Br. J. Anaesth. (1978) **50**, 1173

DECISION-MAKING BEHAVIOUR DURING INHALATION OF SUBANAESTHETIC CONCENTRATIONS OF ENFLURANE

S. BENTIN, G. I. COLLINS AND N. ADAM

SUMMARY

The effect of subanaesthetic concentrations of enflurane on decision-making behaviour in risk situations was assessed using a signal detection task. The subject heard noise alone (white noise) or a signal superimposed on the noise (1000-Hz tone) and had to report what he heard in each trial. Risk situations were manipulated by changing the monetary reward and penalty associated with correct and incorrect responses. Eight male volunteers participated in this study. It was found that under anaesthetic influence they did not avoid the same risks which had been avoided under control conditions. The findings are explained in terms of influence of the gas on loss of control and lessened responsibility for the result of behaviour.

The effects of subanaesthetic concentrations of widely used inhalation anaesthetics on mental functions are of interest to the anaesthetist because this knowledge will add to better understanding of anaesthetic action and because trace anaesthetic concentrations such as exist in the operating room may have similar, though less noticeable, effects. Such small effects may add to others like a negative influence on attention to result in significant and yet unmeasurable deterioration of complex mental functions.

Attention was found to be extremely vulnerable to the anaesthetics; decreased attention was shown even with trace concentrations of halothane, enflurane and nitrous oxide (Bruce and Bach, 1975, 1976). Bruce and his group have also reported impaired perceptual and motor skills (Bruce, Bach and Arbit, 1974) and decreased digit span (Bruce and Bach, 1975, 1976). However, Smith and Shirley (1977) have repeated these studies and have failed to observe the reported effects. By contrast, with higher concentrations, constant effects have been found. Subanaesthetic concentrations of general anaesthetics were shown to disturb time perception (Steinberg, 1954; Robson, Burns and Welt, 1960; Adam et al., 1971; Adam, Castro and Clark, 1974) and impair memory functions, particularly storage and retrieval of word memory (Steinberg, 1954; Steinberg and Tomkiewicz, 1968; Adam, 1973). Furthermore, intellectual impairment has been observed for several days following anaesthesia (Davison et al., 1975; Adam, 1976). Decreased attention and slower processing of incoming information (Adam and Collins, 1978) probably account for most of the deficiencies in time perception and psychomotor skills based on reaction time. Verbal memory functions, however, are adversely affected even when the attention factor is taken into account (Adam, 1973). The extent of anaesthetic effect on other complex cognitive functions such as thinking, verbal behaviour, reasoning and decision making has not been investigated.

The present paper focuses on decision-making behaviour. Previous unreported observations from our laboratory on behaviour of normal subjects under anaesthetic influence pointed to possible anaesthetic effects on this function. More specifically, we were impressed that the subjects were more impulsive in their responses and willing to adopt risky strategies. Since risk-taking tendency is known to be a major factor in decision making, it was the aim of this paper to assess the influence of subanaesthetic concentration of enflurane (Ēthrane) on the risk-taking tendency in human volunteers.

METHOD

Material

Risk taking was tested with a standard signal detection task (Swets, 1964; Green and Swets, 1966). An auditory stimulus was delivered to the

S. BENTIN,* M.SC.; N. ADAM, PH.D.; Department of Behavioral Biology, Aba Khoushy School of Medicine, Technion, Haifa, Israel. G. I. COLLINS, M.B., B.S., Department of Anaesthesia, Rothschild University Hospital, Haifa.

* Present address: Aranne Laboratory of Psychophysiology and Neurobehavioral Studies, Department of Neurology, Hadassah University Hospital, Jerusalem, Israel.

Reprint requests to N. Adam, Department of Behavioral Biology, Gutwirth Building, Technion, Haifa, Israel.

0007-0912/78/0050-1173 $01.00

subject through earphones. The stimulus was either a white noise (N) or a pure tone superimposed on the same white noise (signal+noise, SN). Intensity of the N and SN stimuli were arranged to make discrimination between the two stimuli difficult. The subject's task in each trial was to decide whether the stimulus had been noise+signal or noise only. The subject's response can be classified into four different outcomes. If the signal was presented with noise: (1) a "yes" response would be correct (a hit) and (2) a "no" response would be incorrect (a miss). If the signal was not presented: (3) a "yes" response would be incorrect (false alarm) and (4) a "no" response would be correct (correct rejection) (table I).

