ELSEVIER

Biological Psychology 51 (1999) 77–81

BIOLOGICAL PSYCHOLOGY

www.elsevier.com/locate/biopsycho

Short communication

Harm avoidance and serotonin

Michel Hansenne *, Marc Ansseau

Psychiatric Unit, Centre Hospitalier Universitaire du Sart Tilman (B-35), B-4000, Liège, Belgium

Received 1 April 1999; received in revised form 10 April 1999; accepted 16 April 1999

Abstract

The relationships between the Tridimensional Personality Questionnaire (TPQ) and serotonergic activity has been described in some studies with controversial results. These studies have focused on specific patient populations rather than normal controls. Therefore, the aim of the present study is to examine the relationships between the TPQ and serotonergic activity in a group of non-patient subjects. Twenty-three normal subjects answered the TPQ, and the serotonergic activity was assessed by the prolactin response to a highly potent and selective 5-HT1a agonist (flesinoxan). A positive relationship between harm avoidance and PRL response to flesinoxan was found. This study is consistent with the hypothesized link between serotonergic activity and the harm avoidance dimension of the biosocial model of Cloninger. © 1999 Elsevier Science B.V. All rights reserved.

Keywords: TPQ; Serotonin; Personality; Flesinoxan

1. Introduction

Cloninger and his colleagues have proposed a biosocial model of personality based on three fundamental dimensions: novelty seeking; harm avoidance and reward dependence (Cloninger 1986, 1987). Briefly described, novelty seeking is related to behavioural activation, harm avoidance to behavioural inhibition and reward dependence to behavioural maintenance. According to this model, these three dimensions have been postulated to be heritable and independent. More

* Corresponding author. Tel.: + 32-4-3667960; fax: + 32-4-3667283.
E-mail address: michel.hansenne@ulg.ac.be (M. Hansenne)

PII: S0301-0511(99)00018-6

interestingly, each dimension has been associated to a specific central neurotransmitter. Novelty seeking has been theoretically associated to dopaminergic activity; harm avoidance to serotonergic activity; and reward dependence to noradrenergic activity.

Higher scores on the harm avoidance dimension should theoretically reflect increased serotonergic activity. This is directly supported by the fact that an inverse relationship has been noted between aggression and harm avoidance, as well as between aggression and central 5-HT functioning (Coccaro et al., 1989; New et al., 1997). In a recent study (Hansenne et al., 1997), we have reported a positive association between the prolactin (PRL) response to flesinoxan, a highly potent and selective 5-HT1a agonist, and the harm avoidance dimension in a group of depressed patients. This result appears consistent in light to the studies noted above. However, a major pitfall of this study was the state dependence of harm avoidance dimension in depression. Indeed, since harm avoidance has been shown in our and other studies (Chien and Dunner, 1996) to correlate with the severity of depression, the positive relationship between harm avoidance and the PRL response to flesinoxan could be due to the depressive status. Therefore, the aim of the study is to replicate the same design in a sample of non-depressed subjects. According to the literature, we expect a positive relationship between harm avoidance and PRL response to flesinoxan.

2. Methods

The sample comprised a total of 23 normal subjects (13 women), with a mean age of 38.5 years (standard deviation (S.D.) = 10.4). The subjects underwent a medical interview to exclude psychiatric and somatic disorders. They all presented a score lower than eight on the 17-item Hamilton depression rating scale (HDRS), with a mean of 1.8 (S.D. = 1.57) and a score lower than two on item 1. They completed a French version of the 100-item self-questionnaire TPQ the day before the flesinoxan neuroendocrine test. The protocol was approved by the Ethical Committee of the University of Liège Medical School, and the subjects gave their informed consent. Flesinoxan (1 mg/70 kg), diluted in saline solution to obtain 20 ml, was injected intravenously in 10 min, and blood samples of 10 ml were collected 30 min before, immediately before the injection, and 15, 30, 60, 90 and 120 min after the injection. PRL was measured by radioimmunoassay (RIA) with intra-assay and inter-assay coefficients of variation of $10.0 \pm 10.0\%$ and a detection limit of 8 mIU. Hormonal response following flesinoxan was assessed by peak relative value following the injection. The peak relative value is quantified as the difference score between the higher PRL value after the injection and the pre-injection value. To evaluate the linear relationships between the TPQ dimensions and the PRL responses to flesinoxan, partial correlations were computed to control for age, gender and depression scores.

