Review Article

Biochemical Markers of Flying Stress

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A variety of approaches have been made to characterize and quantify the physiological consequences of flying stress. In earlier studies, post flight changes in the plasma/urinary levels of 17-hydroxycorticosteroids (17-OHCS) were measured. Later, a large number of urinary biochemical parameters viz Epinephrine (E), norepinephrine (NE), NE/E ratio, 17 OHCS, urea, uric acid, Phosphate (Pi), Sodium (Na^+) Potassium (K^+), Na/k' ratio expressed either in absolute terms (µg, mg, meq) or as creatinine based ratio (µg, mg, meq/100 mg creatinine) were used to quantify the long and short term effect of flying stress. Several workers have demonstrated that for the evaluation of short term effect of flying stress post flight changes in urinary E, NE, NE/E ratio are adequate. The recent concept however recommends measurement of flight induced change in the urinary level of 3 methoxy 4 hydorxy phenylglycol (MHPG), NE/5-hydroxy tryptamine (5-HT) ratio and Salivary Cortisol as indices of flying stress. The details of these biochemical indices used in the evaluation of flight stress are reviewed and discussed.

Key words : Flying Stress, 17-OHCS, E, NE/E Ratio, MHPG, NE/5HT Ratio, Salivary Cortisol.

Stress has been defined as the nonspecific response of the organism to any demand made upon it. The word stress is a synonym for the factor (stressor) which elicited the response. Aviation leads to wide ranging stresses. During a flight involving aerobatics, aircrew may be subjected to stresses which may be environmental, physical and psychological. Stress affects human performance by influencing some common intermediate variable, termed as arousal. The arousal reaction prepares the organism to meet the threatening situation often referred to as 'fight or flight reaction' which involves the autonomic nervous system, certain endocrine glands and many metabolic activities. This article reviews reported changes in the sympathoadrenal, adreno-cortical and metabolic activities during short and long term exposure to flying stress and discusses their significance as markers of flying stress.

Endocrine and Metabolic Changes

Hale et al[1] reported significant post-flight increases in plasma corticosteroid level in crew members of B-52 bombers after a non stop flight of 12 hours duration. Marchbanks[2,3] observed significant post-flight increase in urinary 17-OHCS in personnel flying B-52 aircraft for periods of 20 and 22 1/2 hrs while Kramer et al[4] noted a significant post-flight increase after 18 hrs of continous flight in F4C aircraft. The observation of near agreement in the values of E, NE, NE/E ratio, 17-OHCS and 17-ketogenic steroids (17-KGS) after 12 and 35 hrs of continous work in simulated and actual flight conditions in the fliers indicated that the sympatho-adrenal and adreno-cortical activity were affected to the same extent under conditions having identical work load, but the fliers in general had a lower adreno-cortical response as compared to that seen in non-fliers[5,6]. This suggested that flight simulator could be used effectively for assessing the work load and stress intensities.

Hale et al[7] demonstrated that flying proficiency is high when the endocrine-metabolic displacement is low. This was indicated when they assessed the work load and stress intensities of fliers and non-fliers performing two hours of bombing strafing events in F-100 aircraft or working in a simulated flight environment. They formulated a physiologic stress index which was based on the percentage deviations of eleven urinary variables viz E, NE, NE/E ratio, 17-OHCS urea, uric acid, Pi, Na^+, K^+, Na/k ratio and urinary volume. When the physiologic stress index was compared with the proficiency score of the pilots, it was noted that the inferiorly performing sub-groups showed a greater deviation with respect to these urinary variables, as against those seen in the superior group. The control data of NE/E ratio, pi excretion and the post-flight values of E, NE and 17-OHCS obtained in non-fliers were much higher than those noted in fliers indicating a higher degree of physiological activity in the former and a greater degree of adaptability in the later group. These battery of urinary variables was also employed for assessing the physiologic cost of pilot engaged in prolonged C-141 flying operation[8]. These data indicated a higher anticipatory stress in the crew than the flying stress that followed, modifying effect of crew position on the inflight and post-flight trends, modifying influence of flight on the pre-existing circadian periodicity and times of day which represented night at home were the highest sensitivity to flight. The data also suggested that the recovery from prolonged continuous operations required nearly 4-5 days and when the crew developed extraordinary fatigue, there was a 12 hour pattern change in the physiologic stress index which suggested an overload reaction.

