Cardiac- and noncardiac-related coherence between sympathetic drives to muscles of different human limbs

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Kocsis, Bernat, Tomas Karlsson, and B. Gunnar Wallin. Cardiac- and noncardiac-related coherence between sympathetic drives to muscles of different human limbs. Am. J. Physiol. 276 (Regulatory Integrative Comp. Physiol. 45): R1608–R1616, 1999.—Partial coherence analysis was used to evaluate the extent to which coherence between resting muscle sympathetic activity (MSA) in different pairs of limbs in humans is explained by the common baroreceptor input and by other noncardiac-related factors. Multunit MSA in two or three nerves, arterial blood pressure, and electrocardiogram were recorded simultaneously. Correlated MSA consisted of a sharp periodic component at the heart rate and a wideband component of relatively low power distributed between 0 and 2–2.5 Hz. Quantitative analysis revealed stronger coupling between MSAs in close limbs than in distant limbs (peak coherence leg-leg, 0.94 ± 0.03; arm-leg, 0.76 ± 0.11). Furthermore, the wideband component, unaffected by partialization with circulatory signals, was significantly stronger between leg-leg (0.67 ± 0.10) than between arm-leg pairs (0.29 ± 0.10), i.e., noncardiac-related components explained 71% of leg-leg and 38% of arm-leg coherences at the frequency of the heart. Our results indicate that nonuniform relationship exists between resting sympathetic outflow to muscles in close and distant extremities which is, however, partially masked by the effect of the common rhythmic baroreceptor input.

There is a remarkable similarity between human resting muscle sympathetic activity (MSA) recorded simultaneously from nerves in the two legs or in the arm and leg (19, 21, 22, 24), indicating that common mechanisms are involved in the generation of resting activity to muscles in different extremities. During maneuvers such as mental stress (1), postcontraction muscle ischemia (24), or voluntary activity (22), there are, however, clear differences between MSAs recorded simultaneously in arm and leg nerves or even in nerves to different legs. An important mechanism modulating MSA is the rhythmic input from the peripheral baroreceptors, and there is evidence that the effect of baroreceptor input on sympathetic outflow may change dynamically and that such changes may show regional specificity. During mental stress, for example, sympathoexcitation was reported to override baroreceptor inhibition in the leg but not in the arm MSA (1).

In an earlier report, the contribution of common drives was quantified for leg-leg recordings by calculating the peak coherence between the neurograms (24). Inasmuch as MSA occurs in pulse-synchronous bursts, the highest coherence was found at a frequency corresponding to the heart rate (HR). At this frequency the baroreflex imposes a high degree of similarity between MSAs, and it is not known whether, in addition to this dominating influence, other factors contribute to the MSA-MSA coherence.

The purpose of the present study was to evaluate to what extent MSA-MSA coherence is explained by the common baroreceptor input and by other noncardiac-related factors. To this end, we have analyzed mean voltage neurograms of MSA obtained in simultaneous recordings from different arm and leg nerves using the method of “theoretical barodenervation” (16). This partialization technique eliminates that part of the nerve-to-nerve coherences that can be explained by variations in the cardiac rhythm and therefore allows an analysis of the residual coherence reflecting the effect of other common noncardiac-related drives. Similar analysis of the discharge in functionally different sympathetic nerves was used earlier to reveal patterns of differential coupling between generators within the central sympathetic network in the anesthetized cat (2, 10, 16).

METHODS

Subjects. After approval of the ethics committee of the Sahlgren University Hospital of Göteborg and with the informed consent of the subjects, experiments were made in 11 healthy subjects, aged 44 ± 6 (range 23–73) yr. None of the subjects was on any form of medication.

Nerve recording technique. Simultaneous recordings of resting multunit MSA were made from nerves in different extremities. In four subjects recordings were made in the right radial nerve at the spiral groove and in the left peroneal nerve at the fibular head, in six subjects from the two peroneal nerves at the fibular heads, and in one subject in the two peroneal nerves and the left radial nerve. The nerve recordings were made with tungsten microelectrodes that were inserted manually into a muscle nerve fascicle of the respective nerve and adjusted until a position was found in which bursts of sympathetic activity could be recorded. The neural activity was amplified (∼50,000), filtered (700–2,000 Hz), and led to an audiomonitor and through a resistance-capacitance integrating circuit (time constant 0.1 s) to obtain a mean voltage record of the sympathetic activity. Details about the technique have been published previously (21).

