

Sensation seeking amongst healthy volunteers participating in phase I clinical trials

MAGÍ FARRÉ, XAVIER LAMAS & JORDI CAMÍ

Department of Pharmacology and Toxicology, Institut Municipal d'Investigació Mèdica, Universitat Autònoma de Barcelona, Barcelona, Spain

- 1 Phase I clinical trials are usually carried out in healthy volunteers. In addition to economic gain, factors that may influence willingness to participate include scientific interest, curiosity and choice for risky activities.
- 2 We assessed the relationship between personality variables and volunteering for clinical pharmacology research. Two personality questionnaires, the Sensation Seeking Scale (SSS, form V) and the Eysenck Personality Questionnaire (EPQ), were administered to 48 male healthy university students who volunteered to participate in a phase I clinical trial and to 43 male university students who were not willing to participate in phase I clinical trials. General norm data were also used for the comparison of results.
- 3 When healthy volunteers were compared with unwilling subjects, significant differences were found in thrill-and-adventure seeking (7.9 vs 6.7, $P = 0.0034$), experience seeking (6.4 vs 5.2, $P = 0.0012$), disinhibition (6.2 vs 4.3, $P < 0.0001$), boredom susceptibility (3.9 vs 2.8, $P = 0.0073$), total sensation seeking trait (24.3 vs 19.0, $P < 0.0001$), extraversion (15.1 vs 13.3, $P = 0.0490$), and psychoticism (4.4 vs 3.5, $P = 0.0086$). When healthy volunteers were compared with general norm data similar statistically significant differences were found in all these scales, except for boredom susceptibility and psychoticism.
- 4 The personality profile of healthy volunteers was characterized by a higher sensation seeking trait and extraversion as compared with individuals who were not willing to participate in phase I clinical trials and general norm data.

Keywords clinical trials, phase I personality assessment voluntary workers psychology

Introduction

Phase I clinical trials are usually carried out in healthy volunteers, frequently university students, and the financial reward offered for their participation seems to be the main motivation for volunteering [1]. In contrast, when attitudes of patients to participation in therapeutic trials are assessed, altruistic motives appear to be relevant [2]. However, the economic gain might not fully explain why only a subgroup of subjects decides to take part in clinical trials. Other factors, such as scientific interest, curiosity or choice for risky activities may influence the willingness to participate [3].

In a previous study carried out by our group [4] in which the personality profile of healthy volunteers participating in phase I clinical trials was assessed,

volunteers showed higher impulsivity and sociability scores and lower susceptibility to stress than a sample of university students with similar sociocultural characteristics as measured by the Eysenck Personality Questionnaire (EPQ). Similar results have recently been reported by Ball and associates [5]. Some personality traits, such as sensation seeking, were studied by Pieters *et al.* [6] in healthy volunteers participating in pharmacological research, which in some cases involved the administration of psychoactive drugs. These authors observed that volunteers presented higher sensation seeking scores than the general norm. A statistically significant correlation between sensation seeking trait and some EPQ scales has also been described by other investigators [7].

Moreover, an association between willingness to participate in risky or novel activities and sensation seeking has been demonstrated [6].

In order to assess differences in the sensation seeking scale and EPQ profile, results obtained in male university volunteers who participated in phase I trials were compared with 1) a group of male university students who denied willingness to participate in clinical trials (unwilling group), and 2) normative data obtained in university students. As far as we are aware, concurrent data of both questionnaires in these population settings have not been previously reported. Since the association between sensation seeking and volunteering for psychological research [9, 10] could bias the results, the present phase I trials did not involve the administration of psychoactive drugs.

Methods

Healthy volunteers

Healthy volunteers consisted of 48 male undergraduate or postgraduate university students (two-thirds came from the School of Medicine) who participated for the first time in phase I clinical trials, other than those involving the use of psychoactive drugs, which were carried out in our centre between 1991 and 1992. All participants were recruited by means of advertisements at the university, information spread by former volunteers, or directly by the investigators. None of the subjects had history of psychiatric disease or drug abuse, and were found in good health according to physical examination and routine laboratory tests. A signed written informed consent was obtained from all participants. It was made clear to volunteers that responses to questionnaires (Sensation Seeking Scales (SSS) and EPQ) will not have any influence on their participation in the study. Questionnaires were administered to all volunteers before participation in the clinical trial.