Aircraft characteristics and flying experience had modifying influences on post-flight increase in plasma/urinary biochemical variables. Hale et al[9] reported a significant post-flight increase in plasma cortisol level along with hypocapnia after a flight of 50 min in single place supersonic F-100 aircraft. When the pilot performance had reached a high level of plateau after months of practive the adrenocortical and adrenomedullary response to flight were not evident. Sodium excretion showed a significant post flight rise which represented a compensation for flight induced respiratory alkalosis. The diminished endocrinal response suggested adaptation. Marchbanks et al[10] appraised flying stress in two military groups after a transoceanic flight of six hours in single place supersonic aircraft (F-100, F-104). Although flight times for the two flights were similar, stress intensities were not found to be equal. Even though the F-100 was more demanding aircraft, there were two factors which elicited a greater stress in F-104 group : (i) F-100 pilots had twice the flying experince as compared to F-104 group, (ii) F-104 group experienced two hours of turbulence while the F-100 had a smooth flying. There was evidence of homeostatic disruption, both groups showing relatively high excretion of nitrogenous metabolites and the two flying groups were differentiated on the basis of their symatho-adrenal and adreno-cortical response which were found to be higher for the F-104 group.

Repeated exposures to aerial combat manoeuvres (ACM) with and without high G exposure did not appear to modify the post flight stress response of pilots. This was demonstrated by Burton et al[11] who noted a post flight increase of 54% in E, 90% in NE and 20% in 17-OHCS in two groups of pilots flying F-16 and F-106 aicraft even though the former group exerted more relative effort associated with high G exposure. Stress was not found to be correlated with sympathetic activity and state of fatigue and appeared to be independent of the character of ACM.

The work of Hale et al[8], Marchbanks et al[10] and Melton et al[6] demonstrated that the fliers in general had higher resting levels of E, NE and 17-OHCS than the non flier. Burton et al[11] observed that fliers who were repeatedly performing ACM had higher resting levels of E, NE, and 17-OHCS, both on ACM and non ACM days than those noted in fliers engaged in lengthy flights without any significant G loading.

Salivary Cortisol : Salivary cortisol has been shown to reflect free cortisol that is the unbound steroid concentration in plasma. This parameter has been used by Kakimoto et al[12] for assessing workload of captains and co-pilots during transport flight. Changes in salivary cortisol level represent current stress rather than the accumulatory stress. It showed a good correlation in relation to variation in the respective responsibilities of captains and co-pilots.

Blood Lactic Acid : Increase in blood lactate level were demonstrated in passengers and crew of commercial aircraft and was attributed to muscular contraction produced by tiredness during flight. Lactate showed maximum increase of 180% in relation to flying hours as compared to increase of 24% in relation to number of landings. Changes showed good correlation with subjective sensation of fatigue[13].

Blood Sulphydryl Groups : Our studies have shown that estimation of blood sulphydryl (bl-SH) groups is a simple repeatable method for assessing the stress under various simulated condition[14]. A study was undertaken to prove the usefulness of this parameter in assessing the stress involved during transport and fighter flying. Pilots flying transport aircraft with a total duration of one to three hours did not show any significant change whereas pilots flying fighter aircraft with a flight duration of 50-70 min showed a significant fall[15].

Adrenomedullary and Sympathetic Activity

The adreno-medullary and sympathetic response were found to be significantly altered after flights in fast fighter aircraft with a flight duration of approximately one hour[16-23,25].

Paolucci and Blundo[16] determined the catecholamines (CA) excretion response of young aviators and suggested that post flight CA excretion level of 333 ng/min and below can be considered acceptable. In relation to CA response, the individuals can be classified as "indifferent" with no changes in CA excretion, "susceptible" with CA excretion value varying from 250-333 ng/min while in "emotional" group CA excretion exceeded beyond a value 333 ng/min.

