5th Conference of the European Study Group on Cardiovascular Oscillations

Hypnotizability-related complexity of heart rate variability during long lasting relaxation.

E. L.Santarcangelo, R. Balocchi, G. Paoletti, C. Palombo, C. Morizzo, G. Carli, M. Varanini

Abstract*— Aim of the experiment was to compare heart rate and HRV of healthy subjects with high (Highs) and low (Lows) susceptibility to hypnosis during long-lasting relaxation. HRV indexes extracted in the frequency and time domain as well as related to the complexity of the tachogram (entropy) were analyzed through repeated measures ANOVA. The results indicated a parasympathetic prevalence in Highs all over the session and a sympathetic modulation across the session in both groups reflected in the sd2 dimension of the Poincaré plot and in entropy. The possible role of the Very Low Frequency spectral component in these changes, supported by the different correlations between entropy and frequency/time related indexes of HRV, is suggested.

I. Introduction

The susceptibility to hypnosis, or hypnotizability, is a cognitive trait responsible for the possibility to accept suggestions and modulate perception and behaviour accordingly (2). It can be measured through scales and has its anatomo-functional basis in the supervisory attentional system, located in frontal and cingulate cerebral areas.

In non hypnotic conditions and without specific suggestions, individuals with high (Highs) and low susceptibility to hypnosis (Lows) differ in the performance of many tasks in the cognitive, somatic and autonomic domain. In particular, studies of endothelial function allow hypothesizing a natural protection of Highs against the vascular effects of cognitive stress and acute pain (3,4) and studies of heart rate and heart rate variability in subjects receiving various stimulations (1,5) suggest that Highs might be less vulnerable than Lows to heart disease.

At variance with stimulation conditions, the differences between Highs and Lows in basal (no task) conditions are less clear-cut. In particular, some authors report a higher heart rate and a lower vagal tone in low (Lows) with respect to highly susceptible subjects (Highs), while others have found no significant difference between Highs and Lows in heart rate and in heart rate variability (see ref 6). However, in spite of the lack of difference between not hypnotized Highs and Lows in heart rate and HRV along a long-lasting relaxation period, previous finding from our laboratory showed different EEG activities suggesting an increased and decreased integrative activity in Highs and Lows, respectively (6). This suggested that relaxation can be considered a cognitive task and that the cardiac output observed might be the result of complex control mechanisms not reflected in the HRV indexes considered, but related to the Very Low Frequency component of the RR power spectrum and/or to components induced by non stationarities of heart activity. Since decreased entropy is expected when the sympathetic activity increases (11), aim of the present study was 1) to identify possible hypnotizability related changes in the HRV complexity occurring during long-lasting relaxation and 2) to compare the sensitivity of complexity indexes with that exhibited by the classical time and frequency domain HRV indexes.

II. Methods

After signing an informed consent, 8 Highs and 10 Lows (healthy males, age 18-25), selected according to the Stanford Hypnotic Susceptibility Scale, form C joined the study. They were asked to relax as much as possible according to their usual strategies (simple relaxation) for 15 minutes, with eyes closed but without hypnotic induction. The RR time series, obtained from the recorded ECG sampled at 1000 Hz, were corrected from artefacts using a linear predictive filter with a threshold on the prediction error. A posteriori the session was divided into 3 consecutive epochs (E1, E2, E3), each of them including 300 beats.

The following parameters, mean RR (RRm), RR standard deviation (SD), root mean square of successive RR differences (RMSSD) (7), normalized powers in low frequency (LFn) and high frequency (HFn) bands, LF/HF (7), sd2 and sd1 dimensions of the Poincaré plot and their ratio (CSI, cardiac sympathetic index) (8), approximate entropy (ApEn) (9), sample entropy (SmE) (10) and corrected conditional entropy (CCE) (11) were computed for each epoch. The normalized power of

the Very Low Frequency spectral component (VLFn) was also computed all over the session (15min).
Spectral analysis was performed according to Welch method, using a frequency resolution of 0.0167Hz; window length, overlapping and number of intervals were automatically adjusted according to the effective time duration of the 300 beats epoch. Zero padding to 512 length was performed.
The sd1 and sd2 dimensions of the Poincaré Plot as well as the ratio sd2/sd1 (cardiac sympathetic Index, CSI) were also computed (2); sd1 contains only the short-term RR variability, while sd2 includes the HRV corresponding to both the low (LF) and Very Low (VLF) Frequency spectral components.
Entropy-based complexity indices were estimated using the following parameter settings: ApEn, pattern length m=2, tolerance r= 0.2 times standard deviation; SmE, pattern length m=3, tolerance as for ApEn; CCE, pattern length m=3, number of quantization levels=6. Statistical analysis of RRm, SD, RMSSD, LFn, HFn, LF/HF, sd2, sd1, CSI, ApEn, SmE and CCE was performed through repeated measures ANOVA following a 2 Groups (Highs, Lows) x 3 epochs (E1, E2, E3) experimental design. Contrast analysis was used when appropriate. The VLFn values of Highs and Lows all over the session were compared through univariate ANOVA. Spearman correlation coefficients were computed between entropy (SmE,CCE), sd2 and LFn in order to detect a possible role of VLFn in the time related changes of entropy. Level of significance was set at $p<0.05$.

