

## Self-selection for personality variables among healthy volunteers

M. S. M. PIETERS<sup>1</sup>, A. JENNEKENS-SCHINKEL<sup>2</sup>, H. C. SCHOEMAKER<sup>1</sup> & A. F. COHEN<sup>1</sup>

<sup>1</sup>Centre for Human Drug Research and <sup>2</sup>Department of Neuropsychology, University Hospital, Leiden, The Netherlands

- 1 Healthy student volunteers ( $n = 103$ ) participating in ongoing clinical pharmacological research completed the Dutch Personality Inventory (DPI), the Dutch version of the Spielberger State-Trait Anxiety Inventory (STAI-DY) and the Dutch version of the Sensation Seeking Scale (SSS).
- 2 The volunteers were more extrovert ( $P < 0.001$ ), more flexible ( $P < 0.001$ ), more tolerant or less impulsive ( $P < 0.001$ ), had more self-confidence and initiative ( $P < 0.001$ ), and were more satisfied and optimistic ( $P < 0.01$ ) when compared with the general norm. When compared with a student norm, volunteers had lower levels of state ( $P < 0.001$ ) and trait ( $P < 0.05$ ) anxiety. The general sensation seeking tendency of volunteers was higher than in the student norm group ( $P < 0.001$ ). The volunteers had a greater tendency to thrill-and-adventure-seeking ( $P < 0.001$ ) and to disinhibition ( $P < 0.01$ ).
- 3 Hence, volunteers were a selected sample of the total population of students. This may influence the interpretation of pharmacokinetic and pharmacodynamic parameters.
- 4 Personality screening should be added to the screening procedures for volunteers.

**Keywords** volunteers selection personality anxiety sensation seeking

### Introduction

Clinical pharmacological research often uses the cooperation of healthy volunteers, mainly students. A tacit assumption is that student-volunteers, if in good health, constitute a representative sample of the healthy age group to which they belong. Medical data of the volunteers are gathered, but usually only scanty or no information is collected on variables such as socio-demography, motivation and personality profiles.

Relationships between volunteering and personality or temperamental variables such as sensation seeking or level of anxiety, have been frequently studied in behavioural science (Cowles & Davis, 1987; Rosenthal & Rosnow, 1975), but the outcome has not been applied to pharmacological studies. For instance, persons with high scores for sensation seeking appear to be more common as volunteers for behavioural studies (Rosenthal & Rosnow, 1975; Zuckerman *et al.*, 1967). They are also likely to volunteer for the more exciting research topics, among which are the effects of stress, hypnosis, and drugs. General topics, such as learning and reaction times, appear to be less attractive to these subjects (Rosenthal & Rosnow, 1975; Zuckerman, 1978).

However, most studies have only explored the relationship between volunteering and sensation seeking by presenting exciting research topics (Ridgeway & Russell, 1980; Zuckerman, 1974; Zuckerman *et al.*, 1967). A study dealing with both 'exciting' and 'general' research topics demonstrated that male subjects are more likely to volunteer for exciting research, whereas females tend to volunteer for both 'exciting' and 'general' studies (Griffin & Walker, 1976). In a study by Kohn *et al.* (1982), 254 psychology students indicated their willingness to participate as research subjects. Students who were willing to participate had higher scores than non-participants on several measures of sensation seeking.

Volunteers can be less and more anxious than non-volunteers (Rosenthal & Rosnow, 1975). The relationship between volunteering and anxiety seems to be moderated by the sample of subjects, and the task for which the subject volunteered. When the task is perceived as stressful or when the volunteers have recently experienced severe stress, only the less anxious subjects are likely to volunteer. A more fearful person may

be unwilling to expose himself to anxiety-arousing situations (Zuckerman, 1976).

The Clinical Pharmacology Unit at our hospital is involved in numerous experimental drug studies of which the majority is performed with healthy students as subjects. These studies involve cardiovascular and CNS drugs. Whether students who volunteer for these studies represent the target population with regard to personality factors is virtually unknown. This study evaluated the occurrence of self-selection for personality variables among these healthy volunteers.

## Methods

### Subjects

One hundred and three volunteers (94 male, 9 female; mean age 22.7 years, range 19–39 years) volunteered for cooperation in any of the forthcoming studies. They gave informed consent to the physician-investigator, underwent a medical examination, and participated in the present personality study before cooperating in the pharmacological study for which they had applied. The subjects participated in consecutive studies, which are listed in Table 1.

