POSTURAL CONTROL REDUCED BY SUBANESTHETIC NITROUS OXIDE NARCOSIS

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Abstract — The effects of subanesthetic (21%) nitrous oxide (N₂O) narcosis on postural control, as measured by posturography were studied in 12 subjects. Vibration induced body sway, with open and closed eyes, and body sway induced by a visual stimulus were evaluated. Adaptation was measured as the quotient of body sway variance between the second and first halves of each trial. Change in postural strategy was evaluated as change in the variance of shear forces relative to change in body sway. Subjective evaluation of narcosis was recorded. Body sway variance increased significantly during exposure to N₂O, and equally for all body sway inducing stimuli. With the eyes open, adaptation to vibratory perturbation was significantly reduced by N₂O. Postural strategy was unaffected by N₂O, but differed significantly between stimuli, with relatively less involvement of shear forces during vibratory perturbation in the eyes open condition than during the other body sway inducing stimuli. Subjective evaluation of narcosis correlated with body sway variance during the visual stimulus. The present findings indicate that subanesthetic N₂O narcosis reduces postural control. Adaptation to a balance disturbing stimulus, with undisturbed vision, is decreased by N₂O. Visual clues are shown to be crucial to the postural strategy adopted to maintain balance. The effects of N₂O are assumed to be due to impairment of sensorimotor integration in the CNS.

Keywords — posture; adaptation; vision; vibration; N₂O.

Introduction

To maintain postural control in erect stance the human utilizes a complex feedback system involving vestibular, visual and somatosensory input, which is integrated in the central nervous system (CNS) and which affects the motor output required to control posture (1). Sedatives and tranquilizers are widely used in the elderly, causing dizziness, faintings and blackouts (2), presumably due to depression of central nervous sensory integrating centers (3). Of several sedative drugs known to impair human postural control (4–6), some have been shown to impair the vestibuloocular reflex and voluntary eye movements (7–9). These effects have been interpreted as reflecting depressant action on specific neurons involved in the control of eye movements (10,11), though sedation per se has also been postulated as a contributing cause (9,12). Although it is not well understood how sedatives affect human postural control, their effects can be assumed to be either specific (that is, excerpted on specific neural populations), or non-specific (that is, due to general sedation of the CNS).

Inert gas narcosis (for example, induced by N₂O) is assumed to affect behavior by decreasing alertness (13). When induced by hyperbaric air (14) or by N₂O at 1 ATA (15), it has been shown to affect balance. N₂O has been reported to affect the integration of visual and proprioceptive spatial information (16), but not to affect spinal neurons responding to proprioceptive stimuli, or to induce muscular relaxation (17). We thus assumed N₂O would affect postural control mainly by acting on the CNS, possibly by reducing alertness and thus disturbing sensorimotor integration in the CNS.

Received 30 March 1992; Revised 16 November 1992; Accepted 17 November 1992.

173
Although posturography is a useful tool in assessing postural disturbances in patients (1,5), it is difficult to interpret posturography results obtained during quiet stance, as balance is the result of a complex feedback system. On the other hand, the function of postural control can be elucidated by perturbing stance. A vibration stimulus applied to the calf muscles may be used to disturb proprioception, thereby perturbing stance (18). This method has been found to yield reproducible results (1,19). On the basis of a previous pilot study, and to ascertain differences in body sway, a more powerful vibration causing larger body sway was used in the present study than was used in our previous experiments (19). Visual disturbance can also affect balance (5,20). The visual stimulus used in the present study has been shown to disturb balance reproducibly (21).

The aims of the present study were to investigate the effects of subanesthetic N₂O narcosis on sensorimotor integration in postural control during proprioceptive and visual disturbances. Based on the results of other investigators we assumed N₂O would affect ability to adapt to a balance disturbing stimulus (15), and possibly induce a change in postural strategy adopted to maintain balance (6).

