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6.18 Neurobehavioural and neuroendocrine evaluation in operating room personnel exposed to low levels of anaesthetic gases

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Introduction

According to various neurobehavioral field studies [2, 7], occupational exposure to high concentrations of anaesthetic gases can determine early effects on the central nervous system. At lower exposure levels (nitrous oxide - N_2O < 100 ppm), factors other than anaesthetic gases, such as stress and work organization, may play a role in determining performance impairment [9, 6]. These factors were specifically considered in this study by examining a group of subjects working in the same operating theatres, under either gaseous or non-gaseous anaesthesia conditions.

A similarity in the mechanism of neurotoxic action between anaesthetic gases and organic solvents has been identified as an interference of these substances with the dopaminergic system. Similar intermediate reactive metabolites are produced at the tubero-infundibular level, which can condense with dopamine in vitro, determining its depletion [8]. As a consequence, neuroendocrine changes can be produced, such as increased secretion of prolactin (PRL) levels observed in workers exposed to organic solvents [1]. Based on these observations, we also decided to evaluate the PRL secretion in operating room workers.

Methods

A group of 30 operating room workers who usually perform the same job with the same schedule alternatively in gaseous anaesthesia and in non-gaseous anaesthesia conditions was studied. The examinations were repeated in the same subjects during a week with non-gaseous anaesthesia (Time 1) and during a week with gaseous anesthesia (Time 2). The study design (*Table 1*) included measurements of the Simple Reaction Time (SRT) test, the serum prolactin (PRL) and cortisol level, at Time 1 and Time 2 at the beginning and at the end of the first and the last day of the working week. The measurements were scheduled according to the "quasi-experimental" balanced design of Gambberale [3]: half of the workers were tested first at the beginning and then at the end of the shift, whereas the other half were tested first at the end and then at the beginning of the shift. The atmospheric concentrations of N_2O (A-N_2O) were measured during the shift, while the urinary levels of nitrous oxide (U-N_2O) where measured at the end of it. In addition, a group of 30 controls, composed of hospital workers not exposed to anaesthetic gases or other neurotoxins were examined with the same protocol. The general characteristics (age, sex, life habits, length of exposure and educational levels) of the exposed and control groups are reported in *table 2*. Additional information was collected regarding the females' menstrual cycle at the time of testing.

Table 1: Study

Working Week	
First day	Last day
Beginning of the shift	**Beginning of the shift**
Simple Reaction Time	Simple Reaction Time
Prolactin	Prolactin
Cortisol	Cortisol
During the shift	**During the shift**
Atmospheric N_20	Atmospheric N_20
End of the shift	**End of the shift**
Simple Reaction Time	Simple Reaction Time
Prolactin	Prolactin
Cortisol	Cortisol
Urinary N_20	Urinary N_20

Table 2: Characteristics of exposed and control subjects

	Exposed (n = 30)			Controls (n = 20)		
	Mean	S.D.	%	Mean	S.D.	%
MALES			43			41
FEMALES			57			59
DOCTORS			33			31
NURSES			67			69
AGE (years)	30	6.6		29.3	7.5	
EDUCATION*	2.7	0.8		3	0.4	
ALCOHOL (g/day)	20	4		20	4	
SMOKE (index)	0.7	0.9		1.3	1.9	
COFFEE (N°/day)	2	1.02		2.1	1.4	
EXPOSURE LENGTH (months)	50.4	51.5		73.4	72.8	
VOCABULARY	67.2	4.5		66.8	4.4	

(*): index based on number of school years

Table 3: Atmospheric (ppm) and urinary (µg/l) concentrations of N_2O

	TIME 1			TIME 2		
	N°	Geom. Mean	Geom. SD	N°	Geom. Mean	Geom. SD
URINARY N_2O first week day	30	2.5	1.63	30	21.54	9.2
URINARY N_2O last week day	30	2.7	1.79	30	25.67	10.88
ATMOSPHERIC N_2O first week day	30	5	3.3	30	50.9	20.8
ATMOSPHERIC N_2O last week day	30	6	3.8	30	54.2	22.1

The SRT test was selected from the Swedish Performance Evaluation System [4]; PRL levels were detected by means of radio-immuno-assay (Prolactin MAIA-Clone, Ares Serono, Milan); cortisol levels were analyzed with radio-immuno-assay (RIA-Coat Cortisol, Byk Gulden Italy, Cormano, Milan). A-N_2O concentrations in the breathing zone were measured during a 3-hour period by molecular sieves personal samplers. U-N_2O was measured in urine samples collected at the end of the shift. Environmental and biological concentrations were analyzed by the head space method, using a HP 5880-A gas chromatograph connected to a HP 5970-A mass selective detector, according with the method of Imbriani [5].