Analysis of CA alone, however, does not give an account of different types of stress encountered during the flight. Therefore, subsequent workers gave more emphasis on the analysis of E, NE and NE/E ratio[17-23,25]. It has been reported that E increases during emotional arousal and shows elevation under environmental conditions that are disturbing due to their novelty, uncertainty and change. The E response correlates with the feelings of anxiety and apprehension. Moderate rise in E enhances efficiency whereas a high rise leads to impairment of performance. NE is less sensitive to emotional arousal but has been shown to relate to both physical and mental activity of controlled and appropriate nature. NE reflects the activity of sympathetic nerves and shows elevation in assoication with attentiveness, aggression and task oriented responses. The post flight decrease in NE/E ratio suggests involvement of psychological factors and a high preflight NE/E ratio approaching a value of unity post flight indicates incapacitating psychological stress[17].

Debijadji et al[22] and Sarviharju et al[23] noted a significant post flight rise in the urinary output of E, NE after 40 min of supersonic and 30 min of aerobatic flight respectively. Repeated exposure to flying stress[22] and progressive endurance training programme[23] had been found to modify post flight changes in urianry E, NE and NE/E ratio.

Similar post flight changes in E, NE and NE/E ratio which were indicative of better flight adaptability were reported during T-37 flight training programme[17]. During basic cockpit emergency procedure post flight changes in E, NE and NE/E ratio were within normal limits. The First spin-ride appeared to be the most stressful exercise with a maximum post-flight rise of E; NE rise was the least and NE/E ratio showed the maximum fall. Solo and check-flights were equally stressful but resulted in more balanced rise in excretion of catecholamines. As the student progressed from first spin to solo and check flights, there was a progressive decrease in the % rise of E; NE started to show a rise and the post flight reduction in NE/E ratio was significantly less[17]. Similar balanced % rise in E versus NE was observed in the experimental group receiving 80 min of Advanced Simulator for Pilot Training (ASPT) practice on power-on-stall and spin recoveries than in control group who did not receive any ASPT practice[18]. The comparison of CA excretion response of the pilot during the sorties performed either in ASPT or in A-10 rides also showed a similar trends[18,19]. During earlier sorties, both in ASPT and A-10 rides, the relative % increase in E, NE and NE/E ratio were similar; but in the final sortie, E excretion showed a reduction, NE started to show a rise and the NE/E ratio showed a lesser fall. Instructor pupil teaching relationship was also found to be one of the factor which affected CA excretion response of student pilots. Students placed under instructors who relied on criticism and scolding showed higher post flight rise in CA as against students placed under instructors who relied on acceptance and praise behaviour[20]. These observations suggest that repeated exposure to flying stress, practice on ASPT and the proper instructor-pupil relationship modifies the post flight changes in E, NE and NE/E ratio and thus can help student pilot to reach a desirable hormonal balance which may facilitate them to cope successfully with the stress encountered during the flight[17-20].

Our studies also showed a similar trend with respect to post flight changes in E, NE and NE/E ratio[24]. In flight cadets during earlier sorties (solo, 27th sortie) there was a greater NE/E imbalance indicating a greater psychological stress. But as they advanced from solo to mid-term tests (MTT, 49th sortie) there was a substantial reduction in NE/E imbalance, indicating an improvement in the flight compatibility of the student pilot. Post-flight urinary levels of E, NE and NE/E ratio after Power-on-Stall and Spin recovery lesson units indicated dominance of psychological stress in student pilots whereas instructors showed more aggressive reaction.

In pilots, when post flight changes in E, NE and NE/E ratio after a medium stress tail chase sortie were analysed in relation to their flying experience, a lesser rise of E and a greater rise of NE were observed in pilots with greater flying experience (>2000 hrs) as against those seen in pilots with lesser flying experience (<1000 hrs), though differences were not significant. On the other hand, pre flight NE/E ratio did not show any signficant post flight change in more experienced fighter pilots whereas in less experienced fighter pilots the values showed a post-flight reduction. A post flight reduction in NE/E ratio suggest the presence of inflight psychological stress in less experienced fighter pilots. This indicated that NE/E ratio is a better parameter for evaluating psychological stress than epinephrine.

Our study also indicated that a certain amount of post flight rise in E is absolutely essential for a successful flight performance[24]. This was brought out when the post flight changes of these amines were analysed separately in the flight cadets who were declared passed or failed in their MTT. The former showed a significant post flight rise in the urinary levels of E and NE, whereas in the latter none of these changes were significant. In the passed cadets the NE/E ratio showed a post flight rise whereas in the failed cadets the ratio showed a tendency of post flight reduction[24].

