PLASMA GLUCOSE LEVELS AND FLIGHT

Glicemia e volo aereo

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Key words: hypoglycaemia, flight, noise, waiting for the flight

Parole chiave: ipoglicemia, volo aereo, rumore, attesa del volo
Abstract

Background: Noise is able to exert many adverse health effects, ranging from damages on various organs and systems to changes in biochemical and humoral markers. In literature, the effects of chronic exposure to noise on blood glucose levels have been reported, although these results are conflicting: some authors reported hyperglycaemia, others hypoglycaemia and many others recorded no changes in blood glucose levels.

Objectives: Considering that the plasma glucose levels are not used as a biomarker of noise exposure, we conducted a pilot study on 6 subjects, 2 females and 4 males, working as clerks in a low noise environment in order to evaluate the possible occurrence of changes on plasma glucose levels in healthy subjects, non-diabetic and not accustomed to flight, exposed to noise and to flight-related stressors.

Methods: The subjects completed a specific clinic-anamnestic questionnaire and underwent a general clinical examination. In the first phase of the study, participants underwent blood tests in order to assess the plasma glucose levels at three different times: at 8:00 a.m., on board of a turboprop transport aircraft before the take-off with the engine switched off, after 60 and 120 minutes’ flight. The second phase of the study was carried out one month after the first one and while working in the office; three blood tests were performed again, at fasting and after 60 and 120 minutes. The plasma glucose levels were measured on capillary blood by the refractometry method through the use of Glucoscan One Touch device.

Results: The results show an increase of plasma glucose levels during the waiting for the flight and a statistically significant decrease of plasma glucose levels in the first hour of flight (p <0.001), persisting even at the second hour (p <0.001). No significant changes were found in the blood tests performed at work.

Discussion: The data show an initial hyperglycaemic response, followed by a persistent and moderate decrease of glycaemia; a similar response was not observed in the same subjects during ordinary work activities. The Authors believe that the initial increase of the plasma glucose levels, recorded in absence of noise on board, could be related to the response to other stressors, such as anxiety linked to the waiting for the flight. The decrease of the plasma glucose levels observed after 60 and 120 minutes’ flight, that is in conditions of prolonged exposure to flight-related stressors and to noise, may be linked to the intervention of several mechanisms: partial phenomenon of adaptation-exhaustion of the neuroendocrine response to stress; hypoglycaemic effect of noise, CCK-mediated and VIP-mediated with consequent insulin release and decrease of the plasma glucose levels; synergistic action of the above mechanisms. The absence of changes on the plasma glucose levels during the usual work activity is probably due to the absence of those stressors considered able to induce the alterations of the plasma glucose levels recorded during the first phase of the study.

Conclusions: These preliminary results suggest that exposure to flight-related stressors and in particular exposure to noise can cause a hypoglycaemic response.
**Abstract**

**Introduzione:** Il rumore è in grado di esercitare numerosi effetti negativi sulla salute, che vanno da disturbi a livello di vari organi e apparati a modificazioni degli indici biochimici ed umorali. In letteratura sono riportati gli effetti dell’esposizione cronica a rumore sulla glicemia, benché tali risultati non sono univoci: alcuni autori riportano iperglicemia, altri ipoglicemia ed altri ancora non hanno registrato modificazioni del tasso ematico glicemico.

**Obiettivi:** Tenuto conto che la glicemia non è utilizzata come marcatore di esposizione al rumore, abbiamo eseguito uno studio pilota su 6 soggetti, 2 femmine e 4 maschi, che effettuavano lavoro di ufficio in ambiente non rumoroso, con l’obiettivo di valutare l’eventuale occorrenza di modificazioni dei livelli ematici di glucosio quando tali soggetti, non diabetici e non abituati al volo aereo, venivano esposti a stress da volo ed al rumore presente in un aereo.

**Metodi:** I soggetti partecipanti hanno compilato un questionario clinico anamnestico mirato e sono stati sottoposti ad un esame clinico generale. In una prima fase dello studio, i partecipanti sono stati sottoposti a prelievi ematici per la determinazione della glicemia in tre diversi momenti: alle ore 8, su un aereo da trasporto a turboelica prima del decollo, a motore spento; dopo 60 e dopo 120 minuti di volo. La seconda fase dello studio è stata effettuata dopo un mese dalla prima e durante l’attività lavorativa in ufficio; sono stati effettuati nuovamente tre prelievi, a digiuno e dopo 60 e 120 minuti. La glicemia è stata valutata su sangue capillare con metodo refrattometrico mediante l’utilizzazione di un apparecchio Glucoscan One Touch.

