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# Changes in autonomic and EEG patterns induced by hypnotic imagination of aversive stimuli in man

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ABSTRACT: Autonomic and electroencephalographic (EEG) responses to aversive stimuli presented by means of hypnotic suggestion have been studied in man. Healthy volunteers with simple phobia were screened for susceptibility to hypnosis. The experimental paradigm included periods of rest during which the hypnotized subjects were asked to produce an emotionally neutral mental image and periods of emotional activation in which they were asked to image a phobic object. Heart rate (HR), respiratory frequency (RF) and EEG were processed to obtain the HR-related indexes of sympatho-vagal balance and the EEG spectral components. The results showed a significant increase in HR and RF with a shift of the sympatho-vagal indexes towards a sympathetic predominance during the hypnotic emotional activation. EEG activity showed a significant increase in the gamma band with a left fronto-central prevalence. There was also a less pronounced increase in the beta band. In conclusion, by means of hypnosis, autonomic and behavioral responses to fear-like stimuli can be induced in man in a reproducible and controlled manner. Such a paradigm could be applied in human neuroimaging studies to identify central nervous structures that modulate stress and fear-related reactions. © 2000 Elsevier Science Inc.

KEY WORDS: Hypnosis, Emotions, Heart rate, Respiration, Behavior, Humans.

## INTRODUCTION

In animals, including humans, the engagement with emotionally relevant environmental situations is always accompanied by distinct modifications of autonomic and behavioral variables. These reactions usually fall into two main categories: one, consistent with aggressive behavior, is represented by an active type of response to a fearful stimulus and is characterized by a massive sympathetic activation and by desynchronization of the electroencephalogram (EEG); the other is typical of a passive response or withdrawal and displays an opposite pattern of autonomic and behavioral response [3]. In general, these emotional reactions have evolved in the different animal species to produce the optimal behavior to fulfill basic defensive/offensive requirements or to cope with stressful situations produced by physical (pain, exercise, postural adjustments, etc.) or purely emotional (fear, anxiety, anger, etc.) stimuli.

The adaptation of the responses to different purposes is assisted by the coordinated action of several central nervous structures. Animal studies have indeed shown that fear-related autonomic and behavioral responses are under the control, besides the hypothalamus [62], of specific forebrain areas, such as the central nucleus of amygdala [27,35], the medial prefrontal cortex [52] and specific cerebellar lobules [29,59,65]. Although specific autonomic and behavioral responses can be recorded in man when exposed to noxious or stressful stimuli [47], very little is known about their dynamics in controlled situations. Further, the role exerted in man by these central nervous structures, identified in the animal, in the integration of stressful stimuli and in the adaptation of these responses to the environmental context, remains unknown.

Experiments on fear-related behaviours in man can be advantageously performed using hypnosis as a cognitive tool to administer a complex stimulus to subjects whose attention can be strictly focussed on the task. In fact, subjects highly susceptible to hypnosis exhibit remarkable attentional and disattentional abilities [15]; their mental processing is strongly associated with vivid imagery [16,17,71] and good visuo-spatial skills [24]. They also exhibit an all-encompassing involvement towards specific attentional objects, which is defined as "absorption" [67], as well as a "fantasy proneness" [38], involving immersion in a private world of fantasy and vivid daydreaming. Furthermore, expectation of hypnosis, in susceptible subjects, enhances the vividness of visual imagery [46] and a hypnotic induction can improve some of their cognitive abilities [12,13,40,63]. Hypnosis appears more effective than simple suggestion in the regulation of some mind-body relationships, like relaxation, vasomotor and pain control [32]. Due to the neuro-psychological traits of highly susceptible subjects and to their possible amplification after a hypnotic induction, hypnosis can be very useful in allowing subjects to accept complex cognitive aversive stimuli, such as suggestion of fear, so that they can experience their emotions very deeply and vividly [20,21,74].

It is known that marked changes in autonomic patterns are present in subjects with a simple phobia when exposed to their specific phobic object [18,44] and that these individuals display cognitive capabilities very similar to those found in subjects highly susceptible to hypnosis [26]. Then, on the basis of the psychological traits of phobic and hypnotizable subjects, a paradigm based

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on the comparison between the autonomic and behavioral responses obtained during a hypnotic phobic and a neutral hypnotic suggestion, offers many advantages. In fact, hypnosis allows us to present a stimulus very similar to the natural one, to control the cognitive channels involved in the requested imagery and the duration of the stimulation, to avoid any effect of stimulus expectation and to control both the long-lasting cognitive stimuli and the baseline conditions. On the basis of the stereotyped reactions exhibited by phobics [18] and controlled through hypnosis, the present experiments were aimed to study the patterns of autonomic and EEG responses evoked by fearful stimulation and to identify the best markers to chose proper acquisition times in neuroimaging experiments.