Materials and Methods

Twelve paid volunteers took part in the study, 7 females and 5 males aged 25 to 42 y, mean age 32.4 y. All 12 subjects were free from concomitant otoneurological disease, and none had any history of such diseases. The subjects were instructed to abstain from alcoholic beverages and sedatives during the 24-h period preceding each test session. During all tests the subjects stood on a force platform, heels together, feet at an angle of 30° and arms crossed over the chest. Auditory positional clues were blocked by headphone relayed music (Concierto de Aranjuez, Joaquin Rodrigo). During the week preceding the tests all subjects underwent a practice test session without the respiratory equipment. During the equilibration phase, and during the 2-min pauses between tests with different stimuli, the subjects were seated on a chair. A computer (Compaq 486/25) with data recording software sampled the signal from the force platform at 10 Hz through an AD-converter. Signal analysis was done with a mathematical software package (386-Matlab).

Body sway was induced either by disturbing proprioception with two vibrators attached to the calf muscles, or by exposure to a whole-field visual stimulus which gives the illusion of movement in the sagittal plane. The vibration stimulus sequences lasted 256 s, and visual stimulation 240 s, both preceded by a stabilization period of 30 s.

The two vibrators were turned on and off simultaneously according to a pseudorandom binary stimulus (PRBS) schedule with a minimal switching time of 1 s and a period of 256 s. The amplitude and frequency of the vibration were constant (1.0 mm, 60 Hz). Such a stimulus perturbs body posture essentially in the sagittal plane (19,22). During the vibration stimulus, the subjects were instructed either to keep their eyes closed or to fixate upon a spot on the wall approximately 2.5 m in front of them.

To provide the visual stimulus, a movable screen (1.2 m high, 1.5 m broad) was set at an angle of approximately 45° to a mirror of the same size, their bottom edges 1 m above the floor, and the force platform within the 'V' between them. The screen consisted of a matt white sheet of rubberized cloth, 3.0 m long, joined in a looped band around two vertical rollers 1.5 m apart, one of which was driven by a computer controlled servo motor. The surface of the screen was patterned with 2 cm broad vertical black lines at irregular distances from each other (5 to 35 cm), which to the subject standing on the force platform were reflected in the mirror, thus forming, in effect, two screens. (In Figure 1, for clarity the mirror has been omitted.) The visual stimulus itself consisted of the pattern formed by the movement of the vertical lines toward vs. away from the angle formed by the screen and the mirror. The stimulus waveform was a sinus with a mean velocity of 0 m/s, a max-
Postural Control Reduced by \( N_2O \)

**Figure 1.** Experimental set-up and design. For clarity the mirror is omitted from the drawing.

During tests the subjects breathed either air or a mixture of \( N_2O \), oxygen and air. Gas mixtures were inhaled through the face mask of an anesthesia circle system with an in-line soda lime \( CO_2 \)-absorber. Fresh gas flow to the circle system was about 15 liters per minute. Both \( N_2O \) and oxygen concentrations were kept at 21%, as controlled with a gas monitor (Ohmeda 4700 OxiCap Monitor). The subjects breathed each gas mixture for ten minutes before tests to allow blood-brain equilibration (23). Both the inspiratory and expiratory limbs of the anesthetic circuit were 210 cm (as compared to 120 cm in conventional anesthesia practice), the increased...
length of the tubing causing an increase in respiratory resistance. Adequacy of ventilation was monitored with continuous measurements of the end-tidal CO₂ concentration and arterial oxygen saturation (Ohmeda 4700 OxiCap Monitor).

Nitric oxide (NO) is an endogenous vaso­dilator. It is considered possibly to affect excitatory amino acids in the brain (24). The contamination of the inhaled N₂O with NO was less than 1 ppm, and its effects were readily inhibited by hemoglobin (24). Thus NO was considered not to contribute to the results of the present experiments. The increased respiratory resistance caused by lengthening of the tubing resulted in hyperventilation, reflected in a decreased end-tidal CO₂ concentration. Lowered blood CO₂ concentration induces vasoconstriction in the CNS. Hyperventilation is known to cause dizziness and lightheadedness (3). Thus, it is possible that hyperventilation may have contributed to an increased body sway. As data concerning the end-tidal CO₂ concentration were not collected systematically, we do not know whether hyperventilation differed between tests, thus possibly contributing to the difference in body sway. However, as a decreased end-tidal CO₂ concentration was noted in both air and N₂O tests, with no obvious difference between them, it is unlikely that hyperventilation contributed significantly to the differences in body sway between tests.