**Risultati:** I risultati dimostrano un aumento della glicemia in attesa del volo ed una diminuzione statisticamente significativa della glicemia alla prima ora di volo (p<0.001) che persiste anche alla seconda ora (p<0.001). Non sono state riscontrate modificazioni significative della glicemia per i tre prelievi effettuati in ufficio.

**Discussione:** I dati dimostrano un’iniziale risposta iperglicemica, seguita da una persistente e moderata riduzione della glicemia; un’analoga risposta non è stata riscontrata negli stessi soggetti durante le usuali attività lavorative. Gli Autori ritengono che l’iniziale incremento della glicemia, registrata in assenza del rumore dell’aereo, potrebbe essere correlato alla risposta dell’organismo ad altri stressors, come l’ansia da attesa del volo. La riduzione della glicemia riscontrata dopo 60 e 120 minuti di volo, ossia in condizioni di esposizione più prolungata allo stress legato al volo ed al rumore, è verosimilmente legata all’intervento di diversi meccanismi: parziale fenomeno di adattamento-esaurimento della risposta neuroendocrina allo stress; effetto ipoglicemizzante del rumore, CCK-mediato e VIP-mediato con conseguente liberazione di insulina e riduzione della glicemia; sinergismo dei due meccanismi. L’assenza di variazioni della glicemia durante il lavoro in ufficio potrebbe essere spiegata dalla mancanza di quei fattori stressogeni ritenuti responsabili delle variazioni glicemiche registrate durante la prima fase dello studio.

**Conclusioni:** Tali risultati preliminari fanno pensare che l’esposizione agli stressors del volo aereo ed in particolare al rumore possa determinare una risposta ipoglicemizzante.
Background
In recent years, more and more data have been pointed out in literature regarding noise effects on the central nervous system (CNS) (cerebral cortex, limbic system), on the peripheral nervous system (PNS) and on the neuroendocrine system (NES), including the neurohormonal part of gastrointestinal system (1-13). Alterations of some biochemical and humoral markers, among which changes of the plasma glucose levels in response to chronic noise exposure, have been reported (2, 3, 14, 15). The data reported by various authors on the changes in plasma glucose levels in response to noise exposure, are not concordant. The majority of authors reports a hyperglycaemic response (2, 3, 6); Fooladi associates noise exposure to an increased food craving, weight gain and diabetes (16); others show no changes of the plasma glucose levels (14, 15, 17); others consider diabetes as a possible confounding factor in assessing the correlation between noise and cardiovascular effects (18); in studies on animals some authors find a decrease of the plasma glucose levels in response to stress stimuli such as noise (19). In case of noise exposure, in fact, it’s possible to observe a multiple and complex neuroendocrine response, developed from an initial hyperactivity of the pituitary, the adrenal and other endocrine glands, followed by a phase of inhibition or adaptation (2, 3). The neuroendocrine response to noise is considered an adaptive response to stress by some authors (2, 3, 16, 20, 21). The plasma glucose levels are influenced by the interaction existing among different hormones and neurotransmitters (epinephrine, insulin, glucagon, 17OH-corticosteroids, thyroxine, growth hormone) that, in turn, undergo important modifications during the response to stress (12, 20, 22, 23). It’s also known that hormonal and neuromodulator substances, such as the cholecystokinin (CCK) and the vasoactive intestinal peptide (VIP), present in the CNS and in the PNS, control plasma glucose levels through a hypoglycaemic effect mediated by insulin release and that these neuropeptides are released in case of stress (23, 24).

As part of a research we have carried out in recent years about extra-auditory noise effects (5, 7-13, 25-30) and considering that the measurement of plasma glucose is not generally used as a biomarker of noise exposure, we conducted a pilot study in order to evaluate the changes of the plasma glucose levels in healthy subjects, exposed to flight-related stressors.

Materials and methods
We studied six healthy subjects, of mean age 31.6 years old: 2 females (30 and 47 years old) and 4 males (25, 26, 27 and 35 years old). All subjects carried out administrative work in a noiseless environment; working time for females was 8:00-14:00 and for males 8:00-16:30. A clinical anamnestic questionnaire was administered to subjects, in presence of a physician, in order to examine the characteristics of the work, education, lifestyle, family history of hypertension, cardiovascular diseases, obesity and diabetes, past and current diseases and any ongoing drug treatment. Each subject underwent a general clinical examination. Not accostumed to flight, the subjects were exposed to noise on board of a turboprop transport aircraft. The noise, produced by the propellers, was harmonic with a basic frequency determined by the product of the number of the revolutions of the motor by the number of the propeller blades; in the inside the noise was generated and amplified by the vibrations of the walls and the inner surfaces of the aircraft (29). This kind of noise covers all frequencies, being mainly at low frequency (29). At the take-off, the intensity of noise is about 104-106 dB(A); during cruise speed, it varies from 80 to 92 Db(A). The study is divided in two phases (Table 1).