TABLE I. *The four possible outcomes of a response in a signal detection task*

	Response	
	Yes	No
Stimulus		
Signal+noise	HIT	MISS
Noise	FALSE ALARM	CORRECT REJECTION

The delivery of the stimuli was controlled by a PDP 11/45 computer. The subjects were presented with N stimuli in 50% of the trials and with SN stimuli in the remaining 50%. The order of presentation was randomized. The range of the white noise was 20 Hz to 20 kHz and its sound pressure was about 60 dB. The amplitude of the sinusoidal signal was 0.1 V and its frequency 1000 Hz.

A red warning light appeared on a panel in front of the subject, 500 ms before each stimulus. The duration of each stimulus was 100 ms, after which the subject had to decide whether he had heard the signal +noise or the noise only. The response was given by pressing one of two microswitches. A response interval of 3 s was allowed following the offset of the stimulus. At the end of this interval, a new trial began.

In order to manipulate the amount of risk involved, two risk conditions were established by offering monetary rewards and penalties for each of the possible outcomes. The money reward or penalty for each outcome (pay-off matrix) for the two risk conditions are presented in table II.

Since the range of the profits or losses was always higher for "yes" responses than for the "no" response in both conditions, "yes" responses were considered more risky than "no" responses (Lee, 1971). The

TABLE II. *Pay-off matrices for the lower-risk and higher-risk conditions. Reward is indicated + and loss −*

HIT +50 cents	MISS −7 cents
FALSE ALARM −50 cents	CORRECT REJECTION +7 cents
Higher-risk condition	
HIT +25 cents	MISS −7 cents
FALSE ALARM −75 cents	CORRECT REJECTION +7 cents

"yes" response was considered to be much more risky in the second condition (table II) where the maximum penalty for incorrect "yes" responses was bigger than for the first condition (75 cents *v.* 50 cents, respectively), without changing the range of profits (−75 to +25 cents *v.* −50 to +50 cents, respectively).

As a measure of the subject's tendency to choose the "yes" alternative one can take the ratio of the probability of a yes response when signal+noise was presented (P(yes/SN)) to the probability of a yes response when only noise was presented (P(yes/N)) (Swets, Tanner and Birdsall, 1961). This is termed likelihood ratio or decision criterion (CR), and is a good estimate of risk taking, provided that the ability to discriminate SN and the N stimuli remains constant. Since the anaesthetic did affect this ability, the solution was to increase for each subject in the anaesthetic condition the amplitude of the signal relative to the noise, to make discrimination easier. The final signal level was that which yielded success rates comparable to those achieved during control testing. (Discriminability measure is termed d' and is based on the frequency of occurrence of the different possible outcomes.) In summary, with constant discriminability levels, CR can be used as an operational measure for the risk tendency of the subject. Higher criteria imply less risk tendency.

Subjects and inhalation procedure

The subjects were eight paid male student volunteers, between 20 and 30 years of age. The criteria for admission to the study and the inhalation procedure are as described by Bentin, Collins and Adam (1978).

Experimental design

Six subjects formed the experimental group and two subjects the placebo group. The latter did everything performed by the experimental group, only they did not breathe anaesthetic but air, being told that they were breathing an odourless anaesthetic.

Each subject served as his own control, participating in two sessions, control and gas. Three subjects in the experimental group and one in the placebo group began the experiment with the control session followed by the gas session, whereas the other four had the reverse order. Four subjects had the low-risk condition first, then the high-risk and again the low-risk conditions. Two subjects had first the high-risk, then the low-risk and again the high-risk conditions. The repeat conditions served to test the effects of fatigue. The placebo group were not presented with repetitions; one began with the low-risk and one with the high-risk conditions.

Procedure

Two days before the first session, the subjects were trained with the discrimination task. During the training each subject reached his maximal ability of discrimination, and the noise level was adjusted relative to the signal, to allow about 60% of correct answers (d' about 1.000). The training was completed after 1800 ± 300 trials.

In both control and gas sessions the subject received full explanations about the task and the possible profits or losses, before the inhalation procedure began. In the gas session, the subject first breathed air through the anaesthesia circuit for about 5 min, to get used to the new situation. He breathed 0.25% enflurane vaporized in air for about 10 min, and was asked to perform several simple actions such as pressing a microswitch, and follow verbal commands, to assess whether the anaesthetic level would permit task performance. The enflurane concentration was kept unchanged, decreased, or increased, accordingly. The range of changes never exceeded 0.04%. Testing began when the required equilibrium was achieved, when the inspired–expired difference in enflurane concentration was no more than 0.05%. The subject first received a short training period to readjust stimulus parameters in order to keep the performance level at 60% correct answers despite anaesthetic influence on discrimination ability.