Ten of the total number of cooperating volunteers did not participate, because the physician-investigator forgot to ask or the volunteer had no time to complete the inventories.

### Study design

Subjects were recruited by advertisements in a local university-newspaper. Others responded because of information spread by former volunteers. In addition, subjects who had volunteered previously came forward spontaneously for another study ( $n = 24$ , 23%). Recruitment advertisements did not announce the topic of the study or the amount of financial compensation. An appointment was made with applicants to provide both written and oral information on the study for which they had applied. Those who volunteered after an agreed time for reflection were examined medically, after which they were asked to participate in the present study. Both for the pharmacological and the personality study informed consent was given. Volunteers completed the inventories immediately after the medical check-up, being allowed as much time as they needed (mostly between 30–40 min). The data were analyzed anonymously. The reward for participation was HfI 25, (approximately £7.50).

**Table 1** Studies for which the volunteers applied

| Study  | Frequency and Sex;<br>(*) | Drug new (N) or<br>Registered (R) | Payment (HfI)<br>Full study† |
|--|---------------------------|-----------------------------------|------------------------------|
| Kinetics of nitroglycerine   | 6 M; (1)                  | R                                 | 170                          |
| Circadian rhythm of APTT after heparin infusion                      | 7 M; (1)                  | R                                 | 435                          |
| Bioequivalence of nitredipine  | 6 M; (6)                  | N                                 | 280                          |
| Effects of temazepam on saccadic eye movements                       | 3 M, 2 F; (0)             | R                                 | 305                          |
| Transdermal absorption of morphine                                   | 3 M, 2 F; (1)             | N                                 | 238                          |
| Effects of oral nifedipine and exertion on liver blood flow          | 10 M; (2)                 | R                                 | 540                          |
| Effects of changes in body fluid composition on ADH                  | 8 M; (4)                  | R                                 | 120                          |
| Interaction study of ticarcilline and a low molecular weight heparin | 9 M; (2)                  | N                                 | 660                          |
| Effects, kinetics and bioavailability of digoxin in capsule          | 7 M, 5 F; (2)             | R                                 | 825                          |
| Comparison of anticoagulant effects of i.v./s.c. heparin             | 8 M; (1)                  | R                                 | 240                          |
| Renal clearance of betalactam antibiotics                            | 4 M; (0)                  | R                                 | 220                          |
| Tolerability, absorption, and bioequivalence of a renin inhibitor    | 8 M; (1)                  | N                                 | 140                          |
| ACE inhibitor kinetics   | 12 M; (3)                 | N                                 | 650                          |
| t-PA clearance after exercise  | 3 M; (0)                  | N                                 | 160                          |

M = male, F = female.

(\*): number of subjects that participated in previous studies.

†HfI 1 = £0.3.

## Procedures

*The Dutch Personality Inventory (DPI; Luteijn et al., 1975, 1985).* The DPI is based on a translated and shortened version of the California Psychological Inventory (CPI; Gough, 1964). It consists of 133 items, to which subjects respond with 'correct', 'do not know', or 'incorrect', which are distributed over seven non-overlapping scales:

- Inadequacy (IN): vague (physical) complaints, depressed mood and feelings of insufficiency. Inadequacy is related to characteristics such as 'emotional', 'tense', 'dejected', and 'gloomy'.
- Social inadequacy (SI): avoidance of, or unhappiness in social relationships. Social inadequacy is related to characteristics like 'uncommunicative', 'introvert', 'retiring' and 'careful'.
- Rigidity (RI): intellectual fixation, set habits and principles. Rigidity is related to characteristics like 'conservative', 'orderly', 'punctual', 'serious' and 'thrifty'.
- Hostility (HO): criticism and distrust of other people. Hostility is related to characteristics like 'impulsive', 'intolerant', 'impatient' and 'short-tempered'.
- Self-Sufficiency (SS): egoism. Self-sufficiency is related to characteristics like 'self-contentment', 'lack of interest in other individuals and their problems'.
- Dominance (DO): dominance is related to characteristics like 'self-confident', 'give guidance to' and 'take initiative'.
- Self-Esteem (SE): positive attitude towards work, flexibility and adaptation. Self-esteem is related to characteristics like 'active', 'dynamic', 'independent', 'quiet', 'cheerful', 'taking initiative' and 'self-control'.

