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Heart rate variability: sleep stage, time of night, and arousal influences

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Abstract

Spectral analysis was used to assess heart rate variability in consecutive 5-min epochs during the night in 12 normal adults. Simultaneous time coding of EEG and digitized EKG allowed examination of heart rate variability as a function of sleep stage, time of night and presence of EEG arousal. The results replicated previous studies in showing increases in high frequency components and decreases in low frequency components of heart rate variability across NREM sleep stages and opposite changes in REM sleep and wake. These results are consistent with sympathetic nervous system activation during REM sleep and wake periods. The shift in heart rate variability seen during REM sleep began in NREM sleep several minutes prior to standardly scored REM and often continued beyond the end of REM sleep. EEG arousals during Stage 2 and to some extent REM sleep were also associated with changes in heart rate variability which were consistent with sympathetic activation. An examination of beat to beat intervals in proximity to EEG arousals showed heart rate acceleration at least 10 beats prior to the EEG arousal. The arousal data along with Stage 2 sleep transition data support the contention that increases in central nervous system sympathetic activity precede and possibly play a role in the initiation of REM sleep and arousals during sleep. © 1997 Elsevier Science Ireland Ltd.

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1. Introduction

It is known that heart rate decreases during sleep and generally follows the circadian curve of body temperature. However, within this overall pattern, heart rate is also related to sleep stage, awakenings, and body movements (Johns et al., 1976). For example, heart rate was found to be lowest in slow wave sleep and then to increase by about 10% with each stage change from SWS to Stage 2 to Stage 1/REM to wake (Aldredge and Welch, 1973; Snyder et al., 1964; Brooks et al., 1956). Although human heart rate is higher in REM than in NREM sleep, the average heart rate in REM also decreased across succeeding REM periods (Snyder et al., 1964). The graded decrease in heart rate during NREM sleep followed by an increase in REM has been explained as a depression of central sympathetic activity during NREM followed by an instability or increase in rate during REM based upon direct measurement of burst rate of muscle sympathetic nerve activity (Okada et al., 1991; Somers et al., 1993).

Spectral analysis techniques have also been used to link changes in heart rate to underlying central nervous system activity. Spectral analysis has suggested that power in specific frequency bands can be related to parasympathetic and sympathetic nervous system activity. Specifically, relative power in high frequency areas, usually from 0.15 to 0.5 Hz, has been used to infer parasympathetic nervous system activity. Evidence has been published that the peak in the lower frequency component is in the range of 0.09–0.11 with a standard deviation of about 0.02 (Furlan et al., 1990). To include both the peak and surrounding area, a range of lower frequencies from 0.05 to 0.15 Hz has typically been related to a combination of parasympathetic and sympathetic influences (Jaffe et al., 1993; Yeragani et al., 1993; Malliani et al., 1991). Because the lower frequency power is a combination of sympathetic and parasympathetic effects, investigators frequently infer sympathetic nervous system activity from the ratio of low (parasympathetic and sympathetic) to high (predominantly sympathetic) power so

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that parasympathetic power to some extent cancels out of the ratio (Rizzoni et al., 1991; Yeragani et al., 1993; Bigger et al., 1992) leaving a better indicator of sympathetic activity. Jaffe et al (Jaffe et al., 1993) in a study of heart rate changes as a function of posture change found this 'sympathetic index' correlated to heart rate changes. Studies of children (Baharav et al., 1995), and adults (Vaughn et al., 1995), using spectral analysis techniques, have consistently found increased parasympathetic activity during NREM sleep, as measured by high frequency heart rate variability and increased sympathetic activity during REM sleep, as typically measured by the ratio of lower to higher frequency heart rate variability. These findings agree well with earlier studies of heart rate and direct measures of nerve activity (Somers et al., 1993; Hornyak et al., 1991). Other studies of nerve activity in patients with sleep disturbed by apneic events have shown high levels of sympathetic nerve activity during wake and even higher levels when asleep (Somers et al., 1995; Shimizu et al., 1994). However, this unusual pattern was normalized somewhat by the initiation of CPAP therapy (Somers et al., 1995).

