

Effects of mental stress on cardiovascular and endocrine response in Air Force Academy cadets

Paolo Falaschi, Antonella Proietti, Claudio De Angelis*, Antonio Martocchia, Cesare Giarrizzo, Roberto Biselli*, Rosaria D'Urso & Raffaele D'Amelio

Dept. of Internal Medicine, II Faculty of Medicine, University of Rome "La Sapienza",
Via di Grottarossa 1035, 00189 Rome, ITALY.

*Experimental Flight Center – Dept. of Aviation and Space Medicine, Pratica di Mare, Rome, ITALY.

Correspondence to: Prof. Paolo Falaschi,
Via di Tor Fiorenza 13,
00199 Rome, ITALY
TEL: +39-6-86211484, FAX: +39-6-80345401,
EMAIL: paolo.falaschi@uniroma1.it

Submitted: April 20, 2003

Accepted: May 2, 2003

Key words: **mental stress; heart rate; blood pressure; stress hormones; psychometric tests; pilots**

Neuroendocrinol Lett 2003; 24(3/4):197-202 pii: NEL243403A08 Copyright © Neuroendocrinology Letters www.nel.edu

Abstract

OBJECTIVES: Pilots are exposed to the "stress of flight" and the chronically activated stress response may play an important role in circulatory system disease progression. We studied the effect of an experimental mental stress on cardiovascular and neuroendocrine activity, in Air Force Academy cadets, before and after one month intensive course.

DESIGN: Nine cadets were submitted to a psychometric evaluation before *Stroop test* (ST), including Minnesota Multiphasic Personality Inventory, State and Trait Anxiety Inventory (STAI X1 and X2 form) and Reaction Scheme Test. After ST, subjects completed a STAI X1 form. Heart rate (HR), systolic and diastolic blood pressure (SBP and DBP) were monitored and serum prolactin (PRL), growth hormone (GH), adrenocorticotropin (ACTH) and cortisol levels were determined, during ST. The protocol was repeated at the end of the course.

RESULTS: No significant differences were evident in PRL, GH and ACTH levels. Cortisol concentrations were significantly higher before the course. ST did not modify hormone secretion. ST induced a significant and reproducible elevation of HR and SBP. Basal HR, SBP and DBP values were significantly elevated after the course. Two subjects presented a particular psychometric profile, a different cardiovascular response to ST and did not pass the course.

CONCLUSIONS: acute mental stress significantly activated cardiovascular response without modifying endocrine responses, in relation to the psychological profiles. A significant increase of cardiovascular parameters was present after the course, with enhanced dichotomy between the endocrine and sympathetic system, suggesting a careful evaluation and follow-up for circulatory system diseases in cadets.

Abbreviations:

LTD	= long term disability
HPA	= hypothalamus-pituitary-adrenal axis
MMPI	= Minnesota Multiphasic Personality Inventory
STAI X1 and X2	= State and Trait Anxiety Inventory in X1 and X2 form
RST	= Reaction Scheme Test
P	= overt projection
IP	= inhibited projection
D	= denial
R	= rationalization
G	= guilt
ST	= Stroop Test
PRL	= prolactin
GH	= growth hormone
ACTH	= adrenocorticotropin hormone
RIA	= radioimmunoassay
HR	= heart rate
SBP	= systolic blood pressure
DBP	= diastolic blood pressure
Yrs	= years

Introduction

Circulatory system diseases are major causes of long term disability (LTD) in pilots exposed to the stress of flight and to the psychological workload associated with combat military actions [1–2].

An interaction occurs between the hypothalamus-pituitary-adrenal (HPA) axis and the catecholaminergic system in response to stress stimuli, as part of the generalized adaptation syndrome, with an important role in the progression of circulatory system diseases [3–5].

Psychological and biological parameters are currently evaluated during laboratory (mental arithmetics, speech task, *Stroop test*, interview) and/or real-life (academic examination, anticipated loss, every-day work, parachute jumping) stress conditions [6].

The aim of the study was to investigate the effect of experimental mental stress (*Stroop test*) on cardiovascular reactivity and neuroendocrine activity, in a group of Air Force Academy cadets, before and after one month of intensive course for the pilot licence.