Raw scores were corrected for sex and age according to the manual (1985). Because norms for students are not available, the scores of the volunteers were compared with a general norm (manual, 1985), and in addition to a norm table for high school students, comparable with our group with respect to age (range 15–23 years, mean 18.7 years) and educational level (high school higher grades and teaching college) (manual, 1975).

*The Dutch revision of the Spielberger State-Trait Anxiety Inventory (STAI-DY; Ploeg et al., 1980).* The inventory is based on the STAI-DY (Spielberg et al., 1970). It includes two self-rating scales, each consisting of 20 statements, allowing assessment of two distinct concepts of anxiety:

- State anxiety: a transient arousal state of anxiety; an emotional condition marked by subjective feelings of tension or stress, which vary in intensity and fluctuate in time, and by increased activity of the autonomous nervous system. The subject describes his/her present feelings, using the statements.
- Trait anxiety: a general disposition to anxiety; the tendency to react to situations experienced as threatening by increasing intensities of state anxiety (Ploeg et al., 1980). The respondent describes his/her general feelings, using the statements.

Sex-corrected raw scores of the norm table for students, presented in the manual, served as control data (Ploeg et al., 1980).

*The Dutch revision of the Sensation Seeking Scale (SSS; Fey & Zuilen, 1984).* The SSS has been constructed on the basis of several versions of the Sensation Seeking Scale (Zuckerman, 1979). The subjects respond to 68 questions. The SSS is a self-rating scale purporting to measure individual differences in sensation seeking tendency. Various expressions of the need for sensation have been defined (Zuckerman, 1979; Zuckerman et al., 1980), and have resulted in the construction of four subscales. The general tendency to sensation seeking is computed from the scores on these subscales:

- Thrill and Adventure Seeking (TAS): tendency to engage in sports and other activities which emphasize speed and danger (physical risk taking).
- Experience Seeking (ES): tendency to search for new perceptual and psychical experiences and to an unconventional lifestyle.
- Boredom Susceptibility (BS): aversion from dull, routine, boring, and monotonous situations.
- Disinhibition (DIS): tendency to social disinhibition by drinking, parties and sexual variation.

Sex-corrected raw scores of the norm table for students served as control data (Fey & Zuilen, 1984).

## Statistical analysis

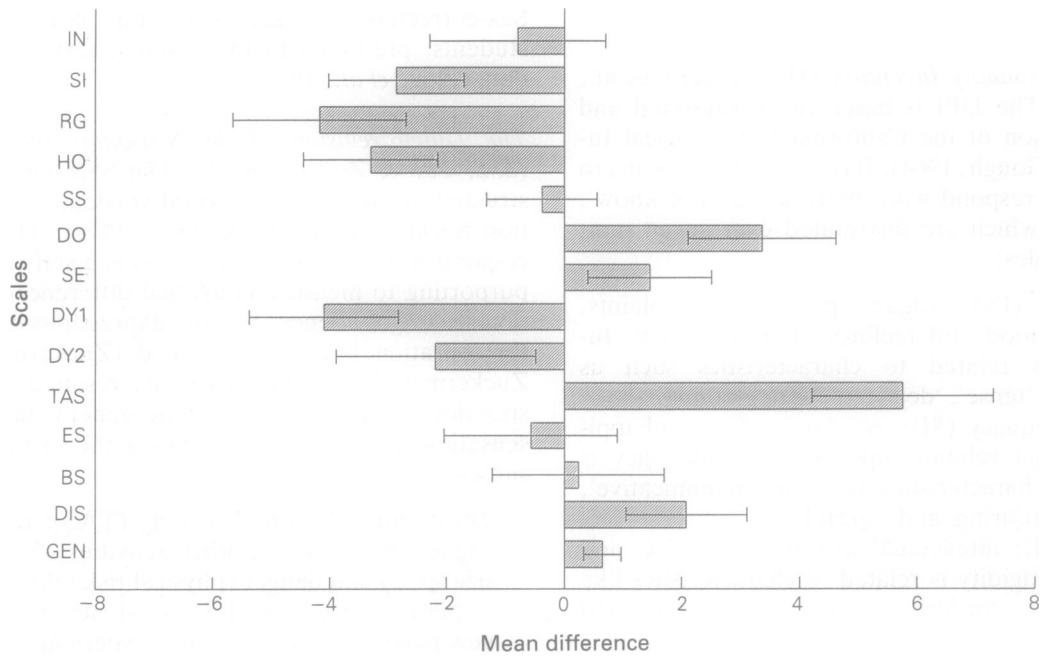
The mean raw scores and standard deviations were calculated for all scales. Differences between scores of the volunteers and the norms of the different manuals were analyzed by Student's *t*-test. Differences reaching a probability level of 0.05 (two-sided) were considered to be significant. All statistical tests were performed using the software package SPSS/PC+ 3.0 (SPSS Inc., Chicago, Illinois, USA).