A positive relation between former flight experience and mean basal activity of E were noted in the fliers who were repeatedly exposed to flying stress[25]. Our study also indicated such a relation[24]. Pilot with greater flying experience (>2000 hrs) had greater basal excretion of E as compared to fliers with lesser flying experience (<1000 hrs).

Urinary Catecholamine Metabolites

Paolucci and Blundo[26] showed that the post flight changes in excretion rate of VMA can be used for evaluating inflight psychic load of student pilots. Compared to basal values the post flight vanillyl mandelic acid (VMA) increased on the average by 24.5%. 20% of the population showed either a decrease or no variation, 31% of the population showed rise between 20-100%, 22% of the students showed rise between 101-200% while the rest showed an increase beyond 200%. They conluded that a moderate increase in VMA excretion (<200%)indicated normal arousal or alerting as required to complete the challenging tasks; decrease or no variation meant boredom and an excessive (>200% rise) rise of VMA may point to over-arousal due to anxiety crisis.

Changes in the excretion of CA and their metabolities were used to assess the stress of student and instructor pilots during exposure to low, medium and high order emergencies[21]. The urinary levels of VMA, the sum of VMA and 3-methoxy 4-hydroxy phenyl glycol (MHPG), dopamine metabolites i.e. Homovanillic acid (HVA) and 3,4 dihydroxyphenyl acetic acid (DOPAC), 5-hydroxy tryptamine (5-HT) and 5-hydroxy indole acetic acid (5-HIAA) were found to be maximum during exposure to medium order emergencies indicating increased noradrenergic, dopaminergic and serotonergic activity. NE/5-HT ratio has been suggested as a useful indicator of excitement and arousal. A greater increase in the value of this ratio was observed during low order emergencies[21]. Urinary MHPG changes were found to be related to intensity of concentration, attention and alertness to perform the task. These changes were not found to be altered with experience[27]. The levels of MHPG in the urine of pilots and navigators were shown to be commensurate with difficulty of landing[27].

Conclusion

Various techniques used for assessing endocrine-metabolic displacement encountered during flying have been reviewed. In earlier studies long term effects of flying stress were evaluated by employing a series of biochemical parameters viz E, NE, NE/E ratio, plasma/urinary 17-OHCS, urea, uric acid, Na^+, K^+, Na/k ratio and urinary volume. By the use of these battery of urinary determinations it was possible to appraise sensitivity to flying stresses in terms of sympatho-adrenal, adreno-cortical and metabolic activities. The findings suggested that in pilots endocrine metabolic displacement is low with high flying proficiency. Subsequent workers however evaluated short term effects of flying stress primarily with the measurements of post-flight changes in urinary E, NE levels and NE/E ratio. It was observed that the first Spin-ride was the most stressful flying event which showed the greatest E and NE imbalance. Solo and check-flights were equally stressful but resulted in a more balanced % rise in the excretion of catecholamines. With increased flying experience, there was progressively smaller elevation of E and greater relative change in NE post flight. Though an upper limit for the post flight excretion of CA (>333 ng/min) and VMA (>200% rise) have been prescribed in young aviators but these cannot be considered as norms for the entire group of pilot population as the excretion levels have been shown to vary with sortie profile, flying experience, aircraft characteristics and weather conditions. Recent trends in flight stress evaluation recommends the use of urinary MHPG, NE/5-HT ratio and salivary cortisol as these parameters are useful indices of cognition, anxiety arousal and status of current stress respectively. In addition to these parameters, there are indications that changes in blood lactic acid and total blood sulphydryl groups can be used for the measurement of in-flight stress.

References

1. Hale HB, Kratochvil CH, Ellis JP Jr. Plasma corticosteroid levels in aircrewmen after long flights. J Clin Endocr 1958;18:1440-3.

2. Marchbanks VH Jr. Effect of flying stress on urinary 17-OHCS levels. J Aviat Med 1958;29:676-82.

3. Marchbanks VH Jr. Flying stress and urinary 17-OHCS levels during 20h mission. Aerospace Med 1960;31:639-43.

4. Kramer ET, Hale HB, Williams EW. Physiological effects of 18h flight in 4-C aircraft. Aerospace Med 1966;37:1095-8.

5. Hale HB, Ellis JP Jr, Williams EW. Endocrine and metabolic changes during 12h simulated flight. Aerospace Med 1965;36:717-9.