When all preparations were complete, the experimenter made sure that the subject understood the consequence of incorrect responses in terms of loss of money, and only then the test began. Three hundred trials were given in each risk condition. The stimuli were presented in blocks of 100 trials, with a 1-min interblock interval, and 5 min rest period following each 300 trials. Before each new risk condition, the instructions were repeated, emphasizing the meaning of the new pay-off matrix. Criterion and d' values were based on 300 trials.

An anaesthetist supervised the subject throughout the whole session, and for half an hour following the end of the experiment.

The procedure was identical in control sessions, apart from the gas inhalation. The control and gas sessions were 4 days apart. The subjects were paid at the end of the second session, to ensure full co-operation.

RESULTS

Control data showed that decision criterion values (CR) in the high-risk condition were always significantly greater than those for the low-risk condition. Greater CR values imply less risk taking. By contrast, no difference was found between the criteria used in both risk conditions, during inhalation of low concentration of enflurane. Figure 1 presents the group mean criterion values for control and gas sessions for all risk conditions; in figure 1A the order is Low risk–High risk–Low risk (L.H.L.) and in figure 1B the order is High risk–Low risk–High risk (H.L.H.).

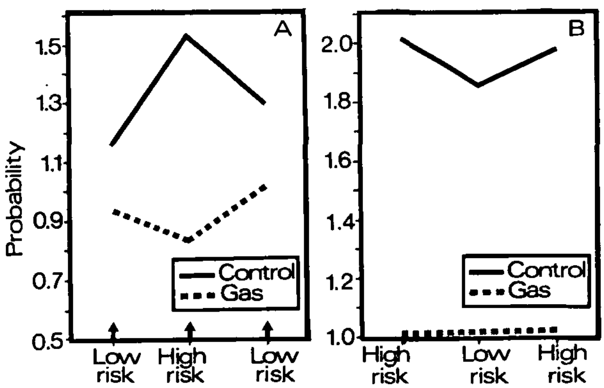

FIG. 1. A: Risk-taking tendency with and without anaesthetic influence for the order of conditions Low risk–High risk–Low risk ($n = 4$). B: Risk-taking tendency with and without anaesthetic influence for the order of conditions High risk–Low risk–High risk ($n = 2$).

Analysis of quadratic trend (Scheffé, 1959) showed that the criteria used by the L.H.L. group in the three risk conditions were significantly different in the control, but not in the gas session. The criteria used by the H.L.H. were not significantly different in either the control, or in the gas sessions, probably because of the small size of this sample.

Since no significant differences were found between CR in repeated risk conditions, the two groups were combined for further statistical analysis, using only the data obtained in the first two risk conditions.

Assuming the same degree of dependence between any pair of observations in each subject, that is a similar influence of conditions and sessions, analysis of variance (model III mixed model, Hays (1973)) was used over the two risk conditions, in gas and control situations. An overall significant difference ($F = 33.05$, $P < 0.01$) was found, allowing multiple t tests for any two matched groups. The CR used in the high-risk condition were significantly greater ($t = 2.9867$, $P < 0.025$) than those used in the low-risk condition in control sessions, but they did not differ significantly in gas sessions. The criteria used in the control sessions were higher than those used in gas sessions for both the high- and the low-risk conditions ($P < 0.001$ and $P < 0.05$ respectively).

Although the homogeneity of the subjects in respect of age, sex, socio-economic background and education might justify the above-mentioned assumption required for the analysis of variance, the non-parametric Friedman's analysis of variance was also used, to avoid any speculative assumption. Again, a significant difference was found between the four groups of results ($\chi^2 = 18$, $P < 0.005$). All subjects showed the same pattern of results.

The placebo group showed similar decision behaviour both in control and in pseudo-gas sessions. Friedman's analysis of variance revealed significant differences between the criteria used in different risk conditions and in different sessions ($\chi r^2 = 27, P < 0.01$). Descriptive data showed that in both sessions the criteria used in the high-risk condition were higher than those used in the low-risk condition, and that the criteria used in the pseudo-gas situation were slightly higher than those used in similar risk conditions during the control session (fig. 2). Considering the small size of this group, the placebo data were unsuited to further statistical treatment.

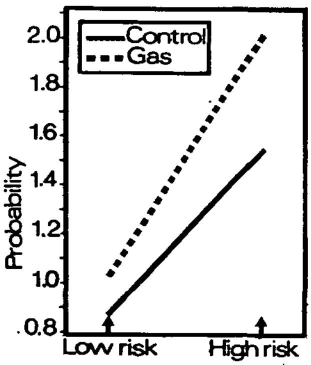

FIG. 2. Risk-taking tendency shown by the placebo group in control and pseudo-gas sessions ($n = 2$).