Other measurements. An electrocardiogram (ECG) was recorded via surface electrodes on the chest. Arterial blood pressure (BP) was measured with the volume clamp technique (Finapres, Ohmeda, Louisville, KY) with a cuff around the third left finger. Analog signals of mean voltage neuro-
grams, ECG, and BP were stored on magnetic tape (V-store, Racal, Southampton, UK) for later analysis.

Experimental procedure. Subjects were supine. When devices for recording ECG and BP had been applied, nerve recording electrodes were inserted and suitable recording sites were defined. After this, resting activity was recorded for at least 10 min. Later in the experiments, other rest periods were also obtained between various maneuvers, such as lower body negative pressure, deep breathing, or isometric hand-grip contractions, etc. (4, 19, 22, 24). Data on the effects of the maneuvers have been published previously, and only rest periods were reanalyzed in the present study (19, 22).

Data analysis. Data analysis from the rest periods consisted of computations of the autospectra for each signal and the ordinary and partial coherences for different signal pairs. Mean voltage neurograms together with BP and ECG were digitized with a sampling frequency of 200 Hz. Fast Fourier transform was performed on sets of three signals either including three MSA signals or two MSAs with BP or ECG. Artifact-free segments of resting activity were selected and divided into contiguous windows of equal length (~5 s, containing 1,024 data points). For each window, the autospectra for all signals as well as the cospectrum and the quadrature spectrum for each pair of signals were computed. The raw spectra were smoothed with a three-point moving average and averaged over the windows. For this calculation, yielding spectra with a resolution of 0.2 Hz/bin, continuous 200- to 600-s data segments were used. To obtain spectra with finer resolution (0.05 Hz/bin), the calculations were repeated for the signals resampled at a rate of 50 Hz. The 20-s windows (n = 22–55) averaged in this case were taken from different parts of the recording, i.e., they were not necessarily contiguous. The autospectra, the squared ordinary coherence spectra, and partial coherences were calculated using the algorithms described by Kocsis and co-workers (15, 17) and by Jenkins and Watts (13).

Coherence spectral analysis gives the following information. The ordinary coherence between two signals measures the linear correlation between these signals, and high coherence indicates that they originate in part from common sources. Because for MSA exhibiting cardiac rhythmicity these will certainly include the common baroreceptor input partialization of the nerve-to-nerve coherence with any signal that reflects the peripheral cardiovascular rhythm, e.g., BP or ECG, will eliminate from this coherence the part that can be predicted from variations of the BP. Thus the residual MSA-MSA coherence, i.e., the partial coherence, will measure the correlation between the two nerves that can be explained by influence of common inputs other than that coming from the baroreceptors.

Statistics. Group data were calculated using coherence values measured at the peak frequency, i.e., at the HR, and are presented as means ± SE. Significance of differences was analyzed using Student’s t-test on coherences subjected first to Fisher’s z-transformation to obtain estimates with approximately normal distribution (15). The variability of peak-to-peak differences was characterized by their group variance and the kurtosis of their distribution. Differences between variances were tested using the F-test. Significance was accepted at P < 0.05.

RESULTS

Figure 1 demonstrates examples of MSA simultaneously recorded in two nerves along with cardiovascular and respiratory parameters in two subjects. In all recordings, MSA was waxing and waning with the frequency of the heart beat, granting the nerve signals

Fig. 1. Specimen recordings of electrocardiogram (ECG), muscle sympathetic nerve activity in left and right peroneal nerves (MSA1 and MSA2), blood pressure (BP), and respiration (Resp) in 2 subjects (A and B) at rest in supine position. The 2 subjects differed in frequency of their heart beat (1.4 and 1 per s in A and B, respectively). Short segment of 3 signals (ECG, MSA1, and MSA2) from A and B (see boxes) are shown on different time scale in C and D, respectively. Falling segment of each burst is indicated by vertical time markers. Length of horizontal markers is equal to latency between peak and end of largest burst in each MSA recording. Horizontal markers are provided to aid visual assessment of fluctuations of peak location relative to this marker due to changes in the burst amplitude.
their characteristic cardiac rhythmicity (3). The nerve signals were not clear sinus waves; however, they rather represented a sequence of rhythmically occurring bursts of variable amplitude and duration with their falling phase synchronized to the cardiac cycle (Fig. 1, C and D; see also Ref. 23). Separation of bursts was especially noticeable when the HR was relatively slow, allowing for a segment of zero activity between bursts occurring even in consecutive cardiac cycles (Fig. 1B), whereas in subjects with higher HR the MSA signal appeared more sinusoidal (Fig. 1A).