# MATERIALS AND METHODS

Five right-handed (Edinburgh Handedness Inventory Score >16) volunteers (three females, 2 males, aged 21–30 years), exhibiting a Diagnostic and Statistical Manual of Mental Disorders, 4<sup>th</sup> edition [1] simple phobia, without any other psychiatric, neurological and medical disorder, were selected. Each volunteer signed a written consent approved by the local Ethical Committee (IRCCS, Stella Maris Scientific Foundation, Pisa, Italy) describing the procedures and the experimental risks and affirming his right to withdraw from the experiment at any time. Subjects hypnotic susceptibility (≥10/12) was assessed through the Stanford Hypnotic Susceptibility Scale A and C [72,73] individually administered. The neuropsychological correlates of hypnotizability related to our task were tested through the Tellegen Absorption Scale (TAS; score: 0-34) [67], the Visual Vividness Imagery Questionnaire (VVIQ; score: 20-80) [41] and the Differential Attentional Processes Inventory (DAPQ; score: 36-252) [30].

During the experimental sessions, subjects sat in an armchair in a semi-dark room. Only the hypnotist remained in contact with them throughout the experiment. Recording instrumentation was not visible and the room was lined with sound attenuating panels to reduce the environmental noise. Experimental sessions consisted of six conditions of 5 min each: (1) Quiet wakefulness (eyes closed, QW); (2) neutral hypnosis (hypnosis without any suggestion except relaxation, NH1); (3) suggestions of a neutral object (NSH); (4) neutral hypnosis (NH2); (5) suggestions of a phobic object (ASH); (6) neutral hypnosis (NH3). The neutral (NSH) and phobic object (ASH) were suggested through the request of a visual and auditory mental imagery; besides, subjects were told that "they were clearly aware" of the presence of such objects in the room. Neutral and phobic stimulation were obviously different in their emotional valence but they were carefully balanced in terms of their sensory-motor aspects. All experimental sessions were carried out between 1500 1900 h. During sessions, EEG, electroonlogram (EOG), frontalis electromyogram (EMG), electrocardiogram (ECG) and respiratory trace were monitored continuously. After awakening, subjects underwent a structured interview to collect experiential data. Subjects rated their negative emotion using a numerical scale of 0 to 10 whose endpoints were no fear-like involvement " and "extremely intense fear-like sensation". To avoid a ceiling effect, subjects were instructed to rate 5 an intense negative emotion, comparable to that usually induced by the presence of the real phobic object.

The analysis was focused on the ASH condition and its NSH control since they are the proper indicators of the methodological efficacy of the present approach to the study of the autonomic and behavioral responses described in typical fight or flight reaction to fear.

ECG and Respiratory Trace Acquisition and Data Analysis

For ECG recording Red Dot<sup>TM</sup> Ag/AgCl electrodes were used while the respiratory frequency (RF) was detected through a polymeric piezoelectric dc-coupled transducer wrapped around the chest. Signals were amplified (ECG: gain = 1 K; RA = 10 K), filtered (ECG: low pass <100 Hz and high pass >1 Hz) and digitized at a 256 Hz.

From the ECG signal a derivative/threshold algorithm provided the series of RR intervals (tachogram) and heart rate (HR). The series of consecutive RR intervals were used to provide the power spectral density using a Fast Fourier Transform (FFT)-based approach. It was evaluated on 128 beats (about 2 min) consecutive epochs-length. This always provided two power spectrum values ("a", "b") for each experimental condition (5 min). The duration of the periodical phenomena in the cardiac signal was measured as a function of cardiac beats, rather than seconds [49,66].

The respiratory frequency signal was sampled once for every cardiac cycle, in correspondence with the R wave, thus obtaining a respirogram synchronized with the tachogram. The two series (tachogram and synchronized respirogram) are generally used for further cross-spectral analysis [8].