There was one week’s interval between tests with the different gases (N₂O or air). The order of gas exposure (N₂O or air) and that of body sway tests (vibration/open eyes, vibration/closed eyes, visual stimulus) were randomized according to a Latin square design. After the last test done during exposure to N₂O, the subjects were asked to evaluate the narcotic effect according to a subjective 20-point logarithmic scale (25). The study design was approved by the Ethics Committee of the Medical Faculty of Lund University.

The moment produced by the displacements of the center point of force actuated by the feet to maintain upright stance was recorded by the force platform and considered to reflect body sway. The variance of the sum of static and dynamic moments throughout each test, being proportional to the amount of mechanical energy consumed (1), was evaluated in the sagittal plane, the unit being (Nm)².

As adaptation has been defined as behavioral adjustment in response to continuous stimulus (26), such adjustment comes with time. Therefore, in the present study the subject’s response was observed in two phases—the first and second half of each test, an adaptation quotient (with no dimension) being calculated from the variance of the second half divided by that of the first. Subdivision of the stimulus period was restricted to two phases in order to minimize variation in the frequency of the vibratory stimulus. This procedure enables the overall relative change in sway variance (that is, adaptation to be observed), but has the disadvantage that it is not possible to follow the time course of adaptation in detail.

The magnitude of shear forces relative to an empirical maximum has been used as a measure of hip strategy utilization (5). During our experiments the subjects were observed to use flexion of both ankles and hips, thus producing shear forces and moment due to ankle torque. We also found correlation between the two (see Results and Table 1), though the relationship between the variance of body sway and that of shear forces changed according to the experimental conditions. Thus the quotient between the two forces exerted in the sagittal direction, in the plane of the platform, with the unit m⁻², was considered to reflect the overall postural strategy, as it is reasonable to suppose body sway and

<table>
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<tr>
<th>Table 1. Pearson’s Coefficient of Correlation (r) Between Variance of Body Sway and Variance of Shear Forces</th>
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<tbody>
<tr>
<td>AIR vibration stimulus/closed eyes</td>
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<tr>
<td>AIR vibration stimulus/open eyes</td>
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<tr>
<td>AIR visual stimulus</td>
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<tr>
<td>N₂O vibration stimulus/closed eyes</td>
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<tr>
<td>N₂O vibration stimulus/open eyes</td>
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<tr>
<td>N₂O visual stimulus</td>
</tr>
</tbody>
</table>

* NS = non-significant.
shear forces to be produced by different movements of the different body segments. Had there been a simple electro-mechanical reason for the positive correlation found, the relationship between the two forces would have been fairly constant and unaffected by the different experimental conditions.

As all data tended to be positively skewed, they were transformed to their natural logarithm to allow the use of parametric tests. The effects of the two variables (gases and stimuli) and their interaction were analyzed using two-way analysis of variance. A post hoc simultaneous analysis (Student-Newman-Keuls multiple range test) was done to determine the level of significance in differences between groups. As sway changes in the sagittal and coronal planes were congruous, and as our stimuli were aimed to perturb body posture essentially in the sagittal plane, only sagittal sway results were used in analysis. RS/1 software (Bolt, Beranek & Newman, Cambridge, Massachusetts, USA) run on an IBM-compatible personal computer was used in all statistical analysis. Differences were considered to be significant at $P < 0.05$.

**Results**

In all stimulus conditions body sway variance was significantly greater during exposure to N₂O than during exposure to air. The three stimuli differed significantly in their efficacy to induce body sway. The vibration stimulus induced greater body sway with greater sway variance with the subjects' eyes closed than with them open. Sway variance was greater with the vibration stimulus irrespective of whether the subjects' eyes were open or closed, than with the visual stimulus. There was no interaction between the effect of N₂O and that of body sway inducing stimuli (Figure 2).

Values for the adaptation quotient indicated adaptation to be significantly better during air breathing than during N₂O breathing in the vibration/open eyes condition, but not in the vibration/closed eyes condition or in the visual stimulus condition. (Figure 3).

The correlation between body sway variance and variance of shear forces was good and statistically significant in most cases (Table 1). The quotient between shear forces and
body sway was unaffected by N₂O, but differed significantly between stimuli, being lower during the vibration/open eyes condition than during the vibration/closed eyes or visual stimulus conditions, whereas it did not differ between the two latter conditions. (Figure 4).

