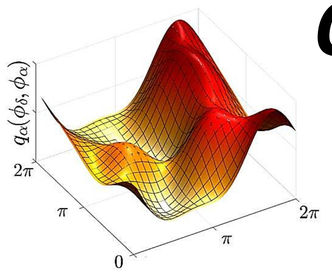

Quantification of the degree of association between left and right muscle sympathetic nerve activity variability in healthy subjects

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Introduction

The sympathetic neural control of the cardiovascular system is influenced by cortical hemisphere laterality [1]. The potential dissimilarity between neural efferent sympathetic activities can be addressed by recording simultaneously muscle sympathetic nerve activity (MSNA) from both left and right peroneal nerves in humans. Previous studies found similar burst rate in left MSNA (lMSNA) and right MSNA (rMSNA) [2,3], while the presence of right lateralization was identified by using normalized burst amplitude and area [4]. **The aim of the study was to assess the degree of association between lMSNA and rMSNA variability as a function of the frequency.** Therefore, in addition to traditional MSNA analysis over lMSNA and rMSNA recordings, we computed the squared coherence function between lMSNA and rMSNA variability (K^2). Analysis was carried out at rest in supine position during spontaneous breathing (SB) and control breathing (CB). The significance of the detected coupling was tested via a surrogate approach [5].

Methods

We studied 10 right-handed volunteers (age 33±9y, 5m) without evidence of disease. Raw MSNA was recorded from the peroneal nerve of the right and left leg simultaneously. The raw MSNA was band-pass filtered, amplified, rectified and integrated to obtain traditional integrated MSNA signals [4,6]. Integrated MSNA [4,6] was sampled at 300 Hz. The experimental sessions consisted of two periods of 15 minutes during SB and CB at 15 breaths/minute. From the integrated MSNA signal we computed traditional parameters such as burst frequency (bf), burst incidence (bi), burst amplitude (ba) and burst area (ba^2).

MSNA variability series was obtained from the integrated MSNA signal (Figure 1a) by counting the number of MSNA bursts inside a moving time window of 5 s and by dividing the count by the length of the time window, thus obtaining a time series expressed in burst/s (Figure 1b). Subsequently, the MSNA variability series was obtained by low-pass filtering the count signal with a cut-off frequency of 0.5 Hz (Figure 1c) and down-sampling the resulting signal once per cardiac beat [9]. Mean (μ) and variance (σ^2) of MSNA variability were computed. Autoregressive spectral analysis provided an estimate of the power in the low frequency band (LF, from 0.04 to 0.15 Hz) (Figure 2).

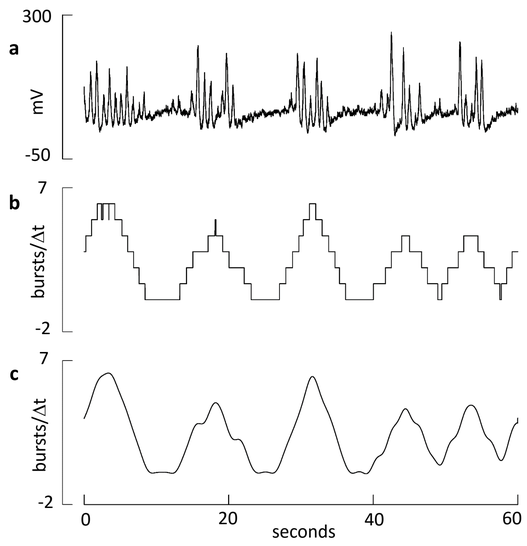

Figure 1: MSNA variability series [9]

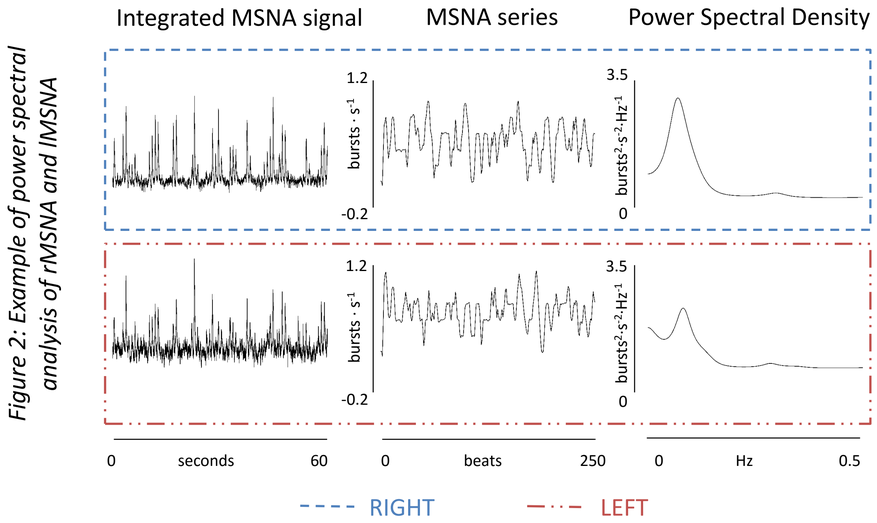

Figure 2: Example of power spectral analysis of rMSNA and lMSNA

K^2 was computed via a bivariate autoregressive approach [5] and averaged in LF and high frequency (HF, from 0.15 to 0.5 Hz) bands to obtain K^2(LF) and K^2(HF) respectively. The computation of the threshold to test the hypothesis of lMSNA-rMSNA coupling was based on the construction of a set of 100 uncoupled isospectral isodistributed surrogates via iteratively-refined amplitude-adjusted Fourier transform method [7]. K^2(LF) and K^2(HF) were deemed as significant if they were larger than the 95th percentile of the K^2(LF) and K^2(HF) distribution computed over the uncoupled surrogates respectively [5,8] (Figure 3). Two way repeated measures analysis of variance (one factor repetition, Holm-Sidak test for multiple comparisons) was applied to check differences between sides and conditions.