Two major oscillatory components are usually detectable in RR variability, one of which, synchronous with respiration, is described as high frequency (HF; about 0.25 Hz and varying with respiration), whereas the other, corresponding to the slow waves of arterial pressure, is described as low frequency (LF; about 0.1 Hz). Areas under the power spectra in LF (0.03–0.15 Hz) and HF (0.15–0.4 Hz) were calculated and used for statistical comparisons. The LF and HF oscillatory components were both presented in normalized units (nu). In addition, the LF-to-HF ratio has been calculated to provide an indication of the sympatho-vagal balance. [43,49].

#### EEG, EOG and EMG Acquisition and Data Analysis

For EEG, EOG and EMG, Ag/AgCl electrodes (d = 8 mm; impedance  $<10~\mathrm{K}\Omega$ ) were used. Monopolar EEG electrodes were placed bilaterally in frontal (F3–F4), central (C3–C4) and posterior (O1–O2) scalp regions and referred to an indifferent electrode (Cz). Signals were amplified (EEG: gain = 100 K; EOG: gain = 1 K; EMG: gain = 1 K) and filtered (EEG: low pass  $<100~\mathrm{Hz}$  and high pass  $>0.3~\mathrm{Hz}$ ; EOG: low pass  $<30~\mathrm{Hz}$  and high pass  $>0.3~\mathrm{Hz}$ ; EMG: low pass  $<500~\mathrm{Hz}$  and high pass  $>1~\mathrm{Hz}$ ). The EEG frequency bands considered were defined as follows: alpha (8–13 Hz), beta (13–36 Hz) and gamma (36–44 Hz).

Digitized signals (sampling rate = 256 Hz), were divided in 2-s epochs. Before performing FFT, data have been filtered by means of a Hanning window. The auto-regressive power spectrum of the signal has been calculated using a 1-s overlap and it was validated by comparing collected data with a power spectrum calculated via FFT [28].

EEG periods altered by body and head movement artifacts have been visually discarded, while the EOG and frontalis EMG artifacts have been automatically removed by means of the Independent Component Analysis (ICA) [34].

#### Statistical Procedures

Because the sample belonged to the same population, two-way general linear model analysis of variance (ANOVA) has been applied to normalized data. The descriptive data of HR and RF as well as the spectral indexes of RR variability relative to the different experimental conditions were analyzed by means of a two way ANOVA. The EEG relative power over periods of five epochs was evaluated and compared across experimental conditions and

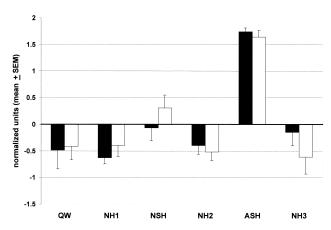


FIG. 1. Heart rate (HR) and respiratory frequency (RF). The effects of each experimental condition on HR (black bars) and RF (white bars), are shown as deviations of the mean normalized values (mean  $\pm$  SEM) from the mean across the whole session (zero line). Abbreviations: ASH, suggestion of a phobic object; NH1, neutral hypnosis (hypnosis without any suggestion except relaxation; NH2, neutral hypnosis; NH3, neutral hypnosis; NSH, suggestion of a neutral ojbect; QW, quiet wakefulness (eyes closed).

channels for each frequency band by means of three separate two-way ANOVAs.

*Post-hoc* Bonferroni test has been performed and threshold for significance has been set at p < 0.05.

#### **RESULTS**

#### Psychological Tests

All subjects exhibited remarkable imaginative and attentional abilities as shown by the high scores obtained in the psychological tests (TAS:  $21.6 \pm 3.9$ ; DAPQ:  $140.8 \pm 21.6$ ; VVIQ:  $61.2 \pm 8.3$ ). At the end of recording sessions, experiential data were collected through a structured interview assessing that each subject had experienced a good hypnotic response and had clearly visualized both the neutral and phobic object. Moreover, it was ascertained that after the phobic suggestion all subjects had felt an intense negative emotion (mean score =  $4.8 \pm 0.2$ ), comparable to that usually induced by the presence of the real phobic object.