Material and methods

Subjects: Nine healthy cadets (19–21 yrs), homogeneous for cultural and social factors, were evaluated. The Academy cadets were attending a one-month intensive course for the pilot licence, with very competitive theoretical and practical trials, including simulated and real flight experience.

The cadets were volunteers and fully informed about the study and in particular that the result obtained were not considered in the evaluation of the pilot course.

Evaluation of psychological characteristics:

All subjects were submitted to a psychometric evaluation, including Minnesota Multiphasic Personality Inventory (MMPI) [7] and State and Trait Anxiety Inventory (STAI) to evaluate trait anxiety (X2 form) [8]. Reaction Scheme Test (RST) [9] was administered to evaluate the subjects's prevalent response pattern

to mildly stressful everyday life situations, in terms of mainly overt (P) or inhibited projection (IP), denial (D), rationalization (R) or guilt (G). At the beginning and at the end of every *Stroop Test*, the subject was requested to complete STAI in X1 form to evaluate state anxiety.

Experimental protocol: before the one-month course, the subjects were submitted to the experimental protocol. After a 12-hour fasting and a 24-hour withdrawal of alcohol and coffee, the cadet compiled STAI in X1 form for the evaluation of state anxiety; between 9:00 and 9:30 a.m., a sphygmomanometer was placed for the continual monitoring of blood pressure and heart rate and a heparinized cannula was inserted to draw blood samples. The subject was permitted to become accustomed to environmental conditions over a period of 1 hour. Blood pressure and heart rate were measured every 3 min. A blood sample was taken for the determination of PRL, GH, ACTH and cortisol levels, immediately before the administration of a 10 min modified version of the *Stroop Test* (ST) [10]. During the ST, blood pressure was monitored every 1 min. At the end of the ST the subject was requested to complete another STAI X1, and a blood sample was taken. Further blood samples were taken 30, 60, and 90 min after the end of the ST for the determination of PRL, GH, ACTH and cortisol levels. Blood pressure and heart rate was measured every 3 min after the task. An identical procedure was repeated at the end of the course, when the cadets already knew if they were excluded or not from the Academy.

Colour-word conflict task:

The task (based on a modified version of the *Stroop test*) consists of a series of slides representing eight colour words (red, blue, green, yellow, orange, violet, pink, brown) randomly projected onto a screen during a 10 min period. The colour words are written in incongruous colours and the subjects are asked to state the colour they see and to disregard the written word and the colour given concomitantly by a disrupting voice. The responses are recorded on a response sheet. The speed of slide presentation is every 2 seconds.

Hormone assay: Serum PRL, GH and cortisol were determined by RIA using kits manufactured by Ares-Serono (Milan, Italy). ACTH was determined by immunoradiometric assay using kits manufactured by IFCI Clone Systems (Bologna, Italy). Normal ranges are: 5–15 ng/ml for PRL; 0–5 ng/ml for GH; 50–250 ng/ml for cortisol; 9–100 pg/ml for ACTH. Intra- and interassay variations in our laboratory are: 2.1 and 4.5% for PRL; 3.4 and 7.6% for GH; 5.7 and 8.9% for cortisol; 3.5 and 6.2% for ACTH respectively.

Heart rate and blood pressure: Heart rate and blood pressure were measured by using a non-invasive auscultatory device (Takeda, TM2420, Japan) attached to the subject's non dominant arm, every 3 min in basal and recovery period, and every min during ST.

Cardiovascular results are divided in basal, ST (*Stroop test*) and recovery. Basal values are expressed as a mean of 10 successive measurements performed in the 30 min immediately preceding the test; ST as a mean of the 10 measurements during the test, and

recovery as a mean of 10 measurements in the 30 min following the test. **Statistics:** The data were presented as mean \pm standard deviation (mean \pm SD). Student's *t*-test for paired samples between tests and analysis of variance within tests were used for hormonal evaluations; Student's *t*-test for paired samples was used for pressure and psychological evaluations. P values <0.05 were assumed as significant. X²-test was applied to evaluate the differences in subgroups of cadets.