Table 1- Summary of the study

<table>
<thead>
<tr>
<th>Phase 1:</th>
<th>T0</th>
<th>T1</th>
<th>T2</th>
</tr>
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<tbody>
<tr>
<td>before and during the flight (E: exposure)</td>
<td>At 8:00 a.m.</td>
<td>60’ on flight</td>
<td>120’ on flight</td>
</tr>
<tr>
<td>without noise</td>
<td>Noise</td>
<td>Noise</td>
<td></td>
</tr>
<tr>
<td>Phase 2:</td>
<td>T0</td>
<td>T1</td>
<td>T2</td>
</tr>
<tr>
<td>at work (NE: non-exposure)</td>
<td>At 8:00 a.m.</td>
<td>After 60’</td>
<td>After 120’</td>
</tr>
</tbody>
</table>
In the first phase (exposure: E), the subjects underwent blood tests in order to assess the plasma glucose levels in three different moments: at 8:00 a.m., on board before the take-off with the engine switched off (T0); after 60 minutes’ (T1) and again 120 (T2) minutes’ flight. All subjects were fasting for at least eight hours. The plasma glucose levels were measured on capillary blood by the refractometry method through the use of Glucoscan One Touch device. After performed the second blood test, a questionnaire was administered to subjects in order to investigate the occurrence of hypoglycaemia-related symptoms, collected with binary system (yes/no): shakiness, nervousness/anxiety, sweating, palpitations, hunger, weakness, confusion and drowsiness.

In the second phase of the study (non-exposure: NE), carried out after a month from the first one, the blood tests were taken at work in the three different moments again; the subjects were at fast for at least eight hours. The same questionnaire on the occurrence of hypoglycaemia-related symptoms was administered.

All subjects consented to their personal details being available, declaring that they had been made aware that these data were ranked as “sensitive information”, and consented that the data arising from the research protocol should be treated in an anonymous and collective way, with scientific methods and for scientific purposes in accordance with the principles of the Declaration of Helsinki.

The statistic evaluation of the data was performed using the Student t test for paired data.

Results
The analysis of the clinical anamnestic questionnaire showed only a family history of hypertension and cardiovascular diseases for three subjects, a family history of obesity for only one of them and a family history of diabetes for a fourth subject. The results of the administered questionnaires show no hypoglycaemic symptoms. The trend of changes of the plasma glucose levels showed no significant differences between the subjects with family history of obesity and/or diabetes and those who had not familiarity.

During the first phase of the study (E), a significant reduction of the plasma glucose levels from T0 to T1 (T0 = 102.2 ± 5.5 mg/dl; T1 = 73.8 ± 10.9 mg/dl; p < 0.001) and from T0 to T2 (T0 = 102.2 ± 5.5 mg/dl; T2 = 75.0 ± 11.4 mg/dl; p < 0.001) was detected (Table 2).

![Table 2- Changes of the plasma glucose levels](image)

<table>
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<tr>
<th></th>
<th>T0</th>
<th>T1</th>
<th>T2</th>
</tr>
</thead>
<tbody>
<tr>
<td>On Flight (E)</td>
<td>102.2 ± 5.5 mg/dl</td>
<td>73.8 ± 10.9 mg/dl</td>
<td>75.0 ± 11.4 mg/dl</td>
</tr>
<tr>
<td>At Work (NE)</td>
<td>95.5 ± 5.6 mg/dl</td>
<td>94.3 ± 6.2 mg/dl</td>
<td>96.2 ± 8.60 mg/dl</td>
</tr>
</tbody>
</table>

No significant difference in the plasma glucose levels measured in T1 (first hour) and T2 (second hour) was found. The plasma glucose levels did not change significantly, when the subjects were at work (NE).

The plasma glucose levels measured during the second phase of the study were studied. At time T0, in the first phase of the study E on board, the subjects showed significantly higher plasma glucose levels compared to those measured during the second phase of the study NE, at work (E = 102.2 ± 5.5 mg/dl; NE = 95.5 ± 5.6 mg/dl; p < 0.02).

At time T1, during noise exposure, a significant decrease of the plasma glucose levels was observed, even compared to the levels observed at work (E = 73.8 ± 10.9 mg/dl; NE = 94.3 ± 6.2 mg/dl; p < 0.001). This decrease continued at time T2 (E = 75.0 ± 11.4 mg/dl; NE = 96.2 ± 8.60 mg/dl; P < 0.001).

