Influence of Arterial Baroreceptors on Heart Rate Variability

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Abstract
Objective: Fluctuations in heart rate, blood pressure and other circulatory parameters have been described since the last century, but only recently the observation that changes in these fluctuations are associated with changes in the sympathovagal balance and with the activity of the arterial baroreflexes has led to the practical use of analysis of cardiovascular variability as a marker of autonomic function. The present review reports the various hypotheses on the origin of fluctuations in cardiovascular variability and the possibility to apply these observations to the clinical field. Method: Two main oscillatory components have been described in the cardiovascular system: one is related to the respiratory activity; a second component whose period is ~ 10 s is independent of respiration. These can be accurately quantified by computerized methods based on spectral analysis. These fluctuations might not only be used as a marker of vagal and sympathetic activity, but also provide information on the activity of the arterial baroreflex. A practical approach to obtain this data is discussed. Results: Practical implications of this methodology involve the non-invasive assessment of baroreflex activity and sympathovagal balance under a large number of physiologic and pathologic conditions. In this article the application to the autonomic assessment during physical exercise and after cardiac transplantation is reviewed in depth. Conclusions: The arterial baroreceptors exert a strong, though not exclusive influence on the cardiovascular fluctuations, through both sympathetic and vagal activity. These might be conveniently evaluated by non-invasive techniques involving spectral analysis of cardiovascular variability.
Introduction

In recent years the introduction of new computerized methods of analysis of cardiovascular variability, i.e. the power spectrum analysis (PSA), has provided an accurate method to describe and quantify the frequency and power of these oscillations. Two major oscillatory components have been described. One is a ‘high-frequency’ (HF) component related to the respiratory activity, i.e. the so-called respiratory sinus arrhythmia, with a central frequency around 0.25 Hz. The second is a ‘low-frequency’ (LF) component that presents a roughly 10-second periodicity rhythm and has a frequency of approximately 0.1 Hz. Other much slower fluctuations are present, related perhaps to sleep, activity, chemoreflex activity and temperature control (fig. 1).

It is often assumed that the spectral indices obtained at the frequency for the HF and LF components reflect vagal and sympathetic tone, respectively [1]. The ratio of these two frequencies has been used to indicate the balance between sympathetic and vagal tone in differing physiological and pathophysiological states [2]. These indices cannot of course be direct measures of autonomic nervous tone since by their nature they can only reflect the variability and not the absolute level of the signal.

These simplified descriptors clearly are not universally applicable. For example indirect measures indicate that although exercise is known to be accompanied by vagal withdrawal and sympathetic arousal [3, 4], the absolute values of LF power are greatly reduced or abolished by submaximal exercise [5, 6]. Similarly patients with severe cardiac failure are known to have high sympathetic tone [7] and reduced sinus arrhythmia (less vagal tone) [8]. But PSA measures in severe heart failure show reduced LF and predominant HF components [9, 10], due to respiratory changes in heart rate of non-autonomic origin. Nonetheless, respiratory-related variations in cardiovascular parameters are increasingly studied as indices of autonomic activity and also because they convey information about pathophysiological processes and their prognosis. For example in healthy and diabetic subjects respiration-related fluctuations in R-R interval (HF) are used as an index of the gain of the baroreceptor cardiac vagal reflex responses [11, 12]. Acute reductions of fetal respiratory sinus arrhythmia during labour predict fetal death [13]; chronic reductions of heart rate variability after myocardial infarction are a marker for subsequent sudden cardiac death [14, 15].

Fig. 1. R-R interval and respiration (time ‘series’) tachograms (a) with autoregressive power spectra (b) in a normal subject. Note the presence of low-frequency (LF) and clear respiratory (HF) fluctuations.
Fig. 2. Model of cardiovascular control. Diagram of the beat-to-beat model of De Boer et al. [16]: baroreflex with two effectors, R-R interval and peripheral resistance. According to this model, changes in cardiac output by effect of respiration modify the blood pressure, and hence baroreceptor response through sympathetic (slow) and vagal (fast) modulation on the R-R interval and peripheral resistance. The delayed sympathetic response causes slow (0.1-Hz) fluctuations, which due to the continuous perturbations induced by respiration, are sustained. For a single circulatory perturbation, this model predicts a damped oscillation in R-R and blood pressure [from ref. 16, with permission].