Indexes	SB		CB	
	rMSNA	lMSNA	rMSNA	lMSNA
bf [bursts/min]	19.7 ± 6.7	20.9 ± 6.2	20.8 ± 5.6	21.1 ± 6.1
bi [bursts/100 beats]	28.9 ± 7.1	30.8 ± 6.4	28.7 ± 6.2	29.1 ± 5.9
ba [a.u.]	72.4 ± 43.2	51.9 ± 22.5	65.4 ± 41.3	48.5 ± 19.0
ba^2 [a.u.^{2}]	21.2 ± 13.4	16.5 ± 8.6	21.9 ± 15.8	16.3 ± 7.6
μ [bursts/s]	0.32 ± 0.11	0.34 ± 0.10	0.34 ± 0.10	0.34 ± 0.10
σ^2 [bursts^2/s^2]	0.039 ± 0.013	0.037 ± 0.010	0.033 ± 0.012	0.037 ± 0.008
LFa [bursts^2/s^2]	0.025 ± 0.015	0.023 ± 0.007	0.022 ± 0.011	0.023 ± 0.011

Table 1: MSNA traditional parameters

Results

None of the traditional parameters (Table 1) showed significant differences in relation to sides or conditions. During SB a significant lMSNA-rMSNA coupling was identified in 80% and 100% of the subjects in LF and HF bands respectively, while these percentages decreased to 60% during CB in both bands.

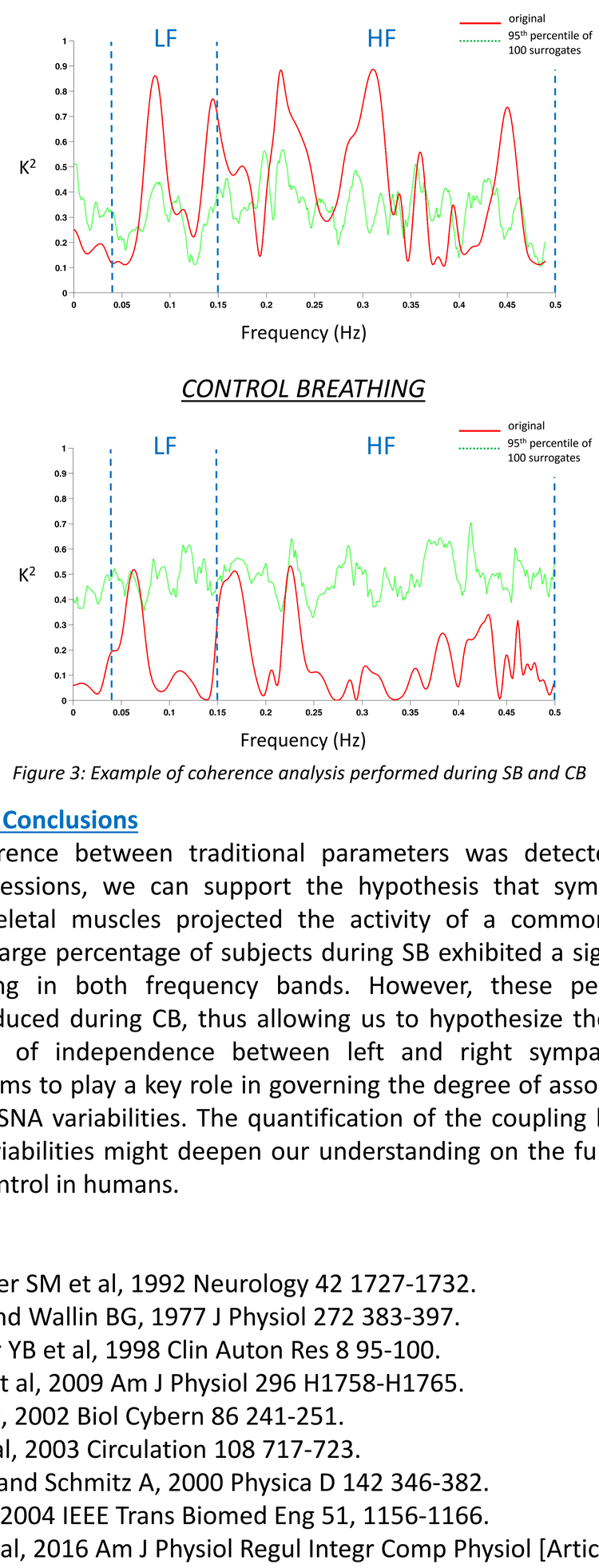

Figure 3: Example of coherence analysis performed during SB and CB

Discussion and Conclusions

Since no difference between traditional parameters was detected during both experimental sessions, we can support the hypothesis that sympathetic nerves directed to skeletal muscles projected the activity of a common central drive. Accordingly, a large percentage of subjects during SB exhibited a significant lMSNA-rMSNA coupling in both frequency bands. However, these percentages were importantly reduced during CB, thus allowing us to hypothesize the existence of a certain degree of independence between left and right sympathetic controls. Respiration seems to play a key role in governing the degree of association between lMSNA and rMSNA variabilities. The quantification of the coupling between lMSNA and rMSNA variabilities might deepen our understanding on the functioning of the sympathetic control in humans.

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