### Heart Rate and Respiratory Frequency

Heart rate was increased during aversive hypnotic stimulation (88.1  $\pm$  8.4 beats/min) compared to the mean rate during the baseline experimental conditions (79.0  $\pm$  3.5 beats/min) and its control during neutral hypnotic stimulation (80.2  $\pm$  8.7 beats/min). Respiration frequency also increased during ASH (19.3  $\pm$  2.1 resp/min) with respect to the mean frequency during baseline conditions (15.2  $\pm$  0.8 resp/min) and its NSH control (16.7  $\pm$  3.4 resp/min). To highlight the effect of the experimental conditions on both HR and RF, data have been normalized. For each subject the normalization has been obtained by subtracting from the values of HR and RF in each condition, the mean value across the whole session and dividing the result by the standard deviation [11]. These deviations are shown in Fig. 1.

For HR normalized values, ANOVA yielded a significant difference among conditions (F(5,20) = 13.33; p < 0.001) with ASH different from all the other conditions as indicated by *post-hoc* test. RF normalized values exhibited a similar pattern except for a slight increase during NSH. When compared across experimental conditions, the values were significantly different [F(5,20) = 12.18;

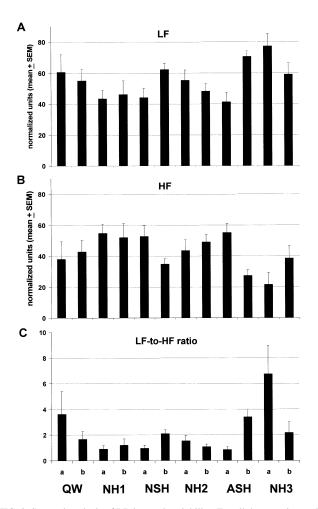


FIG. 2. Spectral analysis of RR interval variability. For all the experimental conditions the low frequency (LF) and high frequency (HF) components and the LF-to HF ratio are shown in (A), (B), and (C), respectively. For each condition, two consecutive spectral index values (a,b) are given (see Materials and Methods). Abbreviations: ASH, suggestion of a phobic robject; NH1, neutral hypnosis (hypnosis without any suggestion except relaxation; NH2, neutral hypnosis; NH3, neutral hypnosis; NSH, suggestion of a neutral object; QW, quiet wakefulness (eyes closed).

p < 9.001] and *post-hoc* test showed that in ASH they were significantly higher than in the other conditions.

#### Power Spectrum Analysis of RR Variability

Figures 2A and B show the mean power of the LF and HF components of the heart period variability in relation to the experimental conditions.

As can be noted in Fig. 2A, the LF component reached its maximum in the second part of ASH (70.6  $\pm$  3.5 nu) and in the first part of NH3 (77.4  $\pm$  7.9 nu). A similar behavior, although less pronounced, could be observed during the second part of NSH (48.2  $\pm$  4.7 nu). LF data calculated among conditions were significantly different [F(11,44) = 4.45, p < 0.001]. Post-hoc test revealed that both the first part of NH3 and the second part of ASH were different from NH1 (43.3  $\pm$  5.6; 46.1  $\pm$  8.7 nu) and NH2 (55.3  $\pm$  6.6; 48.2  $\pm$  4.7 nu)

The HF component depicted in Fig. 2B changed in a reciprocal manner compared to LF, with the lowest values in the second part 108 GEMIGNANI ET AL.

of ASH (27.4  $\pm$  3.7 nu) and in the first part of NH3 (21.5  $\pm$  7.8 nu). Again, ANOVA showed a significant difference among conditions [ $F(11,44) = 4.27 \ p < 0.001$ ] and post-hoc test indicated that the first part of NH3 and the second part of ASH were significantly different from NH1 (54.6  $\pm$  5.8; 51.9  $\pm$  9.0 nu), the second part of NH2 (49.0  $\pm$  4.9 nu) and the first part of both NSH (52.7  $\pm$  7.0 nu) and ASH (55.1  $\pm$  5.9 nu).

Figure 2C shows the LF-to-HF ratio in the same experimental conditions. An increase of the ratio became evident in the second part of ASH (3.4  $\pm$  0.5 nu), reached its maximum in the first part of NH3 (6.7  $\pm 2.2$  nu) and decreased to baseline values during the second part of this condition (2.1  $\pm$  0.8 nu). The comparison among LF-to RF ratios in the different conditions (ANOVA) yielded significant differences [F(11,44) = 4.63, p < 0.001]. However, at variance with the behavior of the previous indexes, post-hoc test revealed that only the ratio computed for the first part of NH3 was different from that of NH1 (0.9  $\pm$  0.2; 1.2  $\pm$  0.4 nu), NH2 (1.5  $\pm$  0.4 nu; 1.1  $\pm$  0.2 nu), NSH (0.9  $\pm$  0.2 nu; 2.0  $\pm$  0.3 nu), the first part of ASH (0.8  $\pm$  0.2 nu), the second part of NH3 and QW (3.6  $\pm$  1.7 nu; 1.6  $\pm$  0.5 nu).