What Is the Origin of the Heart Rate Variability Fluctuation?

Central to this problem is the origin of these fluctuations. Several theories have been proposed.

Peripheral Theory
The peripheral or baroreflex theory follows the De Boer hypothesis (fig. 2) [16]. This model, which is based on a mathematical model of the circulation, examines the interactions of the fast vagal response to baroreceptor stimulation and the slower response of the sympathetic efferents controlling the arterial smooth muscle. Resonance at a frequency of about 0.1 Hz can occur in such a system which has feedback loops with different time constants. Thus the peripheral theory states that the HF fluctuations of heart rate variability (respiratory sinus arrhythmia) result from the inspiratory augmentation of venous return which then leads to a similarly timed rise and fall of peripheral arterial pressure, which is delayed and damped during passage through the lungs. This cycle of blood pressure change is sensed by the arterial baroreceptors which then modulate heart rate. Moreover, respiratory-related changes in venous return to the right atrium are able to induce changes in left ventricular volume which are sufficient to reduce or increase stroke volume so that systolic blood pressure and hence arterial baroreceptor activity change [17–19]. According to this peripheral hypothesis, LF activity is generated by the phase lag in the baroreceptor loop: changes in blood pressure stimulate the baroreceptors, which cause a fast (<1 s) vagal response to the heart and a slow (3–10 s) sympathetic withdrawal to the blood vessels; this delay of the sympathetic branch of the baroreflex in turn determines a new oscillation, which is then sensed by the baroreceptors and so on [12, 13]. Therefore from a practical point of view, respiratory sinus arrhythmia is a relatively
simple index of the gain of the arterial baroreflex, which can give important predictive clinical information.

Central Theory

According to some studies, mostly based on evidence from animals [20–23], the genesis of respiratory sinus arrhythmia (HF fluctuations) and spontaneous LF activity is not due to peripheral factors, such as arterial baroreflexes, but is the result of a ‘common central rhythmicity’. The ‘central’ theory is supported by observations which showed that respiratory sinus arrhythmia may persist in the absence of any respiratory movements, mostly in paralyzed or open chest animals [21, 23], and that heart rate acceleration was still related to inspiratory activity in the phrenic nerve [21, 22, 24]. Finally these studies showed that the amplitude of respiratory sinus arrhythmia was positively correlated to the $P_{\text{CO}_2}$ level of the arterial blood [21]. This theory is also sustained by the evidence of LF and HF components in the discharge variability of brain stem neurones recorded in cats with sino-aortic deafferentation [25]. These oscillations when entrained by afferent stimuli from receptors in the lungs and thoracic wall in time with respiration may result in the oscillations in heart rate called respiratory sinus arrhythmia.

Other Theories

Other theories have been proposed. It has been suggested that heart rate fluctuations could result from reflexes other than the baroreflex, e.g. cardiopulmonary reflexes, including those from lung stretch reflexes [26, 27]. However studies investigating the relationship between lung expansion and the amplitude of respiratory sinus arrhythmia, independent of simultaneous changes in intrathoracic pressure, excluded the role of reflexes from the lungs or the thoracic wall [28]. Another hypothesis is that local stretch of the sinus node causes changes in the spontaneous depolarization rate [28]. Whether and to what extent all these reflexes contribute to RSA is still controversial.

This review presents possible explanations for the discrepancies between the different hypotheses and describes some preliminary and confirmatory experiments based on the peripheral theory which follows from a development of the De Boer model for the origin of the LF and HF peaks in the PSA [16]. The De Boer hypothesis could also explain why conditions which are associated with a reduction in gain of the arterial baroreflex control, such as exercise or heart failure [8, 29, 30], are also associated with diminution of the LF peak, despite other good evidence of increased sympathetic tone [7, 15, 16].