For each scale of the DPI, the STAI-DY and the SSS, the difference from zero and the 95% confidence intervals of the difference were visually presented (Figure 1). The mean scores with their standard deviation, and the *P* values were reported for all scales in Table 2.

## Results

Comparison of scores on each scale of the DPI with the general norm indicated that the group of volunteers differed from the general norm group (Figure 1). The volunteers were significantly more extrovert (SI), more flexible (RG), more tolerant or less impulsive (SS), had more self-confidence and initiative (DO), and were more satisfied and positive (SE) (Table 2).

The pattern of significant differences between scores obtained by the volunteers and the norm of high school students (Table 3) was quite similar, with exception of the inadequacy and rigidity scores. The high school norm group had more vague (physical) complaints than the volunteers. Rigidity could not differentiate volunteers from high school students.



**Figure 1** Differences from the norm data and the 95% Confidence Intervals for all scales of the Dutch Personality Inventory, the State-Trait Anxiety Inventory and the Sensation Seeking Scale. IN = Inadequacy, SI = Social inadequacy, RG = Rigidity, HO = Hostility, SS = Self-sufficiency, DO = Dominance, SE = Self-esteem, DY1 = State anxiety, DY2 = Trait anxiety, TAS = Thrill-and-adventure-seeking, ES = Experience seeking, BS = Boredom susceptibility, DIS = Disinhibition, Gen = General sensation seeking tendency.

**Table 2** Comparison between volunteers and the general norm data of the Dutch Personality Inventory (DPI), and between volunteers and the norm data for students of the State-Trait Anxiety Inventory (STAI-DY) and the Sensation Seeking Scale (SSS); Mean scores  $\pm$  s.d., and the *P* value

| Inventory | Scale                              | Mean $\pm$ s.d. | P     |
|-----------|------------------------------------|-----------------|-------|
| DPI       | Inadequacy                         | 9.6 $\pm$ 7.6   | 0.297 |
|           | Social inadequacy                  | 6.9 $\pm$ 5.8   | 0.000 |
|           | Rigidity                           | 18.5 $\pm$ 7.1  | 0.000 |
|           | Hostility                          | 14.9 $\pm$ 5.9  | 0.000 |
|           | Self-sufficiency                   | 10.8 $\pm$ 4.8  | 0.416 |
|           | Dominance                          | 18.7 $\pm$ 6.3  | 0.000 |
|           | Self-esteem                        | 29.5 $\pm$ 5.4  | 0.007 |
| STAI-DY   | State anxiety                      | 30.3 $\pm$ 6.4  | 0.000 |
|           | Trait anxiety                      | 34.1 $\pm$ 8.3  | 0.012 |
| SSS       | Thrill-and-adventure seeking       | 45.9 $\pm$ 7.8  | 0.000 |
|           | Experience seeking                 | 43.1 $\pm$ 7.5  | 0.450 |
|           | Boredom susceptibility             | 40.6 $\pm$ 7.5  | 0.740 |
|           | Disinhibition                      | 38.5 $\pm$ 7.9  | 0.009 |
|           | General sensation seeking tendency | 13.3 $\pm$ 1.6  | 0.000 |

**Table 3** Comparison between volunteers and norm data for high school students; mean scores  $\pm$  s.d., the difference from the norm value, 95% Confidence Intervals, and the *P* value for each scale of the Dutch Personality Inventory

| Scale             | Mean $\pm$ s.d. | Difference from the norm value | 95% Confidence Interval | P value |
|-------------------|-----------------|--------------------------------|-------------------------|---------|
| Inadequacy        | 9.6 $\pm$ 7.6   | -4.66                          | -6.14, -3.17            | 0.000   |
| Social inadequacy | 6.9 $\pm$ 5.8   | -4.52                          | -5.65, -3.38            | 0.000   |
| Rigidity          | 18.5 $\pm$ 7.1  | 0.32                           | -1.07, 1.72             | 0.650   |
| Hostility         | 14.9 $\pm$ 5.9  | -5.10                          | -6.24, -3.95            | 0.000   |
| Self-sufficiency  | 10.8 $\pm$ 4.8  | 0.88                           | -1.82, 0.05             | 0.063   |
| Dominance         | 18.7 $\pm$ 6.3  | 2.06                           | 0.81, 3.30              | 0.001   |
| Self-esteem       | 29.5 $\pm$ 5.4  | 3.86                           | 2.80, 4.91              | 0.000   |

Similar comparisons were made for the scales of the STAI-DY and the SSS (Figure 1). When compared with the student norm group, volunteers had lower scores of state anxiety and trait anxiety, a higher general sensation seeking tendency, a greater need for thrill and adventure and a higher tendency to disinhibition (Table 2).