Vaughn et al (Vaughn et al., 1995) performed several analyses on 4 10-min samples of EKG from waking, Stage 2, SWS and REM in a group of 10 normal sleepers. They found that sleep stage differences were most clearly seen from the spectral analysis and were consistent with increased parasympathetic nervous system activity during Stage 2, decreasing parasympathetic and sympathetic nervous system activity during slow wave sleep, and increased sympathetic activity during REM. Unfortunately, these data represented short individual observations from different times during the sleep period and therefore may have missed much detail which might exist during the sleep process. In addition, their finding of decreased parasympathetic nervous system activity in SWS as compared with Stage 2 sleep is opposite to that of Baharav et al (Baharav et al., 1995) in a group of younger subjects.

In the current study, spectral analysis was used to examine sequential 5 min blocks across the entire sleep period in a group of normal sleepers. It was hypothesized that the examination of continuous blocks would allow identification of sleep stage and circadian influences as well as the impact of brief arousals and stage shifts on heart rate variability.

2. Methods and materials

2.1. Subjects

Subjects (Ss) were required to be healthy, 18- to 50-year-old males and females. Potential Ss were solicited from sleep center referrals and from ads in the local papers for participants in sleep research. Subjects were required to indicate normal sleep on their screening questionnaire. They were also required to report a sleep latency of less than 30 min. and less than 30 min. of wake time during the night. Potential subjects who indicated excessive caffeine consumption (more than 250 mg of caffeine per day), who were using psychoactive medication or drugs, or who had completed a drug or alcohol abuse program within the previous year were excluded. Ss with a history of depression or psychiatric hospitalization were excluded. Potential Ss who had histories strongly suggestive of circadian desynchrony (e.g. shift workers), sleep apnea, or periodic leg movements were excluded.

Subjects meeting the above criteria were invited to participate in the study after completing an informed consent and two hours of acclimatization to the laboratory with practice on computer tests and questionnaires to be used in the study.

2.2. Design

After practice, subjects were scheduled to spend two nights and the intervening day in the laboratory. On both nights, a standard clinical polysomnogram, including two eye channels, central and occipital EEG channels, chin and leg EMG channels, EKG, airflow, and chest movements was performed. Sleep recordings were scored by Rechtschaffen and Kales criteria (Rechtschaffen and Kales, 1968), and arousals were scored by ASDA criteria (Bonnet et al., 1992). On the day spent in the lab, Ss performed computer tests, completed an MMPI and a sleep history, and were fed the same daily menu of food prepared at the lab during the day. Caffeinated beverages were not available. Subjects usually did not leave the lab during this day and did not engage in any activity more vigorous than walking to the bathroom. Following the second night in the lab, subjects completed some brief computer tests and were allowed to leave.

All subjects were assigned their own room for the course of the study. Each room contained a standard hospital bed and furniture including a desk with an Apple IIGS computer. Subjects participated in the study in groups of 1–2 individuals. Meals and breaks were scheduled in another area of the laboratory, which was also within technician observation.

2.3. EKG data collection

Beginning 30 min prior to lights out on the second night in the lab, EKG data were digitized by a National Instruments NB-MIO-16 AD Board sampling at a rate of 500 samples per second. A time code was digitized by a second channel on the AD board and also printed out on the polygraph paper to allow epoch by epoch matching of digitized EKG with sleep stages and events. The EKG and time code data were collected by LabView 3.0 software running on a Macintosh II computer and stored to optical disk. Data collection was continuous throughout a 20 min resting wake condition and the sleep period which followed. After awakening at their normal time of arising in the morning, Ss

Table 1

Sleep parameters

Sleep stage	Mean	Standard deviation	Range
Sleep latency (min)	6.2	4.6	0.5–14.5
Stage 1%	13.6	7.0	5–25
Stage 2%	52.6	8.4	40–70
Stage 3%	4.5	4.3	0–14
Stage 4%	2.4	4.2	0–13
Stage REM%	21.2	3.8	17–29
Stage wake (min)	26.0	16.1	2–51
Sleep efficiency	94.6	3.3	90–100
Total sleep time (min)	448	19.1	418–476
REM latency (min)	64.0	17.7	39–92
Arousal index	11.3	4.8	5–21

were asked to stand up for a final 10 min EKG recording period.