III. Results

ANOVA revealed a significantly increase in RR during E2 ($F(1,16)=8.219$, $p<0.011$) and E3 ($F(1,16)=14.408$, $p<0.002$) with respect to E1, but no Group difference was observed. RR and HRV indexes values are shown in Table 1.
Frequency domain indexes - No significant Epoch effects were observed for LFn, HFn and LF/HF. A significant Group effect was found for HFn which was significantly greater in Highs (($F(1,16)=9.426$, $p<0.007$) all over the session. Normalized values of the VLF components (VLFn, computed on the entire session) were significantly higher (Group effect, ($F(1,16)=5.706$, $p<0.030$) in Lows (242 $\pm$ 0.021) than in Highs (168 $\pm$ 0.023).
Time domani indexes - SD and RMSSD did not change significantly across epochs and did not differentiate Groups; in the Poincaré Plot, sd2 decreased significantly during E2 with respect to E1 ($F(1,16)= 4.764$, $p < 0.044$), while sd1 and CSI did not change significantly across epochs. A significant Group effect was observed for CSI, which was lower in Highs all over the session ($F(1,16) =7.442$, $p<0.015$).
Entropy - No Group effect was found for entropy. ANOVA revealed a significant increase in SmE ($F(1,16)= 10.278$, $p<0.006$) and CCE ($F(1,16)=5.683$, $p< 0.030$) during E2 with respect to E1, but no significant change in ApEn (E2 vs E1, $p=0.057$). Thus, from a methodological point of view, our findings confirm that SmE and CCE measures are more suitable to estimate complexity of short term HRV with respect to ApEn which does not include the correction of the bias due to short time series (11).
Entropy (SmE and CCE) showed a time course similar to sd2 and different from LFn. In line with this observation, the linear correlation coefficients computed for each epoch showed 1) the absence of significant correlations between LFn and sd2 as well as between both SmE and CCE and LFn; 2) the occurrence of a significant negative linear correlation between SmE and sd2 ($R = -0.542$, $p<0.021$) and of a *quasi* significant correlation between sd2 and CCE ($R=-0.461$, $p=0.054$) during E3.

TABLE I.

		E1		**E2**		**E3**	
variable	**group**	**mean**	**SE**	**mean**	**SE**	**mean**	**SE**
RR	**H**	838,87	45,35	863,75	46,91	861,11	45,48
	L	811,21	40,56	820,66	41,96	821,56	40,68
SD	**H**	60,99	5,49	52,95	7,27	62,13	7,62
	L	57,16	4,91	52,50	6,50	62,54	6,81

RMSSD	**H**	45,31	4,35	44,68	6,13	54,86	10,23
	L	34,07	3,89	32,91	5,48	38,87	9,15
LFn	**H**	0,46	0,04	0,44	0,04	0,46	0,04
	L	0,53	0,03	0,56	0,04	0,53	0,04
HFn*	**H**	0,37	0,03	0,41	0,05	0,37	0,03
	L	0,24	0,03	0,23	0,05	0,22	0,03
LF/HF	**H**	1,49	0,60	1,39	0,75	1,45	0,72
	L	2,79	0,54	3,52	0,67	3,21	0,65
sd1	**H**	32,09	3,08	31,65	4,34	38,86	7,25
	L	24,13	2,75	23,31	3,88	27,53	6,48
sd2	**H**	79,71	7,53	67,53	9,65	78,48	13,97
	L	76,95	6,73	70,17	8,63	80,91	12,50
CSI*	**H**	2,48	0,29	2,21	0,27	2,35	0,29
	L	3,21	0,26	3,05	0,24	3,04	0,26
SmE	**H**	1,37	0,12	1,61	0,13	1,58	0,12
	L	1,26	0,11	1,39	0,12	1,34	0,11
CCE	**H**	0,98	0,08	1,15	0,07	0,98	0,07
	L	0,84	0,07	0,92	0,06	0,97	0,07
	L	0,99	0,04	1,00	0,03	0,98	0,04

***** significant difference between Groups

IV. DISCUSSION

The results failed to identify time-related differences between the Highs' and Lows' heart rate and HRV during long-lasting relaxation, but indicated a parasympathetic prevalence in the former all over the session.