Separation of cardiac- and noncardiac-related components of MSA. Inasmuch as most of the power in muscle sympathetic neurograms was concentrated at the cardiac frequency, all MSA autospectra computed in the present study contained a single large narrow peak at the HR, which was similar in shape to the cardiac peak of BP and ECG autospectra (Figs. 2A and 3). Furthermore, all nerve recordings were highly coherent with both BP and ECG signals, and the relationships between MSA and BP or ECG were similar for different nerves (Fig. 2B). The coherence functions consisted of high narrow peaks at the HR and its harmonics.

There was high coherence between MSAs simultaneously recorded from different nerves, and this coherence also reached its maximum at the HR (Figs. 2C and 3). As revealed by partial coherence analysis, the common baroreceptor input always made a significant contribution to this peak in the nerve-to-nerve coherence functions. In the experiment shown in Fig. 2, for example, mathematical elimination of the cardiac-related components from both neurograms reduced the MSA-MSA coherence at the HR from 0.95 to 0.68, i.e.,
by 28% (Fig. 2, D and E). The coherence between residual MSAs, however, remained highly significant, indicating that rhythmic afferent baroreceptor input was not the sole factor determining MSA-MSA coherence at the HR.

In contrast to MSA-BP and MSA-ECG coherences, the coherence functions connecting different nerve activities contained an additional wideband component, the relative power and the frequency range of which varied between subjects. In subjects with relatively high HR (1.2–1.4 Hz, see e.g., Fig. 1A), this component appeared mainly at low frequencies (<HR) and also as a relatively broad base of the HR peak (Fig. 2C). Partialization in these experiments did not change the shape of the coherence function, only decreased the peak at the HR (by 0.20 ± 0.06, n = 3). When the cardiac cycles were longer (HR = 1 Hz in Fig. 1B), the wideband component distributed over a wider range of frequencies between 0 and 2–2.5 Hz (Fig. 3, A and B). In these cases partialization with BP or ECG signal completely eliminated the HR peak from the MSA-MSA coherence, leaving the noncardiac-related wideband component unchanged (decrease of coherence at HR by 0.31 ± 0.04, n = 4). In either case, the wideband component was not affected by partialization with signals reflecting the cardiac rhythmicity, indicating that it originated from common central generators of sympathetic activity.

Regional differences between MSA in upper and lower extremities. The general characteristics of nerve-to-nerve coherences were similar for arm-leg and leg-leg recordings (compare, e.g., Fig. 3, A and B) in that in both types of pairs both the periodic cardiac and the wideband (noncardiac) components were present and that the two components could be separated by partialization with BP or ECG; i.e., the variance reflected in the cardiovascular signals explained part of the coherence between nerve recordings at the HR but did not affect the coherences at other frequencies.

Quantitative analysis of the coherence functions revealed stronger coupling between MSAs recorded from close limbs than from distant limbs (Table 1). On average, peak coherence values measured at HR between leg-leg recordings were higher (0.94 ± 0.03, range 0.88–0.97, n = 7) than those between arm-leg recordings (0.76 ± 0.11, range 0.54–0.86, n = 6, P < 0.02). More importantly, the proportion between cardiac-related and noncardiac-related fractions of the MSA-