Discussion and Conclusions
The data measured during the exposure show an initial response represented by an increase of the plasma glucose levels, followed by a persistent and moderate decrease of glycaemia, not clinically evident. A similar response was not observed in the same subjects during ordinary work activities. The Authors believe that an increase of the plasma glucose levels adds to an initial and acute stress; the initial increase of the plasma glucose levels, recorded in absence of noise on board, could be related to the occurrence of an acute and initial response to stress due to the waiting for the flight. Actually the waiting for the flight may be considered a psychological stressor, causing anxiety. Flying is a massive exposure to numerous stressors the human body not normally experience, such as cabin pressurization, sitting still, loud...
noise (at the take-off), dry air, sudden loss of support during turbulence, middle ear pain from air pressure changes, etc (31), all able to cause anxiety. In our design there are so all too many stressors, that is unknown variables difficult to evaluate. We hypothesize that noise is the most important stressor, according to literary studies: studies conducted on fearful flyers suggested that they reported higher levels of anxiety when confronted with flight-related sounds (alone or with pictures) than when confronted with pictures without sounds (32). This seems to support the idea that sounds are crucial to evoke fear related to flying (32). According to this, we believe that noise, at high intensity present at the take-off and during the flight, is the first cause in determining the response to the flight-related stressors. It’s well known that stressors are associated to the activation of the autonomic nervous system which causes an increased production of catecholamines (epinephrine and norepinephrine) and to the activation of the hypothalamic-pituitary-adrenal axis with an increase of the plasma levels of the corticosteroids. The increase of the circulating levels of the stress hormones leads to many physiological changes including an increase of the plasma glucose levels (33, 34). Some literary studies point out that normoglycaemia is detected in response to an acute stress; Rostamkhani et al found an increase of insulin levels in response to an acute stress, not associated to instant changes of the plasma glucose levels and believed it to be related to a possible concomitant activation of glycogenolysis and gluconeogenesis, due to the release of catecholamines and corticosteroids (17). This mechanism could explain the increase of the plasma glucose levels found in subjects waiting for the flight. We underline that the subjects were not used to flying. A new stimulus is in fact known to be able to increase the response to psychological stressors.

As to the decrease of the plasma glucose levels observed after 60 and 120 minutes’ flight, that is in conditions of prolonged exposure to this kind of stress, with the addiction of the stress of noise, it’s possible to assume the intervention of several mechanisms:

1) the neuroendocrine response to stress may have incurred a partial phenomenon of adaptation-exhaustion (12, 16, 17, 23);

2) the noise, during the flight, can produce a hypoglycaemic effect connected to an action on the CNS and/or on PNS through the release of CCK and VIP, by the neurohormonal section of the gastroenteric apparatus, causing stimulation of the endocrine pancreas, insulin release and decrease of the plasma glucose levels; so the pancreatic effect would prevail over the catecolaminic and corticosteroid effects, with hypoglycaemia; the stimulation, induced by CCK and VIP, could be connected to the gastrointestinal changes due to the exposure to noise, we noticed, as well as other authors, in some previous research (2, 3, 7, 12);

3) the two mechanisms may act synergistically in causing this phenomenon.

The same experiment has been repeated at work. In this condition the plasma glucose levels at time T0 were lower than the plasma glucose levels measured in the same subjects at time T0 of the first phase of this study (phase of the waiting for the flight). The plasma glucose levels also did not vary at work, with values higher than those recorded in the same subjects during the flight. The absence of changes of the plasma glucose levels during the usual work activity is probably due to the absence of the stressors that induced alterations of the plasma glucose levels during the exposure: waiting for the flight and noise.

These preliminary results suggest that the noise exposure, together with other stressors, can cause hypoglycaemia, compared to a condition of hyperglycaemia measured in the phase of an acute and initial stress related to the waiting for the flight.

Considering that this is a pilot study, it would be worth analyzing a larger sample, taking into account the influence of the different stressors (waiting for the flight and noise) on the plasma glucose levels.

If these data are confirmed, their relevance would be clear above all for those occupational activities exposed to noise and requiring a high level of attention and concentration. In case we could establish that the prolonged exposure to noise causes a lowering of the plasma glucose levels, it would be fundamental to remember that hypoglycaemia can give both neurogenic and neuroglcapenic symptoms. The former are related to the activation of the autonomic nervous system and include increased sweating, hunger, tingling (mediated by activation of the cholinergic system), palpitations, nervousness/anxiety, shakiness (mediated by activation of the adrenergic system). The neuroglcapenic signs and symptoms instead are linked to the brain’s deprivation of glucose and include difficulty in thinking and speaking, decreased attention, weakness, drowsiness, confusion, convulsions until the onset of coma and death in cases of severe hypoglycemia (35). All this implies a possible increase of the risks for the health and safety not only of the worker but also of third party, with not sufficiently investigated and not adequately recognized medical-legal consequences.

Our results must be considered still preliminary and lead to carry out and to study in detail a greater casuistry.
References


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