At variance with previous findings (6) showing an increase in RR during long-lasting relaxation only in Lows, RR increased in both groups, which might be due to gender, since only males were included in the present experiment. The changes occurring in spectral indexes across the consecutive epochs do not account for the RR increases observed, while sd2, extracted from the Poincaré Plot, seems to be a more sensitive index of sympathetic-parasympathetic balance, likely because it includes the contribution of the very Low Frequency spectral component.

Since entropy increases across epochs, paralleling the RR increases and sd2 decreases, it might be hypothesized that this complexity index reflects changes including Low and Very Low Frequency spectral components, as suggested also by the linear correlations observed between entropy and sd2, but not between entropy and LFn. This is not in contrast with previous findings suggesting that when LFn decreases entropy increases (11), but further supports the role of VLF in the autonomic space. Unfortunately VLF cannot be reliably evaluated along short time intervals. However, its prevalence in Lows all over the session might explain the significant Group difference observed for CSI and not for LF/HF between the two groups.

Entropy-based measures of HRV did not differentiate between Highs and Low, while both HFn and CSI revealed a parasympathetic prevalence in Highs all over the long-lasting relaxation. This suggests that the Group differences observed are, mainly, due to parasympathetic components, while the time related changes occurring in both Highs and Lows are the results of a pre-eminent sympathetic modulation. Finally, the analysis of HRV in the frequency domain seems to be more sensitive to group differences, while the indexes extracted in the time domain are more responsive to the time-related changes occurring in heart rate control in both groups during long-lasting relaxation.

ACKNOWLEDGMENT

Research granted by the Italian Spatial Agency (ASI-DCMC project).

REFERENCES

[1] R. Balocchi, M.Varanini, D.Menicucci, E.L. Santarcangelo, S. Migliorini, G. Fontani, G. Carli (2005) Heart rate variability in subjects with different hypnotic susceptibility receiving nociceptive stimulation and suggestions of analgesia. *IEEE Eng Med Biol*., 6996-99.

[2] J.P. Green, A.F. Barabasz, D. Barrett, G.H. Montgomery (2005). Forging ahead: the 2003 APA Division 30 definition of hypnosis. *Int. J. Clin. Exp. Hypn.*, 53, 259-64.

[3] Z. Jambrik, E.L. Santarcangelo, B. Ghelarducci, E. Picano, L. Sebastiani (2004) Does hypnotisability modulate the stress-related endothelial dysfunction. *Brain Res. Bull.*, 63, 213-21.

[4] Z. Jambrik, G. Carli, T.Rudish, A. Varga, T. Forster, E.L. Santarcangelo (2005). Modulation of pain-induced endothelial dysfunction by hypnotisability. *Pain*, 116, 181-86.

[5] E.L. Santarcangelo, R. Balocchi, E. Scattina, D. Manzoni, L. Bruschini, B. Ghelarducci, M. Varanini (2008). Hypnotizability-dependent modulation of the changes in heart rate control induced by upright stance . *Brain Res. Bull.*, in press.

[6] L. Sebastiani, A. Simoni, A. Gemignani, B. Ghelarducci, E.L. Santarcangelo (2005). Relaxation as a cognitive task. *Arch. Ital. Biol*., 143, 1-12.

[7] Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (1996). Standard of measurements, physiological interpretation and clinical use. *Circulation*, 93, 1043-65.

[8] R. Balocchi, F. Cantini, M. Varanini, G. Raimondi, J.M. Legramante, A. Macerata (2006). Revisiting the potentials of time-domain indexes in the short-term HRV analysis. *Biomed. Tech.*, 51, 190-93.

[9] S.M. Pincus (1995). Approximated entropy (ApEnn) as a complexity measure. *Chaos*, 5, 110–17.

[10] J.S. Richman, J.R. Moorman (2000). Physiological time-series analysis using approximate entropy and sample entropy. *Am J Physiol*, 278, H2039 - H2049.

[11] A. Porta, T. Gnecchi-Ruscone, E. Tobaldini, S. Guzzetti, R. Furlan, N. Montano (2007). Progressive decrease of heart period variability entropy-based complexity during graded head-up tilt. *J Appl Physiol*, 103, 1143-49.