Results

Psychological evaluations: All subjects showed normal MMPI profiles and a normal mean STAI X2 score. Basal STAI X1 score was normal in eight subjects, with not significant higher levels at the beginning of the protocol (data not shown). In subject n.2, STAI X1 score was above the normal range before the course and reduced after ST (from 50 to 30); after the course the score was in normal range and increased after ST (from 36 to 41). Seven subjects showed RST scales with an higher R score than normal population (mean \pm SD, R=16.3 \pm 6.7), whereas the other scores were lower (G=6.9 \pm 3.7, D=6.6 \pm 3.6, P=7.3 \pm 4.9, IP=1.0 \pm 1.1). In subject n.2 and n.3, both the R and P score were higher in respect to normal mean (subj.2 R=14 and P=18, subj.3 R=13 and P=14, respectively). The overall ratio R/P was 1.7 in seven subjects (n.1, n.4-9), while in the normal population is 0.8. The ratio R/P in subject n.2 and n.3 was 0.85, not different from normal population value (for range in normal population see reference 9).

Cardiovascular results: Cardiovascular results were divided in basal, ST and recovery. Evaluating the cardiovascular response to ST in each cadet, two subjects (n.2 and n.3) showed cardiovascular results different from the rest of the group (see below) and therefore were presented separately.

Heart rate: ST induced a significant elevation of heart rate (HR) in respect to basal values both before ($p<0.01$) and after the course before ($p<0.02$). A significant increase of HR basal values after the course was evident (basal pre- vs. post-course HR, $p<0.01$). Recovery values were significantly lower than ST values both before ($p<0.01$) and after the course ($p<0.001$) (fig.1). **Systolic blood pressure:** ST systolic blood pressure (SBP) levels were significantly higher than basal SBP values both before ($p<0.02$) and after the course ($p<0.05$). All SBP values were significantly elevated after the course than before the course (basal SBP, $p<0.01$; ST SBP, $p<0.05$; recovery SBP, $p<0.01$). SBP values decreased significantly during recovery either before (recovery vs. ST SBP, $p<0.02$) or after the course (recovery vs. ST SBP, $p<0.05$) (fig.1). **Diastolic blood pressure:** ST diastolic blood pressure (DBP) values showed a trend to be higher in respect to basal DBP levels ($p=0.1$) before the course and were significantly higher ($p<0.05$) after the course. All DBP values were significantly elevated after the course than before the course (basal DBP, $p<0.02$; ST DBP, $p<0.01$; recovery DBP, $p<0.02$). In recovery period,

values decreased significantly either before (recovery vs. ST DBP, $p<0.05$) or after the course (recovery vs. ST DBP, $p<0.01$) (fig.1).

The HR, SBP and DBP values in seven subjects during ST increased immediately after the beginning of the task, with the highest values between the 1st and the 4th minute (data not shown).