The results of the two-way analyses of variance (gases versus stimuli) and of the post hoc comparisons of the effects of different stimuli, where applicable, are summarized in Table 2.

There was a statistically significant correlation between the subjective ratings of narcotic effect and body sway variance during the visual stimulus condition (Table 3).

**Discussion**

In the present investigation subanesthetic N₂O narcosis was found to reduce postural control and reduce adaptation to a balance perturbing stimulus with vision undisturbed, but not to affect the postural strategy adopted to maintain balance. The postural strategy adopted to maintain balance appeared to be dependent on visual information.

Inert gas narcosis induced by hyperbaric air (14) or by N₂O (15) has been shown to affect balance. N₂O has been reported to affect the integration of visual and proprioceptive spatial information (16), but not to affect spinal neurons responding to proprioceptive stimuli and not to induce muscular relaxation (17). Nerve conductance seems either to be unaffected by N₂O (17) or to be enhanced (27).

Certainly spinal reflexes are depressed by N₂O (probably acting on spinal motorneurons), though this depression is not complete even at 85% N₂O (17). Moreover, 60% N₂O has been shown to block the brainstem retic-
Table 3. Pearson's Coefficient of Correlation (r) Between Subjective Ratings of Narcotic
Effect and Variance of Body Sway

<table>
<thead>
<tr>
<th>Condition</th>
<th>r</th>
<th>P</th>
</tr>
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<tbody>
<tr>
<td>N₂O vibration stimulus/closed eyes</td>
<td>0.07</td>
<td>NS*</td>
</tr>
<tr>
<td>N₂O vibration stimulus/open eyes</td>
<td>0.34</td>
<td>NS</td>
</tr>
<tr>
<td>N₂O visual stimulus</td>
<td>0.71</td>
<td>P &lt; 0.01</td>
</tr>
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*NS = non-significant.

ular inhibition of both monosynaptic and polysynaptic reflexes (17).

The presently used subanesthetic (21%) N₂O concentration did reasonably not affect spinal motoneurons significantly. Thus a central nervous depressant effect of subanesthetic N₂O narcosis was assumed to be the most probable explanation of its balance disturbing action.

In the present experiments, when vision was undisturbed, body sway decreased over time (that is, adaptation), though this was less manifest during N₂O exposure. This finding is consistent with a previous report of greater and more rapidly increasing unsteadiness with eyes closed with increasing concentrations of N₂O (15). The finding of reduced ability to use visual information during N₂O narcosis is in agreement with reported reduction of voluntary saccades and pursuit eye movements during N₂O narcosis (28). Moreover, voluntary non-visual suppression of the vestibuloocular reflex gain has been found to be reduced by N₂O narcosis (29), which may reflect reduced spatial orientation during subanesthetic N₂O narcosis, possibly resulting in reduced adaptation in the present experiments.

Postural strategy was found not to be affected by subanesthetic N₂O narcosis. This is somewhat consistent with what has been reported concerning midazolam (6). Thus alertness seems not to be an important factor in the adoption of a postural strategy. Disturbed vision, either due to closing the eyes or due to the presence of a moving surround, was found to be associated with a relative increase in shear forces as compared to the situation with undisturbed vision. The present findings of vision as an important factor in the adoption of postural strategy are consistent with those previously reported (30).

That reduced alertness might be a cause of the balance disturbances, common to N₂O and sedatives, derives a measure of support from the present finding of a correlation between the subjective ratings of narcotic effect and body sway variance during the visual stimulus condition. The reason why correlation was found only with the visual stimulus might be the predictability of that stimulus (as compared to the other stimuli), and the fact that it did not induce sway by acting on spinal reflexes as the vibration stimulus did to some degree.

Conclusions

The present findings suggest that impairment of sensory integration in the CNS, by subanesthetic N₂O narcosis, reduces postural control and impairs the subject's ability to adapt to balance-perturbing stimuli when vision is undisturbed. Visual information would seem to be of crucial importance both when adapting to balance-disturbing stimuli and when adopting a postural strategy.

Acknowledgments - The present study was supported by The Swedish Medical Research Council (grant no. 17X-05693), and the Söderberg Foundation.

REFERENCES