Power Spectrum Analysis of EEG Rhythms

ANOVA did not show any significant change for alpha and beta bands in our experimental paradigm, even if a trend of beta power to increase in NSH and ASH in fronto-central regions could be observed.

For gamma activity (Figs. 3A–C), significant interactions were detected among hemispheres, lobes, channels and experimental conditions. A two-way channels  $\times$  conditions ANOVA [F(25,4002) = 3.45, p < 0.001], showed in NSH (Fig. 3A) a significant prevalence of gamma power in F4 vs. O2 on the right side while in ASH (Fig. 3B) post-hoc tests indicated differences in C4 vs. O2 on the right side and F3 vs. O1 and C3 vs. O1 on the left side.

Lobes  $\times$  conditions [F(10,4020) = 3.23, p < 0.001] interactions were present and *post-hoc* comparisons showed in both ASH and NSH a significant prevalence in frontal vs. posterior and in central vs. posterior lobes. No differences were detected between frontal and central regions.

Significant hemispheres  $\times$  conditions interactions were also observed [F(5,4026) = 5.77, p < 0.001].The comparison for hemispheres in NSH and ASH revealed a significant left side dominance.

In NH3 (Fig. 3C), gamma power did not regain its baseline value. A significant left hemisphere prevalence as well as a lobe effect were present. In addition, comparisons between channels in NH3 revealed a marked fronto-occipital gradient on the left side (F3>C3>O1), which was present, albeit attenuated, also on the right side.

#### **DISCUSSION**

The results of the present study indicate that all subjects experienced an intense negative emotion, as shown by the high scores of the structured interview and by the remarkable changes in the cardiorespiratory output and in the EEG pattern after the hypnotic suggestion of a phobic object. This cognitive tool has proved useful both to amplify the basal psychological characteristics of subjects in which the high hypnotizability was combined with a simple phobia and to provide a reliable model of controlled cognitive stimulation, even if the screening of subjects according to the standard scales of hypnotic susceptibility is an extremely time consuming procedure.

Results also show that the respiratory and cardiac frequencies are significantly increased with respect to the basal condition during the aversive suggestion. The observed changes in cardiovascular variables are strictly related to the suggestions received by the subjects (relaxation during neutral hypnosis and fear during the activation period) and do not depend on the hypnotic state. In fact, when a standard hypnotic induction [72,73] is performed, the effect of the suggested relaxation is a parasympathetic prevalence [20,58], which is considered a simple relaxation response [6].

The comparison between neutral and aversive activation indicated that the affective and cognitive components of the stimuli were able to modulate differently heart and respiratory rates: the former was more influenced by emotion, while the latter was affected by both components of the stimulus. Changes in breathing related to a cognitive task have been described when auditory stimulation (i.e., listening to a story, as in our case) was added to the baseline conditions with eyes closed and whenever a music captured the respiratory rhythm. Such changes may be caused by a volitional respiratory adjustment to the voice or music rhythm [60].

The spectral analysis of the RR interval shows that the changes in cardiac and respiratory frequencies observed during fear-like stimulation are linked to changes in LF and HF components, indicating a shift of the sympatho-vagal balance towards a sympathetic prevalence. The time-course of such modifications showed a delayed onset of the effect which was shifted towards the end of the stimulation period reaching its peak in the first part of the following control condition. These findings were confirmed by the increase of the LF-to-HF ratio, which showed an equivalent trend, and became statistically higher towards the first part of the final baseline condition. These data suggest a sympathetic enhancement typical of an active response to an aversive situation [64]. This is in line with the well-known interaction between cardiovascular and respiratory systems [55], which is even more pronounced in extreme situations when the cooperation becomes essential for survival [31].

An increased sympathetic background is also associated with mental stress [7,33,50] as well as mental and motor imagery [24,57] and it may represent an essential element in the preparation for action as part of an integrated and purposeful behavior.