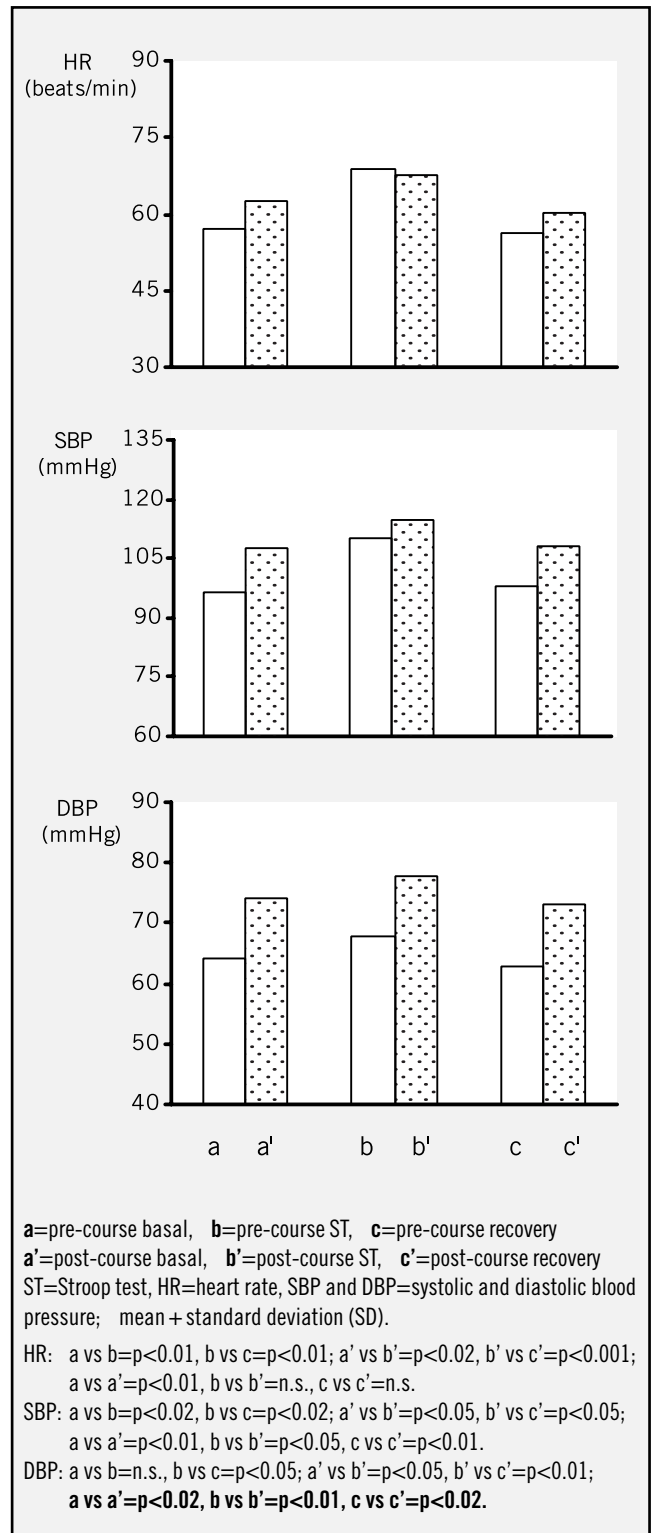


Fig.1. Cardiovascular response to Stroop test before and after the course in cadets (n=7). HR=heart rate, SBP= systolic blood pressure, DBP=diastolic blood pressure.