### Table 1. Quantitative analysis of coherence functions

<table>
<thead>
<tr>
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<th>Ordinal (total)</th>
<th>Partial (noncardiac)</th>
<th>Ordinal-partial (cardiac)</th>
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<tbody>
<tr>
<td><strong>Left leg</strong></td>
<td>0.94 ± 0.03</td>
<td>0.67 ± 0.10†</td>
<td>0.26†</td>
</tr>
<tr>
<td><strong>Right leg</strong></td>
<td>0.76 ± 0.11</td>
<td>0.29 ± 0.19†</td>
<td>0.47†</td>
</tr>
<tr>
<td><strong>Arm</strong></td>
<td>0.83 ± 0.03</td>
<td>0.10 ± 0.08*</td>
<td>0.10 ± 0.06*</td>
</tr>
<tr>
<td><strong>Leg</strong></td>
<td>0.82 ± 0.04</td>
<td>0.42 ± 0.12†</td>
<td>0.09 ± 0.07*</td>
</tr>
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Values are means ± SE; n = number of subjects. MSA, muscle sympathetic activity; BP, blood pressure; ECG, electrocardiogram.

*Significantly different before and after partialization. †Significantly different for nerve pairs of distant and close limbs or for 2 simultaneously recorded MSAs.

MSA coherences showed a remarkable difference when the distant and close nerve pairs were compared. The wideband component was significantly stronger (P < 0.001) between leg-leg (0.67 ± 0.10, range 0.54–0.84) than between arm-leg MSA pairs (0.29 ± 0.10, range 0.19–0.38), whereas the cardiac-related peak, eliminated by partialization with BP or ECG, was stronger (P < 0.03) in arm-leg than in leg-leg recordings (0.47 and 0.26, respectively). Thus the common drives contributing to different nerve pairs had different compositions; noncardiac-related components explained 71% of leg-leg and 38% of arm-leg coherences at the HR.

In the time domain, differential coupling results in dissimilar distributions of the intervals between corresponding MSA bursts, i.e., those occurring within the same cardiac cycle, in two different nerves (Fig. 4). Hence the intervals between corresponding peaks of arm-leg and leg-leg MSA pairs differed not only in their mean value, due to obvious differences in arm and leg MSA latencies (21, 23), but their variance was also significantly different (P < 0.001). The fluctuations of burst latency in one leg MSA closely followed those in the other leg, whereas the intervals between arm and leg MSA bursts were more dispersed. As shown in Fig. 4, the interval between corresponding MSA bursts, i.e., those occurring within the same cardiac cycle, in different nerves (Fig. 4). Hence the intervals between corresponding peaks of arm-leg and leg-leg MSA pairs differed not only in their mean value, due to obvious differences in arm and leg MSA latencies (21, 23), but their variance was also significantly different (P < 0.001). The fluctuations of burst latency in one leg MSA closely followed those in the other leg, whereas the intervals between arm and leg MSA bursts were more dispersed. As shown in Fig. 4, the distribution histograms of peak-to-peak intervals between arm-leg and leg-leg MSA bursts. The 2 histograms were shifted so that their modes appeared superimposed (mean for arm-leg pairs, 350 ms; for leg-leg pairs, 0 ms). Inset: 2 intervals (d1, d2) in specimen arm-leg recording.
4, the interval distribution between corresponding bursts in close limbs was significantly leptokurtic (kurtosis = 6.11) in contrast to the platykurtic distribution of arm-leg burst intervals (kurtosis = -0.12).

In addition to the quantitative differences in the small variations of amplitude and latency of corresponding arm and leg MSA bursts, single bursts occasionally appeared in one of the neurograms without counterpart in the other, simultaneously recorded neurogram (see sample recording in Fig. 5E). The highest number of such unmatched bursts was observed in arm MSA recordings paired with leg MSA (27.0 ± 5.4%), whereas only 3.7 ± 1.9% of leg MSA bursts appeared on the background of silent arm MSA in these same experiments (P < 0.05; n = 4). The number of unmatched bursts in leg-leg pairs was low and balanced between the two MSAs (2.5 ± 1.2 and 3.3 ± 0.9%, P = 0.34; n = 6). Because the unparalleled bursts were locked to the cardiac cycle, these nonuniformities could also be examined by partial coherence analysis (Fig. 5). The effect of partialization of the MSA-BP or MSA-ECG coherences for one of the nerves by the other simultaneously recorded nerve signal was different for leg-leg and arm-leg pairs. In arm-leg pairs, cardiac-related coherence was completely eliminated from leg MSA by partialization with arm MSA, but arm MSA appeared to retain a cardiac-related component, i.e., not explained by the variations in leg MSA (Fig. 5, C and D). On average, the residual arm MSA-ECG coherence was 0.42 ± 0.12 (n = 6), whereas partialization with arm MSA reduced leg MSA-ECG coherence to 0.09 ± 0.07 (Table 1). On the other hand, in leg-leg recordings this analysis yielded symmetrical changes in MSA-BP coherences (i.e., reduction of peak coherences to 0.10 ± 0.08 and 0.14 ± 0.06 for left and right legs, respectively; see Table 1), indicating that such gating of all baroreceptor-related components in leg MSAs was common for the two legs (Fig. 5, A and B).