Baroreceptor Stimulation: The Neck Suction Technique

To study the contribution of the arterial carotid baroreceptors to the origin of fluctuations in physiological signals, we have used the neck suction technique. Activation/deactivation of the arterial baroreceptors can be achieved also by pharmacologic methods (such as phenylephrine and amyl nitrite) [31] and physiologic methods (such as the Valsalva manoeuvre) [32], or by manipulations of respiration [33].

With respect to physiologic methods, the neck suction technique has the advantage that the stimulus is ‘purely’ autonomic. In other words, the mechanical effect of the suction does not extend beyond to the neck region, so any haemodynamic changes that can be observed in the heart, blood pressure, microcirculation or other areas can only be ascribed to reflex effects from the carotid baroreceptors. Respiration per se involves complex changes
in venous return, stroke volume and blood gases, and in addition the Valsalva method provokes major increases in intrathoracic pressures, interfering with cardiac contractility, venous and arterial pressures and peripheral circulation [34]. Pharmacologic stimulation, on the other hand, modifies the blood pressure directly. As a consequence the baroreceptor response on the blood pressure/peripheral vessels cannot be observed. In contrast, neck suction selectively acts at the baroreceptor site, and this enables observation of the effects both on the heart and on the circulation. Figure 3 shows an example of this: a rather strong impulsive suction, lasting 600 ms, from 0 to –55 mm Hg was delivered to the neck region of a subject while a Swan-Ganz catheter was inserted into his right atrium; this resulted in no changes in the right atrial pressure. Similar results can be obtained when a sinusoidal, rather than impulsive, suction is delivered.

**Effect of Arterial Baroreceptor Stimulation on the Cardiovascular System: A Frequency-Dependent Phenomenon**

It is well known that activation/deactivation of the arterial baroreceptors affects not only the heart but also the circulation. Much less effort has been spent on the study of the circulation response. For example, the standard method of testing the baroreflex sensitivity using vasoactive drugs cannot explore the baroreflex effect on blood vessels, since the drugs act directly as well as reflexly on vascular smooth muscle. Furthermore, none of the methods currently used allow direct evaluation of the frequency response of the cardiovascular system to a baroreceptor stimulus. This is probably of primary importance, as most of the interactions in real life are dynamic, and most of the cardiovascular regulation appears to occur through phasic, rather than static changes of different ‘offsets’. Drawing on previous experience [35, 36] we have designed a new method of stimulating the arterial baroreceptors at several frequencies similar to those of the spontaneous rhythms. We used the neck suction with a sinusoidal pattern of constant amplitude for each frequency and examined the responses in various parts of the cardiovascular system. For this kind of experiment it is of the greatest importance that respiration is maintained at a frequency different from that of the stimulation, but not outside the physiologic range. We normally use 0.25 Hz, equivalent to 15 breaths/min. This can be easily differentiated from even fastest stimulation, which is 0.20 Hz (fig. 4). We have consistently found [17, 37] that in a normal subject all components of the cardiovascular system are highly sensitive to stimulation of about 0.1 Hz: R-R interval, systolic and diastolic blood pressure, skin microvessels (fig. 4), and even muscle
sympathetic nerve activity [38] can typically respond to this frequency. In contrast, if the stimulation frequency is in the respiratory band (0.20 Hz), only R-R interval and muscle nerve sympathetic activity are able to respond, but no response can be induced in the blood pressure (either systolic or diastolic) or in the skin microvessels. This finding supports the view that the respiratory fluctuations seen in the vasculature are probably of mechanical origin perhaps resulting from changes in stroke volume induced by respiratory changes in venous return to the left heart, whereas those at lower frequency are primarily due to autonomic activity. This suggests that the vasculature (arteries and microvessels) react to a stimulus of the arterial baroreceptors with a low-pass behaviour.