DISCUSSION

Subanaesthetic concentrations of enflurane increased the tendency to adopt more risky strategies in decision-making situations. This tendency was reflected in the failure of the subject under anaesthetic influence to increase the decision criterion (be more careful) in the higher-risk condition relative to the lower-risk condition. Lower criterion values imply that the subject was more willing to choose the "yes" response when uncertain despite the risk of money loss.

This failure to be more careful under more risky situations did not emanate from lack of understanding of the situation. In an interview following the study, the subjects revealed that they understood perfectly what the best strategy should have been, but they did not care too much about it. This may suggest that, while they did not choose intentionally the risky alternative, neither did they avoid it. Thus, as they were fully aware of the risk involved in the "yes" response, their behaviour may be interpreted as careless and irresponsible.

The data suggest that this effect was the result neither of fatigue nor of the subject's expectation of gas effects. Fatigue would have been reflected by a change in the criterion value for repeated risk conditions. No such change occurred. The data of the placebo group, also obtained with a very small sample, might indicate that the decision behaviour shown by the subjects in the gas session is not the result of subjective expectations about possible gas effects, or any other psychological effect of the situation. The observation that the criterion values adopted by the placebo group in the pseudo-gas session for both risk conditions were slightly higher than control values might be explained by a predisposition to be more careful under what the subject believed to be anaesthetic influence, assuming its negative effect.

The H.L.H. group used significantly higher ($P < 0.05$; t test) criteria than the L.H.L. group in the "control", but not in the "gas" session. This difference reflects the decision criteria of one of the two subjects in the H.L.H. group, who used criteria twice as high as did any other subject. He claimed to be an extremely cautious person when interviewed after the experiment.

The present study also raises the question of trace anaesthetic effects on operating room personnel. The concentrations used in this study, which are about one-sixth to one-eighth of MAC, are greatly in excess of those average values reported for the air of operating theatres. Nevertheless, they suggest an influence, which might, alone or in combinations with other factors like fatigue and tension, interfere with the normal decision-making behaviour of those exposed to anaesthetic agents.

ACKNOWLEDGEMENTS

This study was supported by a grant from the Israeli Ministry of Health. We would like to thank Nissen Preminger Inc. for contributing the Ethrane for this study.

REFERENCES

Adam, N. (1973). Effects of general anesthetics on memory functions in man. *J. Comp. Physiol.*, **83**, 294.

—— (1976). Effect of general anesthetics on search in memory in man. *TIT J. Life Sci.*, **6**, 29.

—— Castro, A. D., and Clark, D. L. (1974). Production, estimation and reproduction of time intervals during inhalation of a general anesthetic in man. *J. Exp. Psychol.*, **102**, 609.

—— Collins, G. I. (1978). Effect of enflurane on electrophysiological correlates of STM. *Anesthesiology* (in press).

—— Rosner, B. S., Hosick, E. C., and Clark, D. L. (1971). Effect of anesthetic drugs on time production and alpha rhythm. *Percep. Psychophys.*, **10**, 133.

Bentin, S., Collins, G. I., and Adams, N. (1978). Effects of small concentrations of enflurane on probability learning. *Br. J. Anaesth.*, **50**, 1179.

Bruce, D. L., and Bach, M. J. (1975). Psychologic studies of human performance as affected by traces of enflurane and nitrous oxide. *Anesthesiology*, **42**, 194.

—— —— (1976). Effects of trace anaesthetic gases on behavioural performance of volunteers. *Br. J. Anaesth.*, **48**, 871.

—— —— Arbit, J. (1974). Trace anesthetic effect on perceptual, cognitive and motor skills. *Anesthesiology*, **40**, 453.

Davison, L. A., Steinhelber, J. C., Eger, E. I., and Stevens, W. C. (1975). Psychological effects of halothane and isoflurane anesthesia. *Anesthesiology*, **43**, 313.

Green, D. M., and Swets, J. A. (1966). *Signal Detection Theory and Psychophysics*. New York: J. Wiley & Sons Inc.

Hays, L. W. (1973). *Statistics for the Social Sciences*. Holt, Rinehart and Winston.

Lee, W. (1971). *Decision Theory and Human Behavior*. New York: J. Wiley & Sons Inc.