After collection, the EKG and time data were visualized and checked for artifacts with the LabView software and output to a separate peak detection program used to construct the tachogram and associated time code. The tachogram data were again examined for artifacts and converted for input into the BMDP 1T (Spectral Analysis) Program[1]. Five-minute sequential time periods were identified from the sleep record with the following constraints:

1. Data from the pre-sleep baseline waking period and post-sleep standing data were blocked and separated from the sleep period data
2. Five-minute blocks were chosen, whenever possible, to contain a single sleep stage: this included, on occasion, shortening or lengthening a block by up to one minute or skipping 1–2 minutes of recording
3. When a block contained a mixture of sleep stages, the 'lightest' stage was assigned (Wake < Stage 1 < Stage 2 < SWS).

Whenever possible Stages 2 and REM were not included in the same block. In practice, all subjects had a number of pure blocks of stages wake, 2, and REM and about 100 total blocks per night. Three Ss did not have sufficient slow wave sleep for any epochs to be labelled as SWS.

2.4. Analyses

Data were compared by sleep stage as defined above, by quarter of the night, by the presence/absence of arousals in the block, and by the the proximity of REM or SWS. Two variability measures were examined: (1) low frequency variability (LFV) was defined as the total spectral power in the 0.05–0.15 Hz frequency band divided by the total spectral power in the 0.15–0.50 Hz frequency band; (2) high frequency variability (HFV) was defined as the the total spectral power in the 0.15–0.50 Hz frequency band divided by the total spectral power (0.0–0.50 Hz) (Jaffe et al., 1993, Kamath and Fallen, 1993). All results will refer to statistically significant differences ($P < 0.05$) except where noted otherwise. Significant F-values from analysis of variance were followed by pairwise comparisons using the Neuman-Keuls procedure at the $P < 0.05$ level with degrees of freedom defined by the Huynh-Feldt correction.

[1] Linear trends were removed from the data using the Detrend option of the BMDP 1T program, and the spectral analysis was performed using the Rectangular option for the shape of the periodogram weighting function (Yeragani et al., 1992).

3. Results

Data from 12 normal sleepers, age 22–48 (mean 32), were analyzed. None of the normal subjects were found to have clinically defined sleep apnea or periodic limb movements. Sleep stage data can be found in Table 1. As shown, sleep parameters for the night were relatively normal.

Fig. 1 is a diagrammatic representation of changes in LFV across the night in one subject. Sleep stages assigned to each 5-min time segment are identified on the abscissa. Changes in heart rate variability as a function of sleep stage are evident. Table 2 presents mean data from the presleep wake period, wake during sleep, and morning standing observation. Examination of the data revealed that the LFV data, especially for the pre-sleep waking and standing conditions, were non-normally distributed because these ratios contained a few large values. A log transformation (of the data plus 1) was therefore used to normalize this data. Analysis of variance for the log transformed low frequency ratio waking data revealed an $F(2,22)$ of 12.75 ($P < 0.002$). Pairwise comparisons showed that low frequency ratio power was significantly greater when subjects

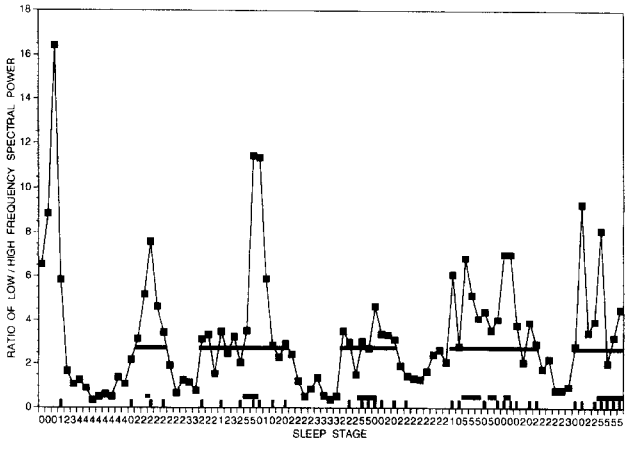

Fig. 1. Low frequency heart rate variability (LFV) in consecutive 5 min epochs across a night of sleep (presleep baseline and post sleep standing periods not included to increase sleep stage detail) in one normal young adult. Wake periods during sleep are indicated as Stage 0; REM is indicated as Stage 5. Short horizontal bars at the bottom of the figure indicate each 30 s epoch scored as REM sleep. Longer horizontal bars higher in the figure indicate consistent periods of increased LFV activity. The vertical lines at the bottom indicate the presence of an EEG arousal in the indicated time block.