Recently, we have further investigated the frequency-dependent effect of arterial baroreflex stimulation in the cardiovascular system by expanding the capabilities of the neck suc-
tion technique [38]. A sinusoidal function of constant amplitude, and with suction from 0 to −30 mm Hg, was used with continuously changing frequencies with time, from 0.02 to 0.20 Hz over a 5-min period. We found that all signals showed the greatest response in the 0.1-Hz region. These results might explain why rhythms of possibly different origin (due to a loop in the baroreflex, or directly originating in the brainstem, or locally) and perhaps with different frequencies might all induce a vascular rhythm in the 0.1-Hz band despite the well-known fact that the sympathetic nerves carry both the respiratory and 0.1-Hz components [2, 39].

Other authors have attempted to characterize the behaviour of the cardiovascular control mechanisms in the frequency domain. Both Saul et al. [40] and Novak et al. [41] used respiration as an input in their models. However, Saul et al. [40] used a ‘random’ signal in order to obtain an ideally equal distribution of frequencies throughout the spectrum, and which entitled them to use a standard spectral method. In contrast Novak et al. [41] only used controlled respiration at different frequencies. In our model, instead of using respiration, we directly stimulated the arterial baroreceptors, and hence we could obtain a result free from the direct haemodynamic consequences of breathing. It is remarkable to note that these three different approaches gave quite similar results: in all cases a low-pass behaviour for the blood pressure was found, and in all models a greater response in the 0.1-Hz region could be obtained for all signals evaluated. The fact, however, that our model primarily interferes only with the arterial baroreceptors suggests that their results also might be explained in terms of the response of the arterial baroreceptors. These results indicate that the arterial baroreceptors can exert a strong influence on cardiovascular fluctuations, which is clearly frequency-de-

**Role of the Arterial Baroreceptors in the Genesis of 0.1-Hz (LF) Fluctuations**

Several researchers [16, 42] have suggested that the 0.1-Hz oscillation is due to the phase lag in the baroreceptor loop. According to this theory, a single fast perturbation of the cardiovascular system (say a single deep breath) should be able to initiate this chain of events and generate an oscillation in the cardiovascular system; however, these will probably damp out if no other stimulus (for example, another breath) arrives. Although respiration can be used to test this hypothesis, a stimulus applied to the neck region appears far more appropriate, as it does not have any direct mechanical/haemodynamic effect.

We therefore applied a short and fast (600 ms, from 0 to −40 mm Hg) suction to the neck of 11 healthy volunteers, and observed the resulting fluctuations in the cardiovascular system. In order to remove the complicating influence of continuous changes in venous return caused by respiration we carried out this transient perturbation during 20 s of apnoea. This apnoea period started at the end of expiration, so that only the delay in the baroreceptor loop could be responsible for the changes observed [43]. In each subject the signals were analysed after averaging of the recordings obtained in 10 neck suctions. A sudden bradycardia from 1,037 ± 47 (mean ± SEM) to 1,204 ± 46 ms (p < 0.001) and a drop in blood pressure was followed in 1 or 2 beats by a peripheral vasoconstriction evaluated by infra-red photoplethysmography. Fol-
following this the blood pressure rose again. After a lag of 1–2 beats after the blood pressure increase, the R-R started to increase again. This created a cycle in the R-R and blood pressure equivalent to a frequency of 0.098 ± 0.007 Hz, which was followed by a second cycle of similar frequency (0.100 ± 0.008 Hz) but at a lower amplitude (fig. 5). Due to the resumption of respiration we could not observe a third cycle in most subjects although this was evident in a few who could better tolerate the apnoea. Therefore the overall trend closely resembled a damped oscillation in the R-R interval, generated by, or related to, an interplay of the blood pressure and arteriolar constriction-dilation phases. This was strikingly similar to a previously published computer simulation of the effect of baroreflex according to the loop theory [44].