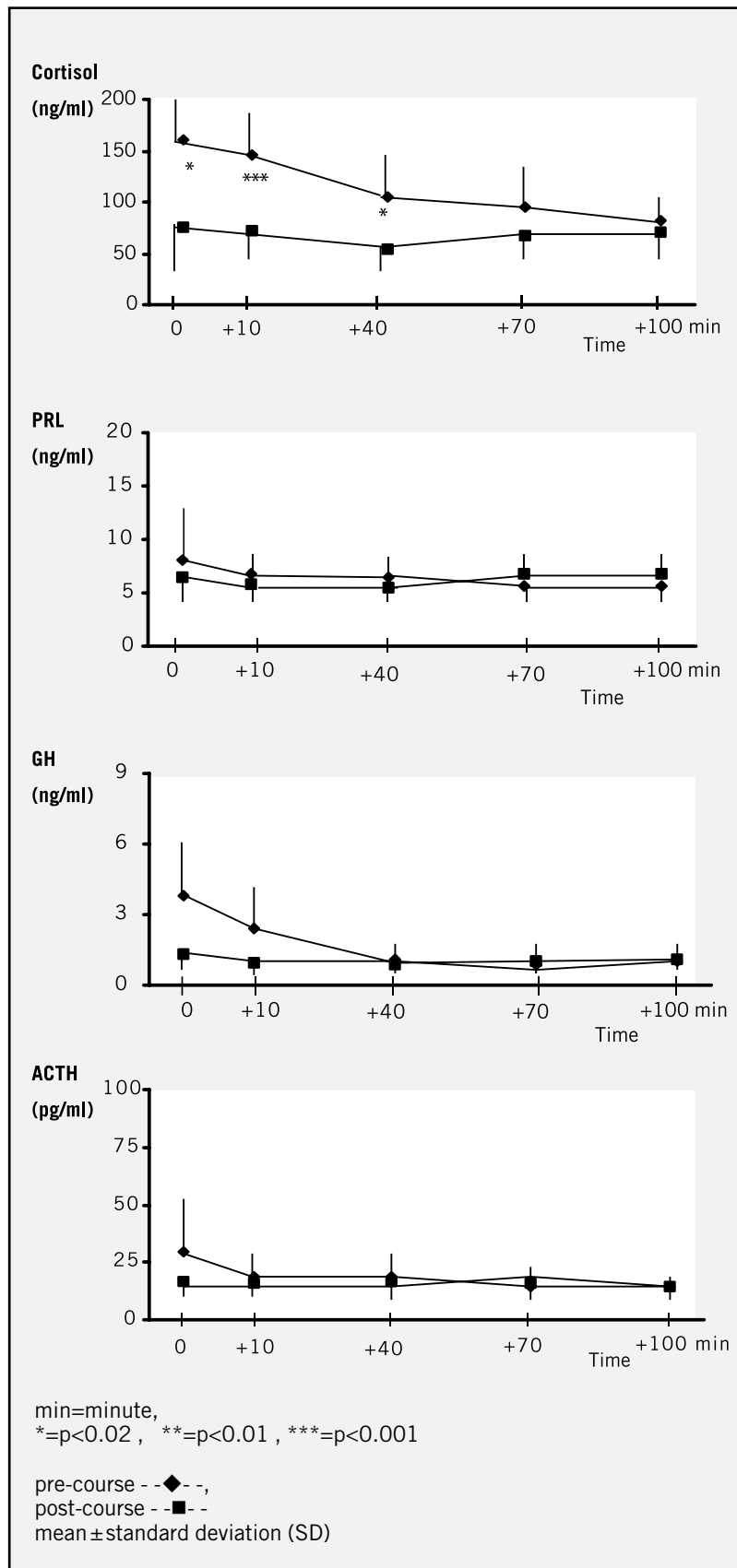


Fig.2. Basal hormonal levels before and after the course and in response to the *Stroop test* (ST) in cadets (n=7).

Regarding the cardiovascular results in the two excluded cadets, subject n.2 showed a diminution of HR during ST (both before and after the course) and a decrease of DBP during ST (before the course); in subject n.3 DBP during ST after the course remained unmodified.

Hormonal results: No statistical significant differences were evident in PRL, GH and ACTH levels respectively both before and after the course, and before and after ST. Cortisol levels before the course were significantly higher than after the course (t.0 min p<0.01, t.+10 min p<0.001, t.+40 min p<0.02). ST did not induce cortisol elevation, neither before nor after the course. Hormonal results of seven subjects (excluding n.2 and n.3) were summarized in fig.2 (n=7). The hormonal pattern in the two excluded cadets (n.2 and n.3) were not different from the rest of the group; in particular, cortisol levels before the course were higher than after the course (data not shown).

Academic results: Seven out of nine subjects successfully passed the one-month intensive course for the attainment of the pilot licence; two subjects (n.2 and n.3) were excluded. In the subjects who passed the course, a significant association was present between the cardiovascular response to ST and the particular psychological profile (high R/P score on RST scale) ($X^2=4.144$ with 1 degree of freedom, p<0.05).

Discussion

In this study, we investigated the effect of experimental mental stress (*Stroop test*) on cardiovascular reactivity and neuroendocrine activity in nine Air Force Academy cadets, before and after one-month intensive course for the attainment of pilot license. The psychological characteristics in seven cadets (n.1, n.4 – 9) resulted homogeneous, and in particular MMPI, STAI X1 and STAI X2 scores resulted comparable to normal subjects. As far as RST score is concerned, the pilots showed higher values of R scale, and lower values in P scale than general population [9], with an R/P ratio almost twice than normal, indicating a higher coping behaviour in stressful situations, that could reflect the peculiarity of this pilot population. On the contrary, in cadet n.2 and n.3, both R and P scores were higher than normal and R/P ratio was similar to normal population; STAI X1

score was higher than normal in subj.2, reflecting an elevation of anxiety state.

Regarding the hormonal values, cortisol levels before the course were statistically higher than after the course, as the result of expectation anxiety at the beginning of the course. During ST no elevation of stress hormones (ACTH, PRL, GH) neither before nor after the course, was observed.

The lack of elevation of adenohipophyseal hormones during ST (10 min) both before and after the course shows that this kind of mental stress does not induce any activations of these hormones, as previously described [11]. A strong stress stimulus or that of longer duration (ST of 20 and 25 min) is probably required to increase hormonal levels, with a hierarchy of response to acute stress [12, 13].