Correlations between and within the different scales of the three inventories were in accordance with the intercorrelations presented in the manuals (data not shown).

## Discussion

Pharmacological studies are often performed with healthy students as subjects. Although it is widely accepted that these volunteers are not necessarily representative for the general population, a tacit assumption is that they represent, at least, their age group. However, behavioural studies addressing the relationship between volunteering and personality and/or temperamental variables, contradict this implicit assumption. In numerous behavioural studies of self-selection bias in volunteers has been amply demonstrated (Rosenthal & Rosnow, 1975).

Our study shows that this assumption is not justified for pharmacological research either. Volunteers for pharmacological studies are likely to be a self-selected sample of the total population, as demonstrated by their characteristics of extroversion, flexibility, tolerance, activity, optimism and satisfaction. In comparison with the general population of students, the volunteers have a higher general sensation seeking tendency, as manifested in a greater need of thrill and adventure seeking, a greater tendency to disinhibition, and in lower levels of state and trait anxiety.

High scores for sensation seeking in volunteers have previously been shown for behavioural studies (Rosenthal & Rosnow, 1975). Particularly exciting topics, like drug studies, appear to be very attractive to those volunteers (Zuckerman, 1978). In addition, Kohn *et al.* (1982) showed that volunteers in behavioural studies outscored non-volunteers on general sensation seeking tendency, thrill-and-adventure seeking, and experience seeking. Our findings for volunteers in pharmacological studies are in accordance with this, except for experience seeking. Instead we found higher levels of disinhibition. This may imply that volunteers in pharmacological research have more need for physical sensation seeking than for psychological arousal.

The results obtained from the volunteers were compared with those from a historical control group. The reason was the impossibility to recruit students who were not willing to volunteer for pharmacological research. This request would most probably have led to a

biased sample, i.e. non-cooperating students. Hence, we preferred to depend on the norm tables of the inventories. This is an acceptable method because the inventories are known to measure personality or temperamental variables that are stable over time.

Bias in personality and temperamental characteristics of self-selected samples of volunteers may bear upon the interpretation of drug response studies. Personality factors like extroversion, aggression, impulsivity or neuroticism are related to differences in cortical arousal (Fey & Zuilen, 1984), and to differences in drug absorption or distribution (Leopold *et al.*, 1979; Netter, 1990). Degree of sensation seeking has been related to numerous perceptual, cognitive and physiological phenomena (Zuckerman, 1979). Level of neuroticism was a modifying factor in pharmacodynamic studies (Nakano *et al.*, 1980; Wilson, 1976).

Pharmacokinetics may also be affected. Nakano *et al.* (1980) have documented the psychological modification of pharmacokinetic parameters. In their study the rate and the extent of the absorption of diazepam was significantly greater in volunteers with high levels of neuroticism as compared with volunteers with low levels of neuroticism. The authors reasoned that this effect was probably due to enhanced gastric motility and faster gastric emptying in volunteers with high levels of neuroticism. Stressful conditions have been demonstrated to delay the enteral absorption of sulphaperine and indomethacin (Leopold *et al.*, 1979). After cessation of stress the absorption deficit was compensated for. Netter (1988) has demonstrated that differences in benzodiazepine-induced amnesic effects depend on variables like pre-drug level of anxiety, expectations of treatment outcome and past experience with benzodiazepine-type drugs, and interactions between subject variables and dose of drug, type of drug as well as the extent of benzodiazepine-induced changes in anxiety, and in cortical and emotional arousal.

Extroversion, impulsivity, high levels of sensation seeking and low levels of state and trait anxiety characterize the self-selected sample of volunteers at our Unit. These volunteers are likely to represent the typical group of student volunteers. Volunteer-related personality variables may well have implications for the interpretation and the generalizability of the results of pharmacological research.