Analysis of simultaneous arm-leg-leg MSA recording. The above correlation pattern was supported by the results of partial coherence analysis of neurograms recorded simultaneously from the left arm and both legs in one subject (Fig. 6). As indicated by the shapes of the autospectra, all three signals were composed of strong periodic and wideband components (Fig. 6A). Accordingly, in all MSA-MSA (ordinary) coherence functions the HR peak was riding on top of a large wideband component. Peak coherences measured at HR were slightly different for different nerve pairs (0.92, 0.84, 0.79; Fig. 6B), but the cardiac peaks were all eliminated by partialization using the ECG or the BP signal (Fig. 6D). There were more substantial differences, however, between the wideband components. The residual coherence that remained after elimination of the cardiac peak from the coherence functions relating the two leg recordings was significantly stronger than those for the arm-leg pairs at each frequency between 0 and 2.5 Hz, including the frequency of the HR.

Simultaneous recording of three nerve signals allowed, in addition, a detailed analysis of the relationships between distant and close MSAs in the same subject. Partialization of the nerve-to-nerve coherences with the third MSA signal (i.e., instead of the BP or ECG; Fig. 6C) suggested a pattern of coupling in which the wideband components of the MSAs of the two legs appeared to reflect the activity of one single (or strongly coupled) generator, which was separated from that driving noncardiac-related arm MSA. Most of the coherences between MSA in the arm and in either of the legs were eliminated by partialization using the other leg nerve signal, indicating that almost all arm-leg coherences could be explained by the variations in the other leg MSA. The residual partial coherence between the MSAs in the two legs, however, was high in a wide range of frequencies, revealing common components in
leg nerve recordings that were not present in MSA in the arm.

**DISCUSSION**

The primary finding of this study was that nonuniform relationship exists between resting sympathetic outflow to muscles in close and distant extremities that is, however, partially masked by the effect of the common rhythmic baroreceptor input. The part of MSA originating from common drives in different nerves consisted of a sharp periodic component corresponding to the HR and a wideband component of relatively low power distributed over frequencies between 0 and 2–2.5 Hz. Partial coherence analysis revealed that the contribution of this latter component accounted for most of the differences between distant and close nerve pairs, i.e., a wideband component dominated leg-leg coherence functions but appeared relatively weak in connecting arm-leg MSAs.

Methodological considerations regarding the analysis technique. Partial coherence analysis used in this study is a theoretical tool for eliminating the “binding” effect of a certain input directed to two signal generators and to test whether the two generators are connected other than by this common input (11, 13, 14, 18). This method provides a quantitative estimate for the residual coherences between the two output signals, allowing examination of the strength of coupling between their source generators. In our study, the input signal represented the rhythmic changes transmitted by the baroreceptors to the central nervous system, and the generators tested were the ones sending sympathetic nervous output to muscle blood vessels in different regions of the body. Therefore the results of partialization as used here are in many ways similar to the effect of barodenervation used in animal experiments.