Examining the effect of academic stress on the hormonal secretion, it has been reported that academic examination stress does not influence 24-hour values of GH and PRL [14]. The same authors indicated that academic stress increases cortisol levels only in subjects that showed highest scores of Perceived Stress Scale [15]. Also in our study, cadets did not show any increase of anxiety scale score during ST and cortisol levels were not modified after ST, suggesting a positive coping with the challenging contingency.

Therefore it has to be emphasized that the psychosensorial strain of the modified *Stroop Test* was unable, in spite of its severity (300 consecutive slides in 10 minutes, accompanied with distorting verbal stimuli), to affect the HPA activity; on the contrary, it clearly affected the cardiovascular activity. A significant elevation of cardiovascular parameters (HR and SBP) was constantly present in seven subjects (n.1, n.4–9) after ST, either before or after the course, demonstrating the high reproducibility of the task. It is noteworthy that the excluded cadets showed a psychological and biological behaviour different from the rest of the group, when evaluated separately. In fact, these cadets presented high P score on RST scale (n.2 and n.3), high STAI X1 score (n.2) and showed a blunted cardiovascular response. The association between the attenuated cardiovascular response and the particular psychological profile of these two cadets (high R and P score on RST scale) with negative academic performance needs further evaluation in a larger group of subjects.

Mental stress is well recognized as a stimulus to sympathetic nervous system and, in fact, increased cardiovascular activity (elevation of HR, SBP and DBP) after ST was previously described [11, 16]. The rapid increase of hemodynamic parameters (1–4 min) suggests that neuronal catecholaminergic pathways could play a central role in the cardiovascular response to mental stress.

The dissociation between the sympathetic nervous system and HPA axis activity after ST suggests that mental stress elicits behavioural response through complex interactions between multiple cortical and subcortical brain area, in addition to the hypothalamus and the brain stem [3, 17–19].

Preliminary functional studies showed that ST induces significant activation of visual cortex (Brodmann's area 18 and 19), left insula (involved in autonomic response) and right-middle cingulate gyrus (implicated in inhibition of response to the word name in respect to the colour of the word), with a widespread network of coordinated activities of anterior brain structures (in particular, the prefrontal cortex) [17, 20] and a preferential tonic opioid inhibition of HPA axis activity in coping individuals [11, 21].

All cardiovascular parameters (HR, SBP and DBP) showed a significant activation after one-month of the intensive course, whereas the endocrine program did not show any activation; consequently, the dichotomy between the endocrine program and the sympathetic program appeared enhanced. Such result needs further studies, since chronic cardiovascular hyperactivity may induce pathological changes [6, 16, 22] and epidemiological studies in pilots have demonstrated that circulatory system diseases (essential hypertension, ischemic heart disease and cerebrovascular disease) are major cause of LTD and premature retirement in pilots [2]. Subjects with parental history of hypertension and delayed recovery of baseline blood pressure after acute mental stress may be at particular risk of developing sustained elevated resting blood pressure when exposed to stressful situations [23].

In conclusion, our study shows that acute mental stress significantly activates cardiovascular response without modifying endocrine responses in Air Force Academy cadets. The dichotomy between the endocrine and the sympathetic system appeared enhanced after one-month of the intensive course. Such findings appear to be clinically relevant, since repeated stressful situations and sympathetic hyperactivity could alter control mechanisms of blood pressure inducing hypertension and could influence the progression of atherosclerosis. Since circulatory system diseases are major causes of LTD and premature retirement in pilots, with consequent high cost for the community, we suggest a careful evaluation and control of risk factors. Furthermore, our observation suggests that modifications of cardiovascular response could be related to particular psychological profiles. This aspect needs further studies and could be relevant during selection procedures to flight duty.

REFERENCES

- 1 Leino TK, Leppäluoto J, Ruokonen A, Kuronen P. Proopiomelanocortin activation and simulated interceptor combat flight. *Aviat Space Environ Med* 1998; **69**:486–490.
- 2 Rotondo G. Italian Air Force Medical Service statistical survey on the clinical causes of temporary grounding and permanent unfitness of Italian Air Force aircrews. AGARD Conference Proceedings 1971, n.89, AI–1.
- 3 Sternberg EM, Chrousos GP, Wilder RL, Gold PW. The stress response and the regulation of the inflammatory response. *Ann Intern Med* 1992; **117**:854–866.
- 4 McEwen BS. Protective and damaging effects of stress mediators. *N Engl J Med* 1998; **338**:171–9.