Unwilling group

During the second semester of 1992, a text explaining the purpose and methods of a hypothetical standard phase I clinical trial* together with SSS and EPQ was distributed amongst students of both sexes in the third, fourth and sixth years at the School of Medicine. At the end of a lecture, one of the authors (MF) was introduced by the professor and gave a brief explanation of the purposes of the questionnaires with the understanding that answering was voluntary, anonymous and will take approximately 15 min. The yes/no questions 'Have you participated in a clinical trial before?' and 'Would you be willing to participate in the above-mentioned clinical trial?' were printed on the first page following the hypothetical trial and preceding the questionnaires. From a total of 150 participants there were 67 males. Forty-three persons replied negatively to both questions, 17 subjects had previous experience

in clinical trials and expressed willingness to take part again, and the remaining seven subjects had not participated in clinical trials but expressed willingness to participate. The records from the 43 subjects with negative answers to both questions were selected and constituted the unwilling group.

Normative group

Normative data were obtained from two published studies that reported results of SSS [11] and EPQ [12] in two samples of university students attending the first or second year at the School of Medicine.

Questionnaires

Sensation seeking is a personality trait associated with a variety of activities and behaviours involving a moderate degree of risk that provides exciting experiences [8]. The form V of the SSS is a 40-item yes/no self-administered questionnaire which provides a total sensation seeking score as well as scores for the four subscales 'thrill-and-adventure seeking', 'experience seeking', 'disinhibition' and 'boredom susceptibility'. A validated version in Spanish of the SSS was used [11]. The EPQ [13] is a 101-item yes/no self-administered questionnaire which provides scores for four scales that correspond to the three dimensions of personality proposed by Eysenck ('extraversion', 'neuroticism' and 'psychoticism') plus a 'lie' scale. A validated version of the EPQ in Spanish [12] was also used. Both questionnaires were administered to both healthy volunteers and subjects in the unwilling group in the same order (SSS first).

Statistical analysis

Sample size calculations were based on preliminary unpublished data from SSS in healthy volunteers and in Spanish reference groups [11]. Taking the total score in the SSS as the main variable, 90% power, $\alpha = 0.05$ and two-tailed contrast, a sample size of 31 subjects for each group was calculated. The mean scores of the three groups of subjects for each scale in the SSS and EPQ were compared using analysis of variance (ANOVA). Multiple comparisons between groups were carried out using the Tukey test. All tests performed were two-tailed. Differences associated with P values < 0.05 were considered statistically significant. Pearson's correlation coefficients between subscales of SSS and ESQ were calculated.

Results

Results of the SSS and EPQ questionnaires in healthy volunteers and unwilling group are shown in Table 1. Mean ages of subjects included in both groups were not significantly different. Healthy volunteers scored significantly higher than subjects in the unwilling group in the four SSS subscales as well as in the total

*Written information provided to students is available from the authors.

Table 1 Sensation Seeking Scale (SSS) and Eysenck Personality Questionnaire (EPQ) scores in healthy volunteers and unwilling group (mean ± s.d.)

	Healthy volunteers (n = 48)	Unwilling group (n = 43)	P ¹
Age (years)	24.4 ± 3.0	23.3 ± 4.0	NS ²
SSS			
Thrill-and-adventure seeking	7.9 ± 2.0	6.7 ± 1.8	0.0171
Experience seeking	6.6 ± 1.8	5.2 ± 1.7	0.0046
Disinhibition	6.2 ± 1.9	4.3 ± 1.9	0.0001
Boredom susceptibility	3.9 ± 2.0	2.8 ± 1.3	0.0064
Total score	24.3 ± 4.8	19.0 ± 3.9	<0.0001
EPQ			
Neuroticism	8.3 ± 4.3	8.2 ± 4.7	NS
Extraversion	15.1 ± 3.9	13.3 ± 4.5	0.0317
Psychoticism	4.9 ± 2.8	3.5 ± 2.3	0.0057
Lie	7.3 ± 4.1	8.8 ± 4.1	NS

¹ANOVA (Tukey test for multiple comparisons).