6. Melton CE, MacKenzie JM, Kelln JR et al. Effect of general aviation trainer on the stress of flight training. Aviation Space Environ Med 1975;46:1-5.

7. Hale HB, Duffy JC, Ellis JP Jr, Williams EW. Flying stress in relation to flying proficiency. Aerospace Med 1965;36:112-6.

8. Hale HB, Hartman BO, Harris DA et al. Physiologic stress during 50h double crew mission in C-141 aircraft. Aerospace Med 1972;43:293-9.

9. Hale HB, Ellis JP Jr, Kratochvil CH. Effects of flying supersonic aircraft on plasma corticosteroids and bicarbonate. J Appl Physiol 1959;14:629-31.

10. Marchbanks VH Jr, Hale HB, Ellis JP Jr. Stress response of pilots flying 6 h over water mission in F-100 and F-104 aircraft. Aerospace Med 1963;34:15-8.

11. Burton RR, Storm WF, Johnson LW, Leverett SD Jr. Stress response of pilots flying high performance aircraft during aerial combat manoeuvres. Aviat Space Environ Med 1977;48:301-7.

12. Kakimoto Y, Nakamura A, Tarui H. Crew work load in JASDFC-1 transport flights. I changes in heart rate and salivary cortisol. Aviat Space Environ Med 1988;59:511-6.

13. Prelooker JA. Quantificatioin of Pilot Fatigue - A New approach to a crucial problem. Int J of Aviat Safety 1985;197-204.

14. Iyer EM, Dikshit MB, Suryanarayana S. Effect of exposure to heat, hypoxia, cold, acceleration and vibration stress on the total blood sulfhydryl groups in human subjects. Aviat Space Envrion Med 1985;56:1097-101.

15. Iyer EM. Total blood sulfhydryl group changes during flight trials. Aviat Med 1985;29:127-30.

16. Paolucci G, Blundo G. Catecholamine excretion from air cadets. Riv Med Aer 1972;36:97.

17. Krahenbuhl GS, Marett JR, King NW. Catecholamine excretion in T-37 flight training. Aviat Space Environ Med 1977;48:405-8.

18. Krahenbuhl GS, Marett JR,Reid GB. Task specific simulator pretraining and inflight stress of student pilots. Aviat Space Environ Med 1978;48:1107-10.

19. Krahenbuhl GS, Constable SH, Darst PW et al. Catecholamine excretion in A-10 pilots. Aviat Space Environ Med 1980;51:661-4.

20. Krahenbuhl GS, Darst PW, Marett JR et al. Instructor pilot teaching behaviour and student pilot stress in flight training. Aviat Space Environ Med 1981;52:594-7.

21. Krahenbuhl GS, Harris J, Malchow RD, Stern JR. Biogenic amine/metabolic response during inflight emergencies. Aviat Space Environ Med 1985;56:576-80.

22. Debijadji R, Perovic L, Varagic V. Evaluation of sympathoadrenal activity in pilots by urinary catecholamines during supersonic flight. Aerospace Med 1970;41:677-9.

23. Sarviharju PJ, Huikk ME, Jouppila PI, Kaerki NT. Effect of endurance training in the urinary excretion of noradrenaline and adrenaline during ground and flying activity. Aerospace Med 1971;42:1297-303.

24. Iyer EM, Banerjee PK, Baboo NS. Development of new criteria for work load and stress assessment of the flying cadets with the help of urinary biochemical stress parameters. AR&DB Project Report No 434 IAM,IAF, Bangalore, 1990.

25. Svensson E, Thanderj MA, Sjoberg L, Gillberg M. Military flight experience and sympathoadrenal activity. Aviat Space Environ Med 1988;59:411-16.

26. Paolucci G, Blundo G. Inflight psychic load in student pilots evaluated by means of vanil mandelic acid changes in urinary excretion. In "Clinical Psychology and Psychiatry of the Aerospace operational Environment" AGARDCP 133. France B-13-1-B-13-2, 1973.

27. Rubin RT, Miller RG, Clark BR et al. The Stress of aircraft carrier landing. II. 3 methoxy 4- hydroxy phenylglycol excretion in naval aviators. Psychosomatic Med 1970;32:589-97.