The effect of mathematical elimination of the cardiac-related component from pairs of simultaneously recorded sympathetic nerve activities on the coherences between them was studied earlier in animal experiments (10, 16). It was found that after partialization by the BP signal, both the peak values and the relative pattern of the coherences between different sympathetic neurograms were similar to those observed in baroreceptor denervated animals (16). However, the effects of the two procedures (i.e., theoretical and surgical barodenervation) were not identical. In addition to the shared input from the baroreceptors, there is a central coupling between sympathetic generators that is subject to dynamic changes depending on the state of the central networks. This cross-talk will not be affected by partialization but may be altered by changing the level of ongoing baroreceptor afferent input. It was found, for example, that the effect of partialization was weaker in unanesthetized decerebrate cats (10) than in cats under chloralose-urethan anesthesia (16). Most likely, this was due to different inherent rhythms of the brainstem networks characteristic for these preparations (i.e., 8–12 Hz and 2–6 Hz, respectively). Furthermore, the effect of partialization increased after vagotomy, a procedure that by itself did not change sympathetic nerve-BP coherence (10). Thus the method
of theoretical barodenervation does not replicate in each experiment all consequences of real baroreceptor denervation. It rather provides an estimate of the residual nerve-to-nerve coherence without changing the noncardiac-related interconnections between sympathetic generators. When these interconnections are strong, the part of the common variance in MSAs explained by the BP and ECG signals will be relatively small, and therefore the partialization will have a weaker effect. This may explain why partialization was less effective in states when the sympathetic circuits generated stronger rhythmic sympathetic nerve activity both in the cat (16) and in humans (this study, compare Figs. 2 and 3).

Possible mechanisms generating nonuniform MSA-MSA coherent discharges in close and distant limbs. The origin of the wideband component in the MSA spectra and its various features can be understood by comparing the present results with a previous time domain analysis of the morphology and baroreceptor latency of the MSA bursts (23). As shown earlier, human MSA signals are not clear sinus waves, but they rather represent a sequence of rhythmically occurring bursts of variable amplitude and duration. It was also demonstrated that the rhythmic baroreceptor inhibition strongly synchronized the falling phase of the bursts to the cardiac cycle and consequently the latency of the MSA peak varied in close correlation with changes in the amplitude of the bursts (23). Thus stronger MSA bursts exhibiting higher amplitude and longer duration start and peak earlier in the cardiac cycle than smaller ones but terminate about the same time, independent of the size of the bursts. Because of this amplitude-latency “conversion,” the amplitude modulation of the rhythmic MSA signal results in corresponding variations in the peak-to-peak intervals, producing therefore a jitter in the MSA frequency around the HR. The variations in the frequency, manifested as a wideband component in the frequency domain, were most evident at low HR. Because the average duration of the MSA bursts is 0.54–0.69 s (23), a continuous signal composed of a sequence of such bursts will look more and more sinusoidal as the frequency of their occurrence approaches and drops below 1 Hz, i.e., when the period becomes about twice the duration of the bursts.

Compared with the autospectra, the wideband component was even higher in the coherence functions, indicating that whatever the mechanism producing the amplitude and latency modulation of the MSA bursts it was in part common for different nerves. In subjects with faster HR where the coherence peak was relatively narrow this component was less obvious in the ordinary coherence functions but could be separated from the rhythm imposed by the common baroreceptor input using the partialization technique.

The high coherence that remained after elimination of the cardiac-related coherences may signify specific coupling between different MSA generators or may be an indication of noncardiac-related inputs of either central or peripheral origin. As shown here, these inputs have a certain level of specificity indicated by the quantitative differences between the coherences connecting the MSAs in close and distant extremities and by the fact that high leg-leg coherences remained after partialization with the arm MSA signal. Time domain observations concerning baroreflex latencies of radial and peroneal MSA bursts are in agreement with this finding. First, the latency of individual bursts in simultaneous arm-leg recordings showed a lesser degree of correlation than in simultaneous leg-leg recordings ([23]; see also Fig. 4). Second, the absolute latency variability was less in the arm than in the two-leg MSA (23). Differential input to close and distant MSA pairs was also indicated by the differences in the number of unmatched bursts in arm-leg and leg-leg MSA recordings ([24]; see also Fig. 5). Because arm MSA contained the highest number of such bursts, it appeared that some other mechanism interfered with the baroreceptor input and caused either a transient increase of excitability in sympathetic neurons to arm muscles or a decrease of excitability in neurons to leg muscles. In contrast, this mechanism affected neurons to the two legs in a similar way, resulting in a balanced neural drive. These nonuniformities could be effectively revealed and quantified by partialization of the MSA-BP (or MSA-ECG) coherence using another MSA (see Fig. 5 and right column of Table 1).