²NS: not significant.

sensation seeking trait. Extraversion and psychoticism scores of the EPQ questionnaire were also significantly higher in healthy volunteers than in the unwilling group. No differences in neuroticism and lie scores were detected.

Table 2 shows the results of the SSS and EPQ questionnaires in healthy volunteers and the normative group. Ages were significantly different, normative subjects being younger than volunteers. Healthy volunteers scored significantly higher than subjects in the normative group in three items (thrill-and-adventure seeking, experience seeking, disinhibition) of the four SSS subscales as well as in the total sensation seeking trait. Extraversion scores of the EPQ questionnaire were also significantly higher in healthy volunteers than in the normative group. No differences in neuroticism, psychoticism and lie scores were detected.

Subjects in the unwilling group were significantly ($P < 0.0001$) older than subjects in the normative groups (Tables 1 and 2). Unwilling subjects scored lower than normative persons in the disinhibition (4.3 ± 1.9 vs 5.1 ± 2.5 , $P = 0.0444$) and boredom susceptibility (2.8 ± 1.3 vs 3.6 ± 2.2 , $P = 0.0225$) subscales of SSS, as well as in the total sensation seeking trait (19.0 ± 3.9 vs 21.3 ± 6.4 , $P = 0.0209$). In the EPQ questionnaire, neuroticism scores were lower in the unwilling group in comparison with normative subjects (8.2 ± 4.7 vs 10.0 ± 5.2 , $P = 0.0055$).

The analysis of correlation between the SSS and EPQ scores showed statistically significant positive correlations between extraversion and psychoticism as well as between total SSS score and each of the four subscales. The highest values of Pearson's coefficients were 0.42 for psychoticism vs total SSS score; 0.41 for

Table 2 Sensation Seeking Scale (SSS) and Eysenck Personality Questionnaire (EPQ) scores in healthy volunteers and normative group (mean ± s.d.)

	Healthy volunteers (n = 48)	Normative group ^{a,b}	P ¹
Age (years)	24.4 ± 3.0	21.0 ± 3.6 ^a 19.8 ± 1.9 ^b	<0.0001 <0.0001
SSS^a			
Thrill-and-adventure seeking	7.9 ± 2.0	6.8 ± 2.6	0.0051
Experience seeking	6.6 ± 1.8	5.7 ± 2.1	0.0251
Disinhibition	6.2 ± 1.9	5.1 ± 2.5	0.0040
Boredom susceptibility	3.9 ± 2.0	3.6 ± 2.2	NS ²
Total score	24.3 ± 4.8	21.3 ± 6.4	0.0001
EPQ^b			
Neuroticism	8.3 ± 4.3	10.0 ± 5.2	NS
Extraversion	15.1 ± 3.9	12.4 ± 5.1	0.0014
Psychoticism	4.9 ± 2.8	4.2 ± 2.6	NS
Lie	7.3 ± 4.1	8.6 ± 3.7	NS

¹ANOVA (Tukey test for multiple comparisons).

²NS: not significant.

^aSSS (n = 173), from reference 11.

^bEPQ (n = 96) from reference 12.

psychoticism vs disinhibition; 0.38 for psychoticism vs boredom susceptibility; and 0.38 for extraversion vs thrill-and-adventure seeking. In contrast, lie scores correlated negatively with experience seeking, disinhibition and total SSS score. No significant correlations between neuroticism and SSS scores were observed.

Discussion

This study provides evidence of a personality profile of healthy volunteers characterized by a higher sensation seeking trait, and extraversion, which is different from that of individuals who are not willing to participate in phase I clinical trials or normative subjects.

The personality traits of healthy volunteers were compared with those of subjects who expressed unwillingness to participate in clinical trials and who also had no previous experience as participants in these types of studies. The condition 'no previous experience in clinical trials' and 'willingness to participate' could not be selected for comparison purposes because only seven subjects were encountered in this category. Although historic controls or general norm data have been used in other studies [4–6], the possibility that subjects who were willing to take part in clinical trials could be included was the reason to design a different selection method in our study. However, in order to confirm that individuals who volunteer are different from unwilling subjects, a further comparison between volunteers and general norm data was also assessed.