Robson, J. G., Burns, B. D., and Welt, P. J. L. (1960). The effect of inhaling dilute nitrous oxide upon recent memory and time estimation. *Can. Anaesth. Soc. J.*, **7**, 399.

Scheffé, H. (1959). *The Analysis of Variance*. New York: J. Wiley & Sons.

Smith, G., and Shirley, A. W. (1977). Failure to demonstrate effect of trace concentrations of nitrous oxide and halothane on psychomotor performance. *Br. J. Anaesth.*, **49**, 65.

Steinberg, H. (1954). Selective effects of anaesthetic drug on cognitive behaviour. *Q. J. Exp. Psychol.*, **6**, 170.

—— Tomkiewicz, M. (1968). Drugs and memory; in *Psychopharmacology* (ed. D. H. Efron). U.S. Government Printing Office PHS Publication, 1936.

Swets, J. A. (ed.) (1964). *Signal Detection and Recognition by Human Observers*. New York: J. Wiley & Sons Inc.

—— Tanner, W. P., and Birdsall, T. G. (1961). Decision processes in perception. *Psychol. Rev.*, **68**, 301.

COMPORTEMENT DANS LA PRISE DE DECISIONS PENDANT L'INHALATION DE CONCENTRATIONS SOUS-ANESTHESIANTES D'ENFLURANE

RESUME

On a évalué l'effet des concentrations sous-anesthésiantes d'enflurane sur le comportement lors de la prise des décisions dans les situations dangereuses à l'aide d'une tâche de détection de signaux. Le sujet a entendu, dans certains essais, le bruit seul (bruit blanc) ou un signal superposé au bruit (tonalité 1000 Hz) et a dû faire un rapport lors de chaque essai sur ce qu'il a entendu. Les situations dangereuses ont été manipulées en changeant la récompense ou la pénalité monétaire associée aux réponses correctes ou incorrectes. Huit volontaires ont participé à cette étude. On a trouvé que sous une influence anesthésiante, ils n'ont pas évité les mêmes risques qu'ils auraient évité dans des conditions contrôlées. Les résultats de l'étude sont expliqués en termes d'influence du gaz sur la perte de contrôle ou sur la diminution de responsabilité.

DAS MENSCHLICHE VERHALTEN BEIM TREFFEN VON ENTSCHEIDUNGEN WÄHREND DER INHALATION VON SUBANÄSTHETISIERENDEN KONZENTRATIONEN VON ENFLURAN

ZUSAMMENFASSUNG

Die Wirkung, die subanästhetisierende Konzentrationen von Enfluran auf das Treffen von Entscheidungen hat, die in Situationen mit verbundenem Risiko getroffen werden, wurde in einem Versuch, bei dem Signale entdeckt werden mussten, bewertet. Die Versuchsperson hörte entweder nur ein Geräusch, ein sogenanntes "white noise", oder ein Signal zusammen mit dem Geräusch (1000 Hz Ton), und musste bei jedem Versuch berichten was sie hörte. Das Risiko in den Situationen wurde durch den Weschel von Straf- und Belohnungsgeldern für falsche und richtige Antworten geschaffen. Acht männliche Versuchspersonen nahmen an dieser Untersuchung teil. Dabei wurde gefunden, dass sie unter dem Einfluss der anästhetisierenden Droge nicht wie die Kontrollgruppe die Risiken vermieden. Die unterschiedlichen Resultate im Verhalten werden als Kontrollverlust und abnehmende Verantwortungsgefühle, vom Einfluss des Gases herrührend, erklärt.

COMPORTAMIENTO DE ADOPCION DE DECICIONES DURANTE LA INHALACION DE CONCENTRACIONES SUBANESTESICAS DE ENFLURANO

SUMARIO

Se evaluó el efecto ejercido por concentraciones subanestésicas de enflurano sobre el comportamiento de adopción de decisiones en situaciones de riesgo, valiéndose de una tarea de detección de señales. El sujeto escuchó solamente ruidos (ruidos blancos) o una señal superpuesta sobre el ruido (tono de 1000 Hz), debiendo informar en cada prueba lo que había escuchado. Las situaciones de riesgo fueron manipuladas mediante el cambio de las recompansas y multas monetaries asociadas con las respuestas correctas e incorrectas. En este estudio participaron ocho voluntarios masculinos. Se descubrió que bajo la influencia de anestesia no evitaron los mismos riesgos que habían evitado bajo condiciones de control. Los descubrimientos se atribuyen a la influencia del gas sobre la pérdida de control y la responsabilidad disminuída en su comportamiento.