Table 2

Mean (SD) for heart rate variability data in three waking conditions

Stage	HFV	LFV
Presleep waking baseline	0.224 (0.18)	2.303 (2.05)
Stage wake	0.235 (0.16)	1.789 (1.33)
Standing	0.100 (0.06)	9.67 (1.50)
$F(2,22)$	8.22	12.75
P-value	0.003	0.002
Differences	Stand < Wake = Wake	Stand > Wake = Wake

LFV data, which were transformed for analysis, have been transformed back for presentation.

were standing but that the presleep and during sleep wake values did not differ. For high frequency activity, the ANOVA was significant ($F(2,22) = 8.22$, $P < 0.003$), and pairwise comparisons indicated that high frequency ratio power was significantly less in the standing condition as compared to the two other waking conditions, which did not differ.

Table 3 presents mean data from sleep stages throughout the night. Statistical comparisons involving SWS were limited to the 9 Ss who had sufficient SWS for at least one block to be designated as SWS. Analysis of variance for the log transformed LFV sleep stage data revealed an $F(4,32)$ of 18.08 ($P < 0.001$). Pairwise comparisons showed that LFV was significantly less in SWS than in Stage 2, which was significantly less than Stage 1, which was equal to REM and wake during sleep values. For HFV activity during sleep, $F(4,32) = 11.52$ ($P < 0.001$), and pairwise comparisons indicated that high frequency ratio power was significantly greater in SWS than in Stage 2, which was significantly greater than Stage 1 which was equal to REM and wake during sleep values.

Stage Wake, 1, 2, and REM observations were averaged within each quarter of the night to test for time of night effects. Insufficient data existed for REM sleep to be included in the first quarter of the night. For both the LFV and HFV analyses, the time by sleep stage interaction was not statistically significant. In both cases the main effect for time of night also was not statistically significant (F-PNS(3,33) = 0.20; F-SNS(3,33) = 0.06). In both cases, the

Table 3

Mean (SD) for heart rate variability data as a function of sleep stage

Stage	HFV	LFV
Stage wake	0.189 (0.15)	1.998 (1.47)
Stage 1	0.217 (0.17)	1.667 (1.60)
Stage 2	0.359 (0.17)	0.984 (1.36)
Stage SWS	0.490 (0.19)	0.589 (1.21)
Stage REM	0.208 (0.17)	1.846 (1.47)
$F(4,34)$ Sleep	11.52	18.08
P-value	0.001	0.001
Differences	SWS > St 2 > others	SWS < St 2 < others

Table 4

Heart rate variability in Stage 2 and REM sleep periods with and without EEG arousals

	Stage 2	REM	F-interaction	P-value	Differences
HFV Arousal	0.329	0.261	19.51	0.001	St 2 > REM
HFV No arousal	0.508	0.292			St 2 No Aro > St 2 Arousal
LFV Arousal	1.366	1.924	6.211	0.03	All differ
LFV No arousal	0.722	1.613			

main effect for sleep stage was significant (F-PNS(2,22) = 37.61, $P < 0.001$; F-SNS(2,22) = 6.51, $P < 0.01$). This sleep stage effect replicated the complete night analysis reported earlier, except that the pairwise comparisons additionally revealed that the HFV value from Stage 1 sleep was significantly greater than the wake value and that the LFV value from Stage 1 sleep was significantly lower than the wake value.