The group of healthy volunteers and the unwilling group had similar age and most of them were students in the School of Medicine at the same university in Barcelona. The fact that subjects in the normative group were significantly younger than subjects in the unwilling group may be the reason for higher scores in two subscales of the SSS (disinhibition, boredom susceptibility), total sensation seeking trait, and neuroticism in the EPQ. It has been shown that age correlates negatively with the scores of the subscales of EPQ and total SSS [11, 13].

Only subjects taking part in clinical trials had their health status evaluated by anamnesis, physical examination and routine laboratory tests. Cost constraints, operational complexity and possible sample attrition was the reason for not applying the same exclusion criteria to apparently healthy subjects included in the unwilling group. An effort was made to provide almost identical information to that given in a standard phase I trial carried out in our centre to subjects in the unwilling group. Although it has been shown that the amount and type of information can exert some influence on the decision of individuals to volunteer for research [1], we have found consistent differences in the personality profile of subjects who were not willing to participate in a hypothetical clinical trial as compared with healthy volunteers. Overall, these differences were similar to those observed in previous studies [4–6].

The results of the SSS questionnaire indicate that healthy volunteers have a tendency towards activities

which involve some degree of risk and novelty. A marked sensation seeking trait has been demonstrated in a wide range of physical-risk activities, such as outdoor sports [14, 15] and amongst some professionals, such as fireman and policemen [16]. Although the risk associated with participation in phase I trials seems low [17, 18], the sensation seeking trait is assumed to be particularly important in situations related to low-to-moderate degree of risk provided by novel experiences [8]. Our finding of statistically significant differences in the four SSS subscales are in agreement with those obtained in subjects volunteering for behavioural research [9] and agree with the findings of Pieters *et al.* [6]. These authors showed that healthy volunteers participating in phase I clinical trials scored higher in the thrill-and-adventure seeking and disinhibition subscales as well as in the total sensation seeking trait as compared with a general norm group, we obtained almost the same results. However, the possible inclusion in normative data of individuals who were willing to participate in clinical trials might account for an enhancement in average scores of sensation seeking, which our results seem to confirm.

Results of the EPQ were consistent with those of the SSS. Significant correlations between SSS and EPQ, similar to those previously documented [7], were also observed. Volunteers were characterized by a greater degree of sociability and impulsivity than unwilling controls as shown by higher scores in extraversion and psychoticism items. This characteristic may favour participation in clinical trials. Overall, these results are consistent with those obtained in a previous study comparing the personality traits of healthy volunteers, measured by the EPQ, with a reference group [4]. In that study, volunteers scored higher on the extraversion and psychoticism dimensions and lower on neuroticism, whereas no differences were found in the lie scale. In the study of Danjou *et al.* [19], subjects who volunteered for psychopharmacological studies scored higher in extraversion than norm controls when the Eysenck Personality Inventory (EPI) questionnaire was administered. Although extraversion and neuroticism scales from EPQ and EPI are interchangeable [10], results should be interpreted with caution since the EPI questionnaire was used by Danjou *et al.* [19] as an eligibility screening procedure for participation in clinical trials. In our study, personality questionnaires were administered after volunteers signed the informed consent. In addition, volunteers who participated in psychopharmacology trials were excluded with the purpose of eliminating the possible association between sensation seeking trait and both the search for new psychological experiences [8] and illicit drug consumption [20] which could bias the results.

Our results raised some questions regarding the interpretation of data obtained in phase I clinical trials. The personality profile of volunteers may have implications in the extrapolation of data to other populations, even amongst individuals taking part in phase I clinical trials. Although the relationship between some personality traits and pharmacodynamic and pharmacokinetic parameters has been previously reported [21–23], the question of whether or not person-

ality in general, and sensation seeking in particular, modulates the response to drugs remains open to further research.

Although healthy volunteers taking part in phase I clinical trials showed differences in sensation seeking (tendency to be involved in novel experiences and risk-taking activities) and EPQ profile (greater degree of extraversion and impulsivity) as compared with

unwilling and general norm data, these personality traits do not constitute an unusual psychological profile. The relevance of these findings in phase I clinical trials merits further investigation.

We thank Marta Pulido, MD, for editorial assistance and copy editing.