The proportion of different inputs necessary to generate coherences quantitatively matching those found in the present study (Table 1 and Fig. 6) is summarized in a simple model in Fig. 7. In this model we assumed that each MSA is a product of activity of five “neurons.” Four of them (i.e., 80%) in each nerve receive baroreceptor input resulting in a MSA-BP coherence of 0.8 for all nerves. Noncardiac-related input is assumed to arise from two different sources. One of them (leg-leg input) only influences three neurons in leg MSA circuits, whereas the other (arm-leg input) affects one neuron in each circuit. Considering the arrangement of target neurons shown in the model, the ordinary coherence between leg MSAs is 1.0 because all five neurons projecting to the legs receive common input from at least one source. Elimination of the baroreceptor input will leave three of the five (i.e., 60%) neurons still connected by sharing other inputs resulting in a leg-leg partial coherence of 0.6. Similarly, 80% of the neurons in arm and leg circuits are connected before and only one neuron after theoretical baroreceptor denervation, corresponding to ordinary arm-leg coherence of 0.8 and partial coherence of 0.2. The effect of elimination of the other two hypothetical inputs could not be tested directly in our experiments, but their contribution could be evaluated using indirect measurements obtained by partialization with one of the MSA signals. Partialization, for example, with arm MSA eliminates all the variance reflected in this signal, i.e., those originating from the baroreceptors or from the arm-leg inputs. Inasmuch as after this maneuver three neurons in leg circuits still remain connected, leg-leg coherence remains relatively high (0.6). On the other hand, arm-leg coherence will drop to zero after partialization.
by leg MSA because this latter signal carries information derived from all three inputs (cf. Fig. 6).

The model shown in Fig. 7 also illustrates another important point. Unmasking of noncardiac MSA-MSA coherences was possible because signals reflecting the rhythmic baroreceptor input were available through direct recordings. The reverse analysis in which the baroreceptor effect would be dissected from the web of other MSA-MSA connections could not be performed. Such analysis would require an auxiliary signal containing a complete set of all coherent components with the exception of the cardiac-related rhythm. Therefore, inferences regarding the possible differential effect of the baroreceptor input on arm and leg MSAs could only be made using indirect evidence which, however, should be used with caution. It is worth noticing that the difference between ordinary coherences connecting close and distant MSAs (0.94 vs. 0.76) was not as high as the difference between the contribution of noncardiac-related inputs (0.67 vs. 0.29). This made the cardiac-related component appear considerably smaller for leg-leg (0.26) than arm-leg pairs (0.47). However, MSA-BP and MSA-ECG coherences were not different for arm and leg nerves, indicating that occlusion of inputs arriving from different sources plays a role in determining the level of MSA-MSA coherences. As shown in the model, even though baroreceptor input was set to be the most influential of all three and to affect the "neuron pools" equally, due to unequal occlusion of other inputs, its specific effect may appear different in different extremities.

Perspectives

There is evidence that sympathetic outflow is differentiated. Human sympathetic traffic differs markedly between nerves to effectors with different function, e.g., muscle and skin blood vessels (3–5, 12). Also when recording from different muscle nerves, i.e., from fibers destined to the same type of sympathetic effector, the responses to certain maneuvers may differ between different extremities (1, 24). At rest on the other hand, mean voltage neurograms of MSA recorded simultaneously in different extremities are very similar (21) and only minor differences have been demonstrated between burst amplitude distributions in arm and leg MSA (22, 23). The results of the present study using partial coherence analysis provided clear evidence of nonuniform coupling between nerves regulating muscle blood flow in different parts of the body also at rest. The relatively high residual coherences between resting leg-leg MSAs compared with arm-leg coherence indi-

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icates that some neuronal activity that contributes equally to MSA in both legs did not influence sympathetic outflow to arm muscles. The composition of MSAs, tested in resting conditions here, may be different in other situations, however, e.g., when the role of the baroreceptor input is lesser and the central drive or other afferent inputs have more pronounced influence on sympathetic outflow to different muscles. In this respect, it is interesting that the prominent cardiac rhythmicity in MSA can be lost when the inhibitory baroreceptor influence is eliminated (9) or weakened, e.g., during general anesthesia and surgery (20). Multiple nerve recordings made during interventions designed to alter baroreceptor firing (6–8) and combined with the analysis procedure of “theoretical barodenervation” may be a useful tool for studying possible central nervous dysfunction in patients with cardiovascular diseases.

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