The impact of EEG arousals on heart rate variability was examined by comparing epochs containing Stage 2 and REM without arousals to epochs containing arousals. Specifically, for each stage for each subject, 5-min epochs containing an EEG arousal were matched with the closest epoch in time (within the same quarter of the night) of the same stage containing no arousal. For each subject, the values for all of the matched epochs for each stage were averaged, and the average value was used in the ANOVA. Mean data are presented in Table 4. There was a significant sleep stage by presence of arousal interaction for both the HFV and LFV values. Pairwise comparisons for the LFV ratios indicated that all four means differed significantly from each other (i.e., LFV activity was greater in REM than in Stage 2 with or without arousals and LFV activity was increased in both stages in epochs containing an arousal). The interaction indicated that the increase in LFV activity after arousal in Stage 2 was greater than the increase seen after an arousal in REM. For HFV, a significant decrease in activity was seen after an arousal in Stage 2 but not in REM (and Stage 2 values were greater than REM values). Smaller changes as a function of arousal in REM may have reflected the fact that heart rate variability values during REM were already relatively close to waking values even before arousals occurred.

From Fig. 1, it may also be noted that abrupt changes in LFV, which were associated with REM sleep, frequently occurred prior to EEG/EOG scoring of REM and frequently lasted longer. To examine changes in heart rate variability in periods of state transition, the following transitions, all in Stage 2 sleep, were identified for each subject: Stage 2 in transition to SWS; Stage 2 immediately following SWS; Stage 2 sleep closely preceding REM; Stage 2 sleep closely following REM. For each subject, all transitions in each category were averaged, and the average values were used in the ANOVA. The mean data over all subjects are pre-

sented in Table 5. It can be seen from the table that heart rate variability in Stage 2 periods varied as Stage 2 approached transition to other sleep stages. Specifically, HFV was significantly increased in Stage 2 periods near the onset of SWS and was decreased significantly in Stage 2 periods both prior to and following REM. LFV was significantly increased in Stage 2 periods preceding REM sleep as compared to periods of stable Stage 2 and Stage 2 prior to transition to SWS.

Individual data (Fig. 1) and the Stage 2 transition data indicated that heart rate variability might begin to change prior to sleep stage shifts. However, due to the relative insensitivity of the 5-min time window required for the spectral analysis, individual heart beat data were examined around EEG arousals during Stage 2 sleep to determine whether EEG or EKG changes occurred earlier. Specifically, for each subject, 3–5 EEG arousals were chosen which occurred during stable Stage 2 sleep. Beat to beat heart rate intervals (tachogram) were obtained from the digitized data for 30 beats prior to and after each arousal. The first 5 beat to beat intervals (25–30 beats prior to arousal) were averaged as a baseline and all succeeding intervals were subtracted from this baseline. As such, all positive numbers reflected a decrease in beat to beat interval (increase in heart rate) and all negative numbers reflected an increase in interval (decrease in heart rate) from the baseline. These data were averaged for 11 of the 12 subjects. For one subject, technical difficulties with the time code for a portion of the recording precluded exact matching of heart rate with arousals. The data for the 11 Ss were averaged and are presented in Fig. 2. It can be observed from the figure that heart rate began to increase about 10–20 beats prior to the first visual change in ongoing EEG associated with an EEG arousal. For statistical analysis, the 25 heart beat intervals prior to arousal were divided into 5 five-beat periods and then averaged over the 5 beats in each period. These 5 periods were tested against the hypothesis of a mean of zero

Table 5

Heart rate variability in continuing Stage 2 sleep and in Stage 2 sleep prior to shifts to SWS or REM and after shifts from SWS or REM

	HFV	LFV
Stage 2	0.406	0.793
Stage 2 – SWS	0.480	0.637
SWS – Stage 2	0.371	1.149
Stage 2 – REM	0.272	1.504
REM – Stage 2	0.294	1.201
$F(4,32)$	7.288	4.338
P-value	0.002	0.02
Differences	Stage 2 – SWS > SWS – St2 Stage 2 – SWS > St2 – REM Stage 2 – SWS > REM – St2 Stage 2 > St2 – REM Stage 2 > REM – St2	Stage 2 – REM > Stage 2 Stage 2 – REM > St2 – SWS