The variations within each group during the week were preliminary analyzed with the ANOVA test for repeated measures. The two way ANOVA test was used to compare the results between the different groups (exposed subjects at time 1 vs. exposed subjects at time 2 vs. control subjects). Simple and multiple linear regression analyses were performed to study dose-effect relationships and correlations between the indicators of exposure.

Results

The highest exposure levels were found on the last day of the working week, when U-N_2O ranged from 10 to 50 µg/l (geometric mean 25.67, geometric SD 10.88) Trace N_2O exposure levels were detected also at time 1, probably due to pollution from adjacent operating rooms (*Table 3*). A significant correlation was observed between U-N_2O and A-N_2O ($r = 0.89$; $p = 0.0001$). PRL and cortisol showed fluctuations during the day, with higher levels at the beginning of the shift, according to the circadian rhythm. Alteration of SRT and increase of PRL levels were observed in the operating room personnel, compared to the control subjects, only when they worked with gaseous anesthesia. These differences were more evident at the end of the shift, the last day of the working week (*Fig. 1* and *2*). Cortisol levels did not differ between the two anaesthesia conditions (*Fig. 3*). No dose-effect relationships were found between SRT and PRL and the indicators of exposure, while a slight association was noticed between SRT and PRL at the end of the shift on the last day of the working week ($r = 0.3$; $p = 0.001$).

