV-interval increase was due to prolongation of the AH interval only, the HV interval remained

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**Figure 1.** Composite graph of the RR-interval prolongation and AV-interval prolongation, together with the decrease in mean arterial pressure, evoked by carotid sinus nerve (CSN) stimulation in patient 1. Percent changes with respect to the mean control value (86 mm Hg for mean arterial pressure; 975 msec for the RR interval and 226 msec for the AV interval) are shown. Calibration is indicated in the graph. The RR interval was measured during spontaneous sinus rhythm, whereas the AV interval was measured during atrial pacing (intervals were 600 and 700 msec). Note the similar time course of the negative chronotropic and dromotropic effects. n = number of stimulation runs.

**Figure 2.** Prolongation of the AH interval (mean ± SEM) evoked by carotid sinus nerve (CSN) stimulation at 100 Hz in the same subject as in figure 1, but on another occasion. The HV interval and QRS duration remained unchanged. n = number of stimulation runs. The atrial pacing interval was 750 msec.

**Figure 3.** Composite graph, as in figure 1, of the cardiovascular effects evoked by carotid sinus nerve (CSN) stimulation before and after cholinergic block in patient 1. The atrial pacing interval was 700 msec before and 450 msec after administration of atropine. AV = atrioventricular.
unchanged (fig. 2). (3) The negative dromotropic effect of CSN stimulation was primarily due to enhancement of vagal tone (fig. 3). (4) CSN stimulation evoked inhibition of sympathetic activity affecting the AV node as well; the resulting AV-interval prolongation started after 2-3 seconds and reached a maximum after 20 seconds (fig. 3). (5) The AV-interval prolongation, whether mediated by enhanced vagal or inhibited sympathetic tone, was roughly parallel to the RR interval prolongation evoked by CSN stimulation without atrial pacing (figs. 1 and 3). Baroreflex control of heart rate and AV conduction is achieved primarily by modulation of parasympathetic outflow to the heart. After cholinergic blockade, CSN stimulation evoked a delayed and sluggish RR-interval and AV-interval prolongation, indicating reflex inhibition of sympathetic tone affecting the sinoatrial node and the AV node. The atropine dose of 0.04 mg/kg body weight must have blocked vagal control of the heart completely, because heart rate rose to 120 beats/min in the 65-year-old subject and the respiratory arrhythmia disappeared completely.

Atonic influence on conduction in the AV node can be examined only when atrial rate is fixed, because in the paced heart the RR interval and the AV interval are inversely related. The interaction between direct and indirect effects on AV conduction is exceedingly complex. We were careful to maintain the atrial rate constant for the measurement of baroreflex effects on AV conductivity.

The time course of vagally and sympathetically mediated effects of CSN stimulation on the RR interval and the AV interval in man show features closely resembling the responses to stimulation of cardiac autonomic nerves in animal experiments. Vagally mediated chronotropic responses have a very brief latency (a few hundred milliseconds) and a short time constant (a few seconds), whereas sympathetically mediated responses appear after only 1-3 seconds and have relatively long time constants (about 10 seconds). Dromotropic responses exhibit a similar difference in time course.

In conclusion, our results give the first demonstration in man of the parallel time course of SA-nodal and AV-nodal inhibition by electrical stimulation of the CSN. The time course of vagally and sympathetically mediated baroreflex effects closely resembled the chronotropic and dromotropic responses to electrical stimulation of the autonomic cardiac nerves in the dog.

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