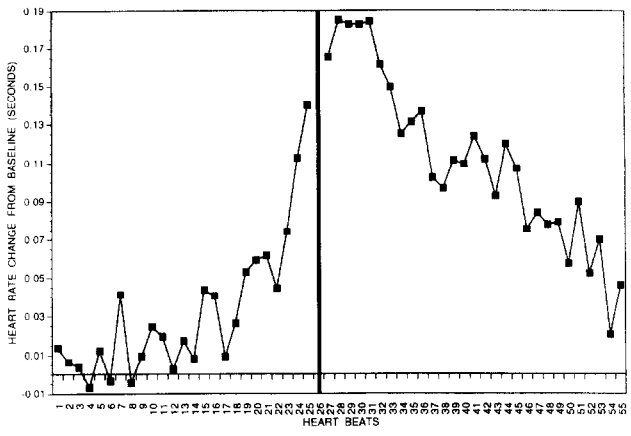

Fig. 2. Change in beat to beat interval preceding and following an EEG arousal (vertical black bar). Positive values indicate decreasing intervals (i.e. heart rate acceleration) compared to baseline, which was the average interval of the 5 beats 25–30 beats prior to the EEG arousal.

by t-test. These data were well fit with an exponential curve. The consecutive 5 t-values (all with 10 df) were 0.489 (NS), 1.296 (NS), 1.994 ($P = 0.07$), 3.358 ($P = 0.007$), and 4.315 ($P = 0.002$).

4. Discussion

These data replicate earlier studies that used both spectral analysis and direct nerve recordings and found that HFV (indicating greater parasympathetic nervous system activity) increased in NREM and decreased in REM while opposite changes were found in LFV, the analogue of sympathetic nervous system activity (Hornyak et al., 1991; Baharav et al., 1995; Vaughn et al., 1995). The results also support the findings of Baharav et al. (1995), which showed a continuing increase in HFV in SWS as compared to Stage 2. Vaughn et al. (1995), who analyzed relatively long (10 min) periods of EKG from older Ss compared to Baharav et al. (1995) found a reduction in HFV in SWS compared to Stage 2. One possible explanation for the discrepancy is that, as a result of selecting longer time periods from older Ss, Vaughn et al. (1995) were sampling closer to the end of SWS periods where early shifts to sympathetic nervous system dominance were found in the current study. Such shifts could have resulted in the appearance of lower HFV in SWS.

The current data also replicate several earlier studies in showing large differences in heart rate variability in waking subjects who stand up, a standard procedure to demonstrate sympathetic nervous system activation. It is of interest to note that the magnitude of change in heart rate variability as subjects stood up as compared to resting awake (an increase of about 420% in LFV and a decrease to about 45% in HFV) was very similar to the magnitude of change seen when moving from SWS to the resting awake values (390% and 46%). In comparison, heart rate variability in periods of wake during sleep was not different from heart rate variability in the presleep waking observation period.

It is important to understand that these global findings concerning heart rate variability as a function of sleep stage operate within the context of: (1) arousals and sleep disturbance; (2) the sleep/wake circadian rhythm; and (3) an extended REM/NREM cycle. Examination of 5-min periods of Stage 2 sleep containing EEG arousals showed a 35% decrease in HFV and an 89% increase in LFV as compared to Stage 2 epochs without arousals. These changes could be interpreted as a decrease in parasympathetic activity and a somewhat larger increase in sympathetic activity associated with the EEG arousals.

Time of night effects were not found for either heart rate variability measure unlike a previous study which found a decrease in heart rate across REM periods during the night (Snyder et al., 1964). As such, the current data indicate that if consistent time of night changes in heart rate variability occur within sleep stages, the changes must be relatively small compared to other components of variability.