References

- 1 Bigorra J, Baños JE. Weight of financial reward in the decision by medical students and experienced healthy volunteers to participate in clinical trials. *Eur J clin Pharmac* 1990; **38**: 443–446.
- 2 Bevan EG, Chee LC, McGhee SM, McInnes GT. Patients' attitudes to participation in clinical trials. *Br J clin Pharmac* 1993; **35**: 204–207.
- 3 Hassar M, Pocolinko R, Weintraub M, Nelson D, Thomas G, Lasagna L. Free-living volunteer's motivations and attitudes toward pharmacologic studies in man. *Clin Pharmac Ther* 1977; **21**: 515–519.
- 4 Camí J, Llorente M, Farré M, Badenas JM, Ugena B. Personality of healthy volunteers participating in phase I clinical trials. *Person Individ Diff* 1989; **10**: 1199–2000.
- 5 Ball CJ, McLaren PM, Morrison PJ. The personality structure of 'normal' volunteers. *Br J clin Pharmac* 1993; **36**: 369–371.
- 6 Pieters MSM, Jennekens-Schinkel A, Schoemaker HC, Cohen AF. Self-selection for personality variables among healthy volunteers. *Br J clin Pharmac* 1992; **33**: 101–106.
- 7 Furnham A. Extraversion, sensation seeking, stimulus screening and type 'A' behaviour pattern: the relationship between various measures of arousal. *Person Individ Diff* 1984; **5**: 133–140.
- 8 Zuckerman M. *Sensation seeking: beyond the optimal level of arousal*. New Jersey: Lawrence Erlbaum Associates, 1979.
- 9 Kohn PM, Hunt RW, Davis CA, Cowles MP. Volunteering in principle, volunteering in fact, and experience seeking. *Psychol Record* 1982; **32**: 205–213.
- 10 Cowles M, Davis C. The subject matter of psychology: volunteers. *Br J Soc Psychol* 1987; **26**: 97–102.
- 11 Pérez J, Torrubia R. Fiabilidad y validez de la versión española de la Escala de Búsqueda de Sensaciones (forma V). *Rev Latinoam Psicol* 1986; **18**: 7–22.
- 12 Torrubia R, Tobeña A. A scale for the assessment of susceptibility to punishment as a measure of anxiety: preliminary results. *Person Individ Diff* 1984; **5**: 371–375.
- 13 Eysenck HJ, Eysenck SBG. *Manual of the Eysenck Personality Questionnaire*. London: Hodder and Stoughton, 1975.
- 14 Zuckerman M. Sensation seeking and sports. *Person Individ Diff* 1983; **3**: 285–293.
- 15 Gomà M. Personality profile of subjects engaged in high physical risk sports. *Person Individ Diff* 1991; **12**: 1087–1093.
- 16 Levenson MR. Risk-taking and personality. *J Person Soc Psychol* 1990; **58**: 1073–1080.
- 17 Zarafonitis CJD, Riley PA, Willis PW, et al. Clinically significant adverse effects in a phase 1 testing program. *Clin Pharmac Ther* 1978; **24**: 127–132.
- 18 Orme M, Harry J, Routledge P, Hobson S. Healthy volunteer studies in Great Britain: the results of a survey into 12 months activity in this field. *Br J clin Pharmac* 1989; **27**: 125–133.
- 19 Danjou P, Warot D, Weiller E, Lacomblez L, Puech AJ. The personality of the healthy subject: normality and paradox. *Thérapie* 1991; **46**: 125–129.
- 20 Pedersen W. Mental health, sensation seeking and drug use patterns: a longitudinal study. *Br J Addict* 1991; **86**: 195–204.
- 21 Claridge GS, Donald JR, Birchall PM. Drug tolerance and personality: some implications for Eysenck's theory. *Person Individ Diff* 1981; **2**: 153–166.
- 22 Nakano S, Ogawa N, Kawazu Y. Influence of neuroticism on oral absorption of diazepam. *Clin Pharmac Ther* 1980; **27**: 370–373.
- 23 Bertilsson L, Alm C, de las Carreras C, Widén J, Edman G, Schalling D. Debrisoquine hydroxylation polymorphism and personality. *Lancet* 1989; **i**: 555.

(Received 12 July 1994,
accepted 2 December 1994)