- 5 Barnett PA, Spence JD, Manuck SB, Jennings JR. Psychological stress and the progression of carotid artery disease. *J Hypertension* 1997; **15**:49–55.
- 6 Biondi M, Picardi A. Psychological stress and neuroendocrine function in humans: the last two decades or research. *Psychosom. Psychother.* 1999; **68**:114–150.
- 7 Dahlstrom WG, Wechs SG, Dahlstrom IE. An MMPI handbook. Minnesota Press, Minneapolis, Minnesota; 1972.
- 8 Spielberger CD, Gorsuch R, Lushene RE. Manual for the State Trait Anxiety Inventory. Consulting Psychologist Press, Palo Alto, California; 1970.
- 9 Biondi M, Peronti M, Pacitti F, Pancheri P, Pacifici R, Altieri I et al. Personality, endocrine and immune changes after eight months in healthy individuals under normal daily stress. *Psychosom* 1984; **62**:176–184.
- 10 Stroop JR. Studies of interference in serial verbal reaction. *J Exp Psychol* 1935; **18**:643–662.
- 11 Morris M, Salmon P, Steinberg H, Sykes EA, Bouloux P, Newbould E et al. Endogenous opioids modulate the cardiovascular response to mental stress. *Psychoneuroendocrinology* 1990; **15**:185–92.
- 12 Richter SD, Schurmeyer TH, Schedlowski M, Hadicke A, Tewes U, Schimdt RE et al. Time kinetics of the endocrine response to acute psychological stress. *J Clin Endocrinol Metab* 1996; **81**:1956–60.
- 13 Henry JP. Biological basis of the stress response. *Integr Physiol Behav Sci* 1992; **27**:66–83.
- 14 Malarkey WB, Hall JC, Pearl DK, Kiecolt-Glaser JK, Glaser R. The influence of academic stress and season on 24-hour concentrations of growth hormone and prolactin. *J Clin Endocrinol Metab* 1991; **73**:1089–92.
- 15 Malarkey WB, Hall JC, Pearl DK, Demers LM, Kiecolt-Glaser JK, Glaser R. Influence of academic stress and season on 24-hour mean concentrations of ACTH, cortisol, and beta-endorphin. *Psychoneuroendocrinology* 1995; **20**:499–508.
- 16 Elkohen M, Clerson P, Mounier-Vehoer CL, Humbert R, Prost PL, Poncelet P et al. Variabilité tensionnelle et tests de stimulation: intérêt du Stroop word color conflict test. *Arch Mal Coeur* 1994; **87**:1073–7.
- 17 Andenaert K, Lahorte P, Brans B, Van Laere K, Goethals I, Van Heeringern K et al. The classical stroop interference task as a prefrontal activation probe: a validation study using 99Tcm-ECD brain Spect Nucl Med Commun 2001; **22**:135–43.
- 18 Roth RH, Tam SY, Lda Y, Yang JS, Deutch AY. Stress and the mesocorticolimbic dopamine systems. *Ann N Y Acad Sci* 1998; **537**:138–47.
- 19 Herbert J. Stress, the brain and mental illness. *Br Med J* 1997; **315**:530–5.
- 20 Martin TE. Using functional magnetic resonance imaging to understand mechanisms of consciousness. *Aviat Space Environ Med* 1998; **69**:1146–57.
- 21 Malarkey WB, Lipkus IM, Cacioppo JT. The dissociation of catecholamine and hypothalamic-pituitary-adrenal responses to daily stressors using dexamethasone. *J Clin Endocrinol Metab* 1995; **80**:2458–63.
- 22 Rozanski A, Bairey CN, Krantz DS, Friedman J, Resser KJ, Morol M et al. Mental stress and the induction of silent myocardial ischemia in patients with coronary artery diseases. *N Eng J Med* 1998; **318**:1005–12.
- 23 Gerin W, Pickering TG. Association between delayed recovery of blood pressure after acute mental stress and parental history of hypertension. *J Hypertension* 1995; **13**:603–610.