In addition, the spontaneous LF component obtained in the R-R interval spectrum of a baseline recording was 0.093 ± 0.005 Hz, similar (p: NS) to the frequencies of the damped oscillations in the R-R interval after neck suction. Furthermore, the frequency of this spontaneous LF component correlated with that of the damped oscillation after neck suction in each subject (r = 0.715, p < 0.025; fig. 6) [43]. These results show that a sudden stimulation of the arterial baroreceptor can initiate a 0.1-Hz oscillation in the cardiovascular system, similar to that observed at rest without any stimulation: its damped effect indicates that the persistence of the stimulus is essential to maintain it, and argues against a role played by the central nervous system in the generation of this particular phenomenon. Although a transient at the carotid sinus might momentarily entrain a pre-existing central oscillation, this would have different time relationships, and one would not expect a damped oscillation. Conversely, the period of this oscillation seems to be entirely due to the delay of response of the whole system (baroreceptor response + nervous transmission + neurovascular coupling + contraction time of microcirculation). This theory can also explain why atropine abolishes most of the LF as well as the HF components. The reduced vagal drive cannot then 'transmit' the 'sympathetic' information produced by the sympathetically induced oscillation in blood pressure.
Origin of Respiratory Sinus Arrhythmia (HF Fluctuations): An Important Role for the Arterial Carotid Baroreceptors

Assuming the 'loop' theory is correct, we should be able to increase or decrease both the LF and the HF component by appropriate manipulation at the site of the arterial baroreceptors. For example, by suppressing respiration, the input to the loop, we should expect no fluctuations in the cardiovascular system. However, accepting the idea that respiration activates the loop due to the respiration-related fluctuations in blood pressure, sensed by the arterial baroreceptors, one should be able to abolish the input to the baroreceptors without really altering respiration. We therefore used neck suction with a sinusoidal function, tuning the suction pressure to be similar to that observed in the respiratory variations of blood pressure for each subject. The frequency of the suction was then synchronized with that of respiration, and the phase between suction and respiration was changed in each recording, in order to approximate a wide range of possible conditions (in phase, phase opposition, quarter of phase leading and lagging). We consistently found in each subject that at a given phase we could reduce by about 50%, rather than increase, the respiratory component of the R-R interval synchronous with respiration and the neck suction; in addition, at that same phase, also the LF was consistently reduced (fig. 7) [45]. Similar results were obtained in the blood pressure. Complete suppression could not be expected, due to the obvious limitations of the experiment, and to the persistence of information from aortic and other baroreceptors, and/or perhaps also because of other operating mechanisms such as a central oscillator. However, this experiment indicates that a stimulus to the arterial baroreceptors does not necessarily cause an increase in fluctuations; this depends critically on the interaction with the frequency and timing of the fluctuations in blood pressure sensed in the carotid receptor region.

During undisturbed apnoea, HF fluctuations were much reduced and at a rhythm similar but generally slower than that of respiration before apnoea. Furthermore, during the first part of apnoea, the LF fluctuations of heart rate variability were also markedly reduced. In addition the blood pressure fluctuations at the respiratory frequency were reduced, which accounted for the decrease in R-R interval fluctuations during apnoea. When the apnoea was performed during neck suction and cycled at the same frequency as the prior respiration, sinus arrhythmia re-
mained unchanged, and at the onset and at the end of the apnoea were almost indistinguishable in the R-R interval patterns.

**Arterial Baroreceptors Are Not Responsible for All 0.1-Hz Fluctuations**

According to other authors, however [20], arterial baroreflexes play no major role in the genesis of LF oscillations, which are considered more as the result of a respiratory ‘entrained’ central oscillation. In fact procedures or interventions that have different effects on arterial baroreceptors, such as nitroglycerin infusion causing increased baroreflex sensitivity, myocardial ischaemia with no change in sensitivity and moderate physical exercise, yielding decreased sensitivity, have been reported to increase the LF [2]. According to the ‘loop’ theory an oscillation should start only if a perturbation such as a deep breath changes the blood pressure, and we have observed that in apnoea this baroreceptor-induced oscillation damps out [43]. As a consequence, if the 0.1-Hz rhythm were only the result of this baroreflex oscillation, no LF should be observed during a prolonged and well-tolerated apnoea. The apnoea seems thus a good model to test the uniqueness of the ‘loop’ theory. We therefore observed the changes in R-R interval and blood pressure after prolonged 30- to 50-second apnoea in healthy subjects.