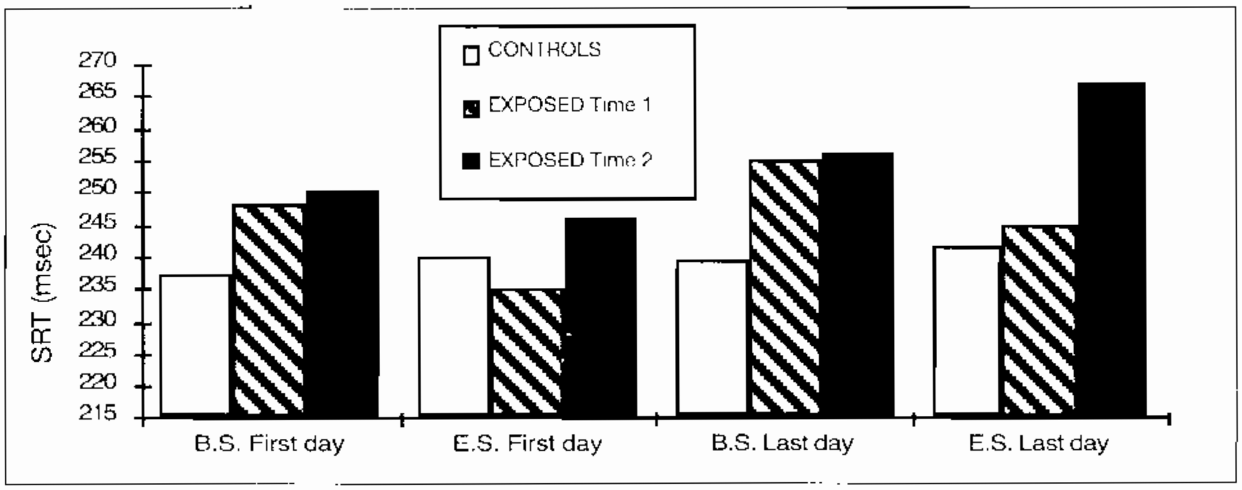

Figure 1: Simple reaction times in exposed and control subjects

B.S. = BEFORE THE SHIFT
E.S. = END OF THE SHIFT

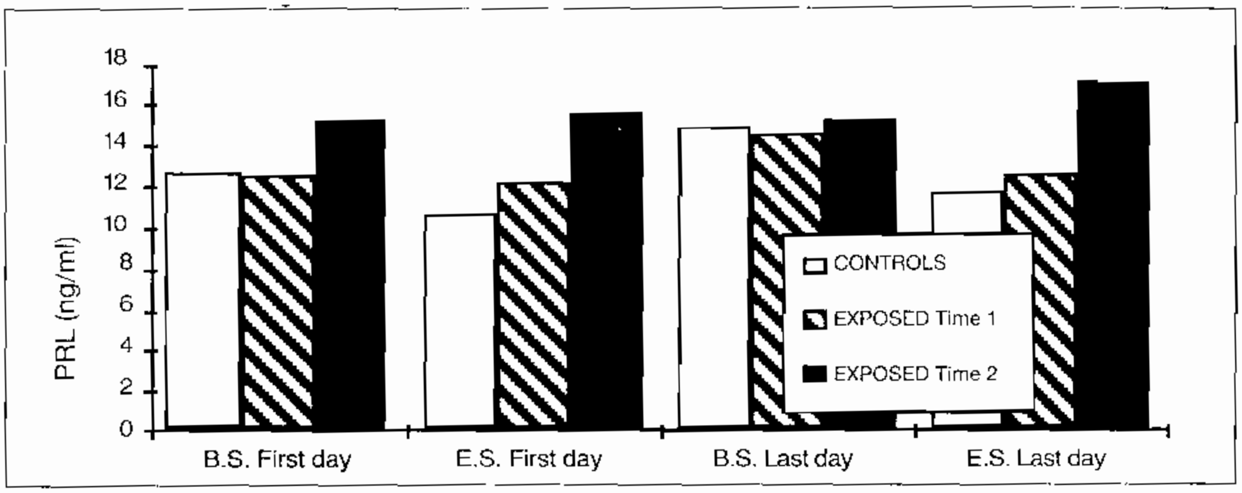

Figure 2: Prolactin levels in exposed and control subjects

B.S. = BEFORE THE SHIFT
E.S. - END OF THE SHIFT

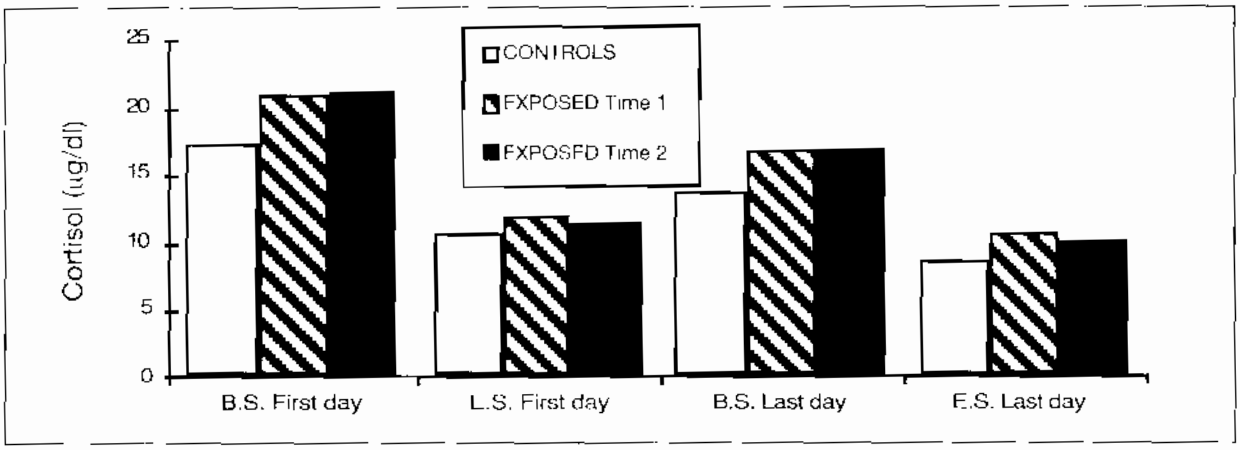

Figure 3: Serum cortisol levels in exposed and control subjects

B.S. BEFORE THE SHIFT
E.S. - END OF THE SHIFT

Conclusions

The existence of neurotoxic effects of anesthetic gases at low exposure levels is confirmed by this "semi-experimental" study. This effect appears not to be related to stress factors, because whenever the identical stress level was present in the same subjects in different operating conditions, the impairment of performance appeared only during anaesthetics exposure. Moreover, the neuropsychological effects could be an expression of anaesthetic gases interference with the dopaminergic system, as shown by the increase of PRL levels. Since most of the operating room personnel are females, consideration should be also given to the possible implications of these neuroendocrine changes on reproductivity.

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