Unless it is proven that particular volunteering-related personality variables are not relevant to the objects under study, investigators should be aware of the chance that personality characteristics of the volunteers may distort or limit the interpretation and the generalizability of pharmacokinetic and pharmacodynamics results found in volunteers. Volunteer screening should include personality or temperamental characteristics.

## References

- Cowles, M. & Davis, C. (1987). The subject matter of psychology: volunteers. *Br. J. Soc. Psychol.*, **26**, 97-102.
- Fey, J. A. & Zuilen, R. W. van (1984). *Spanningsbehoefte lijst (SBL), Handleiding*. Lisse: Swets & Zeitlinger.
- Griffith, M. & Walker, C. E. (1976). Characteristics associated with expressed willingness to participate in psychological research. *J. Social Psychol.*, **100**, 157-158.
- Gough, H. G. (1964). *Manual for the California Psycho-*

- logical Inventory*. Palo Alto: Consulting Psychologist Press.
- Kohn, P. M., Hunt, R. W., Davis, C. A. & Cowles, M. P. (1982). Volunteering in principle, volunteering in fact, and experience seeking. *Psychol. Record*, **32**, 205–213.
- Leopold, G., Pabst, L. G. & Ungethüm, W. (1979). Role of volunteer selection in human pharmacology studies. In *Methods in clinical pharmacology*. The proceedings of an International Symposium held in Frankfurt/M. 6–8 May 1976, eds Rietbrock, N., Woodcock, B. G. & Neuhaus, G. Braunschweig/Wiesbaden: Vieweg & Sohn.
- Luteijn, F., Starren, J. & Dijk, H. van (1975). *Handleiding bij de NVP*. Lisse: Swets & Zeitlinger.
- Luteijn, F., Starren, J. & Dijk, H. van (1985). *Handleiding bij de NVP. Herziene uitgave*. Lisse: Swets & Zeitlinger.
- Nakano, S., Ogawa, N. & Kawazu, Y. (1980). Influence of neuroticism level on diazepam absorption. *Clin. Pharmac. Ther.*, **25**, 239–245.
- Netter, P. S. (1988). Individual differences in benzodiazepine-induced changes in memory. *Psychopharmac. Ser.*, **6**, 90–113.
- Netter, P. S. (1990). Psychological factors related to variability in drug response. *Eur. J. Pharm.*, **183**, 110.
- Ploeg van der H. M., Defares, P. B. & Spielberger, C. D. (1980). *Handleiding bij de Zelf-Beoordelings Vragenlijst: een nederlandse bewerking van de State-Trait Anxiety Inventory (STAI-DY)*. Lisse: Swets & Zeitlinger.
- Ridgeway, D. & Russell, J. A. (1980). Reliability and validity of the sensation seeking scale: psychometric problems in form V. *J. Consult. clin. Psychol.*, **48**, 662–664.
- Rosenthal, R. & Rosnow, R. L. (1975). *The volunteer subject*. New York: Wiley.
- Spielberger, C. D., Gorsuch, R. L. & Lushene, R. E. (1970). *STAI Manual for the State-Trait Anxiety Inventory*. Palo Alto: Consulting Psychologist Press.
- Wilson, G. D. (1976). Personality. In *Human psychology*, eds Eysenck, H. J., Wilson, G. D. Lancaster: MTP Press Ltd.
- Zuckerman, M. (1974). The sensation seeking motive. In *Progress in experimental personality research*, ed. Maher, B. A., Vol. 7. New York: Academic Press.
- Zuckerman, M. (1976). Sensation seeking and anxiety, traits and states, as determinants of behaviour in novel situations. In *Stress and anxiety*, eds Sarason, I. G. & Spielberger, C. D., Vol. 3, pp. 141–170. Washington/London: Hemisphere Publishing Corporation.
- Zuckerman, M. (1978). Sensation seeking. In *Dimensions of personality*, eds London, H. & Exner, J. New York: Wiley.
- Zuckerman, M. (1979). *Sensation seeking: beyond the optimal level of arousal*. Hillsdale: Erlbaum.
- Zuckerman, M., Schultz, D. P. & Hopkins, T. R. (1967). Sensation seeking and volunteering for sensory deprivation and hypnosis experiments. *J. Consult. clin. Psychol.*, **31**, 358–363.
- Zuckerman, M., Buchsbaum, M. S. & Murphy, D. L. (1980). Sensation seeking and its biological correlates. *Psychol. Bulletin*, **88**, 187–214.

(Received 29 July 1991,  
accepted 2 September 1991)