Figure 8 shows that during undisturbed apnoeas slow R-R interval and blood pressure fluctuations appear and tend to be sustained or increase toward the end of the apnoea [38]. The frequency of these fluctuations was significantly lower than that observed during spontaneous or controlled breathing; in addition, different patterns of respiration or different patterns of neck suction, induced in the pre-apnoea period, could not alter, or minimally altered, the power and the frequency of this oscillation during apnoea. These results suggest that the genesis of the fluctuations in the 0.1-Hz band is complex: the presence of 0.1-Hz fluctuations in apnoea contrasts with their origin from the ‘loop’ model and hence with their origin by the arterial baroreflex; these findings rather suggest that a central oscillator might be the cause for this fluctua-
Fig. 8. Effect of apnoea on cardiovascular fluctuations. R-R interval and blood pressure fluctuations during apnoea in a normal subject. Note evident slow fluctuations, in the range of the LF band, different from those determined by respiration in the pre- and post-apnoea periods.

diet, at least when the ‘loop’ phenomenon is not activated. It is also interesting to note that the frequency of this apnoea-LF is significantly lower than that of the spontaneous LF rhythm, which in turn is in general slightly slower but not statistically different from that of the baroreceptor-induced damped oscillation: although no simultaneous experiments with prolonged apnoea and impulsive neck suction were carried out, it is possible to speculate that in normal subjects and/or in normal conditions, when the arterial baroreflex is efficient, the 0.1-Hz fluctuation is predominantly the result of the ‘loop’ phenomenon, whereas when it is inefficient or inactive, other factors could be the main determinants of the 0.1-Hz fluctuation. The results obtained during physical exercise provide some support for this hypothesis: in two groups of healthy subjects, sedentary and trained athletes [6], before the start of bicycle exercise, the period of the LF was 0.093 ± 0.009 Hz in the sedentary and 0.103 ± 0.002 Hz in the athletic subjects, and decreased to 0.060 ± 0.005 Hz (p < 0.05) and to 0.058 ± 0.008 Hz (p < 0.01) at peak exercise, respectively. Although the role of the arterial baroreflexes during physical exercise is controversial, there is general agreement that with increasing intensity of exercise the overall autonomic modulation to the heart decreases, and although the stimulation of the arterial baroreceptors at specific slow frequencies (in the range of 0.07 Hz) can still cause changes in R-R interval [46], the standard methods of testing the arterial baroreflex, such as the phenylephrine method, indicate a reduced baroreflex sensitivity during intense exercise. It is then possible to speculate that this slowing of the LF rhythm is evidence of a reduced influence of the arterial baroreflex on the heart, whereas a slower central oscillator can still influence the cardiovascular system. Further support for this model comes from the observation that subjects with diabetes, a condition known to reduce the efficiency of the arterial baroreceptors [47], exhibit an LF rhythm which is consistently slower throughout the 24 h [12], or, similarly, the well-known observation that respiratory sinus arrhythmia in diabetic subjects with autonomic neuropathy is maximal at a frequency lower than the 0.1 Hz of normal subjects [48]. Further experiments are clearly needed to clarify whether these findings are indeed evidence of rhythms of different origins, or
simply the result of a different mode of functioning of the same mechanism (either baroreceptor or central).

**Clinical Implications**

We now turn to consider how PSA allows evaluation of activity of the arterial baroreceptors both in physiological and pathological conditions.