Our choice to limit the analysis to the alpha, beta and gamma EEG activities rests on the classical assumption that a stressful stimulus should induce a desynchronization of the EEG pattern, with a reduction of the alpha and an increase of the beta and gamma components. However, the interpretation of our results, which showed the alpha rhythm largely unchanged throughout the experimental conditions, is complicated by the co-existence of hypnosis which can elicit, per se, characteristic EEG patterns [14]. In particular the lack of the expected alpha suppression [25] during the activation periods could be linked to hypnosis. A similar result has been reported by Orne and Paskewitz [48], who observed that apprehension or heightened arousal did not always reduce alpha activity.

The tendency exhibited by beta power to increase bilaterally in fronto-central regions could be the consequence of a general arousal due to the presentation of the cognitive stimulus which appears further increased when it is charged by a negative emotional content. The behavior of gamma activity is particularly relevant to the aim of this study, because this frequency band has been related to a series of higher cognitive processes, which include focused attention [54,69], memory [51,61], linguistic processing [53], behavioral and perceptual functions [56], emotional states [23] associative learning [42] and preparation of motor responses [56]. In accordance with recent reports [39,45], our results show a left gamma power increase during the neutral cognitive activation which is further enhanced by the emotional valence of the aversive condition. However, these observations

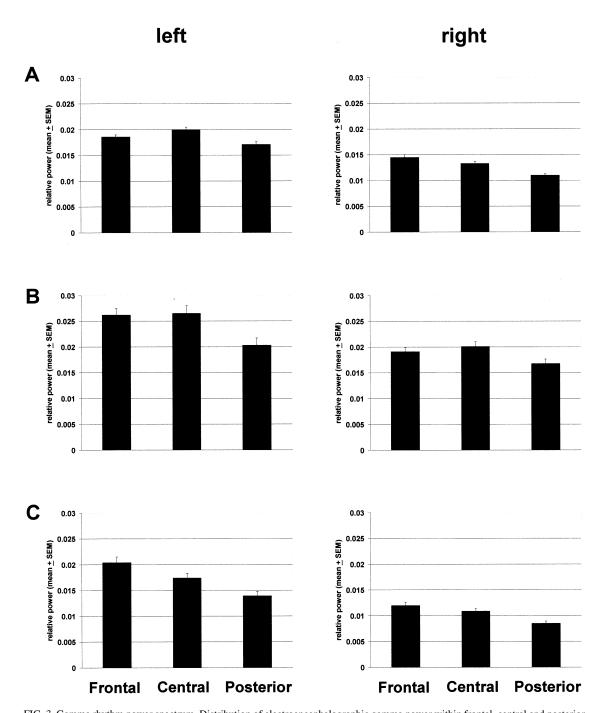


FIG. 3. Gamma rhythm power spectrum. Distribution of electroencephalographic gamma power within frontal, central and posterior regions of both sides as a function of the three most relevant experimental conditions: suggestions of a neutral object (A), phobic object (B) and the following neutral hypnosis (C).

contrast with other studies [19] that report a right side lateralization during negative experiences and with the observation of a right hemisphere predominance of gamma density related to the recalling of a negative emotion during hypnosis [22]. The discrepancy may be explained by the characteristics of the stimulus employed in the different studies. In our case, the stimulus was presented through the verbal channel, required a focused attention and contained suggestions of a complex mental imagery. There-

fore, it was strongly directed to the activation of the left hemisphere [25]. Nonetheless, all subjects reported to have experienced deep negative emotions that were accompanied by marked cardiorespiratory changes. Particularly relevant for the aim of this study is the similar behavior exhibited by the gamma EEG activity in the left fronto-central regions (Fig. 3C) and the sympathetic component of the heart period variability (Figs. 2A,C) which exhibited a parallel increment during the aversive and the subsequent baseline

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conditions, thus supporting the concept of a global involvement, from central command to peripheral output, in human emotional responses. The linkage between cerebral areas and autonomic activities has been investigated in animals in which electrophysiological and neuroanatomical data have shown that frontally located cortical areas such as the medial prefrontal and insular cortex [9] as well as the sensory motor areas [10,70] can modulate the autonomic output by means of direct projections to areas of the amygdala [36,37], and hypothalamus [9], as well as brain steam [5,68] and spinal cord [4] that are involved in neurovegetative control. Thus cognitive, autonomic and somatic-motor activities are integrated in the production of patterned responses, which may differ according to environmental situations. Such integrated responses may represent a reliable index of a specific emotional state and could be used as time markers for scanning procedures in neuroimaging experiments aimed to identify the central nervous structures involved in the control of the different aspects of human affective responses.

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