The broad bands of alternating sympathetic and parasympathetic nervous system activity seen in the current data (Fig. 1) are reminiscent of bands of human sleep-related immobility and mobility presented by Hobson (Hobson, 1983) in support of this concept, that postural changes, analogous to sympathetic nervous system activity here, occur in SWS prior to what has been traditionally seen as the shift toward REM sleep. These findings are also consistent with the report of Muzet et al. (1972) that body movements were unusual in periods of Stage 2 preceding SWS but very common in periods of Stage 2 prior to REM. In fact, based upon their motility data, Muzet et al. (1972) speculated that the difference in susceptibility to movements prior to SWS and REM might reflect 'fundamental physiological difference' or might help produce an aroused CNS necessary for REM. In terms most familiar to human sleep researchers, the shift toward sympathetic nervous system dominance usually occurred at the point during sleep where a body movement initially disturbs, but may not terminate, SWS. This concept is also supported by the current analyses of heart rate variability in Stage 2 periods which are followed by SWS or REM. These analyses clearly indicated that periods of stable Stage 2 or Stage 2 prior to SWS have heart rate variability characteristics much different from Stage 2 sleep prior to or following REM. Whether these heart rate changes reflect early autonomic changes correlated with or leading to changes in ongoing EEG or whether they are produced as a result of other influences was examined with individual beat to beat interval data gathered before and after EEG arousals in stable Stage 2 sleep. These data (Fig. 2) indicate that heart rate acceleration, usually considered to be associated with increased sympathetic nervous system activation, began at least 10 heart beats and perhaps more prior to visual changes in the EEG. Exponential heart rate acceleration prior to EEG changes is consistent with a central process heralding or possibly driving the EEG activation. While the process underlying EEG arousal may be different from the process initiating REM, the concept of the central nervous system leading cortical EEG activation is common.

The current results can be criticized for the use of heart rate data from grouped sleep stages. The use of such grouped data was thought essential in the conceptualization of this project because (1) spectral analysis of heart rate segments shorter than 256 beats is typically considered not reliable and (2) an examination of sleep process effects across the night was not considered possible if all sleep segments containing less than 5 min of a single sleep stage were deleted from the data set. A more important question, which can be answered, is "what is the difference in spectral parameters between a 5-min period which is entirely wake time and a 5-min period of sleep containing 1–2 epochs of wake (because the criteria for this study would classify both 5-min periods as wake)?" A comparison of the presleep waking baseline data, which contain no sleep, to the wake during sleep data revealed no significant difference between these means. The implication of this finding is that short periods of wakefulness during sleep are related to an increase in sympathetic activity which may be longer than the period of wakefulness and are sufficient to shift entire 5-min epochs toward typical waking values. Similar results have been reported in an examination of whole body metabolic rate during and after periods of wake and EEG arousals (Bonnet et al., 1991).

The 5-min classification paradigm also had potential effects on the Stage 2 transition analyses. Based upon the classification rules, epochs classified as Stage 2 could have contained sleep epochs scored as Stage 3, and it is most likely that these epochs occurred in close transition to SWS. As a result, the significant differences noted in the transition from Stage 2 to SWS are likely to be secondary to SWS in the epochs coded as Stage 2 (of course, as sleep scorers know, there are also frequently several delta waves in 30-s epochs scored as Stage 2 prior to epochs scored as Stage 3). This same phenomenon occurred to a lessor extent in the Stage 2 periods which followed SWS. It is of interest to note, however, that these post-SWS Stage 2 periods had heart rate variability more in the direction of REM sleep than in the direction of SWS despite some occurrence of SWS in the Stage 2 epochs. This same reasoning cannot explain the Stage 2 preceding and following REM epochs because an effort was made to separate Stage 2 and REM when the epochs were constructed, and the relatively few mixed epochs were not used in the Stage 2 to REM transitions.

In summary, this study has replicated previous studies in showing systematic changes in heart rate variability as one progresses through the NREM sleep stages and in REM sleep and are consistent with sympathetic nervous system activation during REM sleep and wake periods. The sympathetic activation seen during REM sleep frequently begins in NREM sleep several minutes prior to standardly scored REM and continues beyond the end of REM sleep. EEG arousals during Stage 2 and to a lessor extent REM sleep

are associated with changes in heart rate variability which are consistent with sympathetic activation. An examination of beat to beat intervals in proximity to EEG arousals showed heart rate acceleration prior to the EEG arousal. The arousal data along with the Stage 2 sleep transition data support the contention that increases in central nervous system sympathetic nervous system activity precede and possibly are associated with the initiation of REM sleep and arousals during sleep.

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