**Physical Exercise**

First we used PSA to assess the contribution of the baroreflex in the haemodynamic responses to exercise. In particular we evaluated the mechanisms of the hypotensive effect of exercise both acutely and after long-term physical training. It is well known that after an acute bout of exercise blood pressure falls, sometimes for several hours: the underlying mechanisms are still controversial. In normotensive individuals the role of the autonomic nervous system, haemodynamic, and renin activity have been investigated [30]. The fall in blood pressure lasted for 1 h: this was not attributed to a fall in cardiac output which instead increased, due to a persistent tachycardia. A persistent systemic vasodilatation was present, which induced as reflex responses sympathetic activation and vagal withdrawal. The baroreflex sensitivity was assessed by two methods, i.e. by the slope of the changes in blood pressure against heart rate induced by bolus injection of phenylephrine, and by the spectral analysis of R-R and blood pressure variability alpha index [29]. Both methods demonstrated that baroreflex sensitivity was reduced for the first 30 min after exercise, which was consistent with the sympathetic activation seen after exercise. This suggests that the baroreflex sensitivity plays little if any role in the hypotension during the period immediately after exercise in normals.

The interpretation of autonomic and haemodynamic changes seen after a prolonged exercise in well-trained subjects is more complex. Although it is well known that physical training lowers heart rate and blood pressure [29], the mechanisms which lead to these effects are not well understood. In order to clarify the contribution of autonomic control of heart rate and arterial vessels to prolonged exercise in trained subjects, we studied the arterial baroreflex activity after a 32-mile marathon [49]. Immediately after exercise a sympathetic predominance was also observed in well-trained subjects, with a reduced effect of parasympathetic baroreceptor stimulations. However 24 h later, the effect of parasympathetic stimulation to the baroreflex activity was increased (p < 0.0005) compared to the day before the marathon, whereas the sympathetic stimulation by neck suction was no longer effective on blood pressure. Thus, the post-effect reverses to an increased sensitivity to vagal and reduced sensitivity to sympathetic baroreflex stimulation and suggests a possible mechanism for training-induced increase in vagal tone: while sedentary subjects respond to exercise with prolonged sympathetic activation [as shown in ref. 30] after physical training the effect of exercise induces a prolonged vagal activation, further suggesting that post-exercise vagal overactivity develops as an effect of training. Further studies are warranted to clarify this observation.

**Cardiac Reinnervation after Human Heart Transplantation**

In the immediate period after cardiac transplant, the heart is thought to be denervated. Subsequently during the 2nd year, the presence of reinnervation has been suggested. To evaluate the presence of reinnervation we used power spectral analysis to stimulate the carotid baroreceptors by our neck suction technique [37]. All transplant patients pre-
sented small HF fluctuations which, independent of autonomic tone, result from the stretch of the donor atrium caused by the inspiratory increase in venous return. Instead non-respiratory LF fluctuations were present in 13 of 26 transplant patients and increased with months since transplantation, confirming the hypothesis of reinnervation. After HF neck suction no response was observed in the patients, while LF neck suction induced a small response in the patients; the neck suction-induced increase in LF fluctuations persisted after administration of atropine, but were attenuated by beta-blocker treatment, suggesting sympathetic reinnervation.

Conclusions

In conclusion, these observations indicate that the arterial baroreceptor exert a strong, though not exclusive influence on the cardiovascular fluctuations, through both sympathetic and vagal activity; the LF component appears to be generated not only by resonance in the cardiovascular system, but also by other independent factors, such as a central oscillator. Moreover the baroreceptors seem to play a major part in the genesis of respiratory sinus arrhythmia.

We can only speculate on the conditions that determine the presence or the prevalence of one factor over the other and call for specific investigations. However, some observations do indicate that both physiologic and pathologic conditions such as physical exercise, diabetic neuropathy, cardiac transplantation, can induce marked changes in the frequency of the spontaneous LF oscillation. To what extent this is evidence of the rhythms being of different origin, or just a change in the dynamic interaction between the same parts of the autonomic and cardiovascular system remains to be established.

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