Table 1
Partial correlations between the Tridimensional Personality Questionnaire (TPQ) scores, age and the Hamilton depressive rating scale (HDRS) scores with the prolactin (PRL) response to flesinoxan

	PRL response to flesinoxan
Novelty seeking	−0.23
Harm avoidance	0.46
Reward dependence	0.27
Age	−0.13
HDRS	−0.15

3. Results

The mean scores and S.D.s for each of the three personality dimensions in our sample are 16.5 (5.7) for novelty seeking, 17.7 (4.3) for harm avoidance and 11.4 (4.7) for reward dependence, respectively. PRL peak values ranged from 12 to 1376 mIU with a mean value of 384.0 (S.D. = 326.59). PRL values were not different between males and females ($t = 1.1$, df = 21, $P = 0.32$). Table 1 shows the partial correlations between PRL responses to flesinoxan and the personality dimensions, age and HDRS scores. The harm avoidance dimension was significantly correlated with the PRL response to flesinoxan ($r = 0.47$, $P = 0.04$) (Fig. 1). In contrast, novelty seeking and reward dependence dimensions were not correlated with the endocrine response ($r = -0.23$, $P = 0.33$; and $r = 0.27$, $P = 0.21$, respectively).

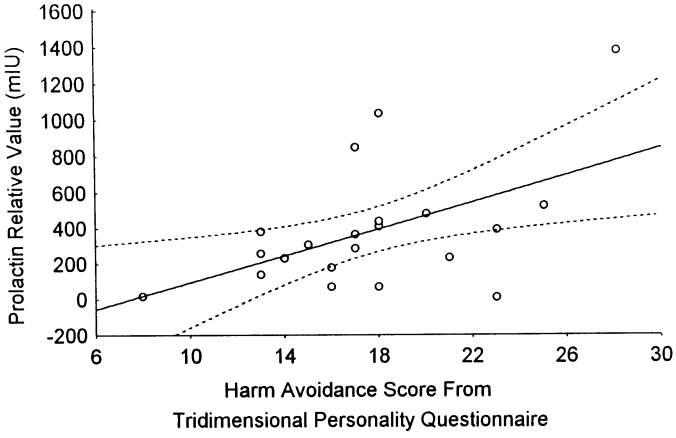

Fig. 1. Relationship between harm avoidance scores from the tridimensional personality questionnaire (TPQ) and prolactin (PRL) responses to flesinoxan among 23 non-depressed subjects ($r = 0.46$, $P = 0.04$).

4. Discussion

The major finding of the present study is a positive correlation between harm avoidance and PRL response to flesinoxan in a group of non-depressed subjects. The study ostensibly replicates and extends a previous study (Hansenne et al., 1997), and it is consistent with the hypothesized link between serotonergic activity and harm avoidance dimension of the biosocial model of Cloninger. However, an important limitation of the previous and present studies is the selective effect of flesinoxan on the 5-HT1a receptors. Indeed, the pharmacologically-induced PRL response to flesinoxan is an indirect index of serotonergic neurotransmission and could involve areas of the brain not related with the neural substrate of harm avoidance hypothesized by Cloninger (Cloninger, 1987, 1988). Moreover, the lack of a placebo-controlled flesinoxan challenge limits the conclusions of this study. It should be noted also that there is no general agreement that the factorial structure of the TPQ is replicable (Earleywine et al., 1992). This suggests that the scales require further revision before the model could be adequately tested.

In the past, three studies failed to report a significant association between serotonergic activity and the harm avoidance dimension (Pfohl et al., 1990; Limson et al., 1991; Waller et al., 1993). In contrast, Nelson et al. (1996) have demonstrated an association between harm avoidance and the sensitivity of the 5-HT2a serotonergic receptors. These controversial results are probably related to the complexity of the neurotransmitter systems, and the different assessment techniques used in these studies. Moreover, these studies have focused on specific patient groups rather than normal controls. Therefore, the present study can be considered as an advancement over the past research. Thus, to exhaustively examine the hypothesized link between harm avoidance and serotonergic activity, future studies should be conducted using agonist and antagonist serotonergic agents in non-patient groups.

References

Chien, A.J., Dunner, D., 1996. The tridimensional personality questionnaire in depression: state versus trait issues. Journal of Psychiatric Research 30, 21–27.

Cloninger, C.R., 1986. A unified biosocial theory of personality and its role in the development of anxiety states. Psychiatric Developments 3, 167–226.

Cloninger, C.R., 1987. A systematic method for clinical description and classification of personality variants. Archives of General Psychiatry 44, 573–588.

Cloninger, C.R., 1988. A unified biosocial theory of personality and its role in the development of anxiety states: a reply to commentaries. Psychiatric Developments 2, 83–120.

Coccaro, E., Siever, L.S., Klar, H.M., Maurer, G., Cochran, K., Cooper, T.B., Mohs, R.C., Davis, K.L., 1989. Serotonergic studies in patients with affective and personality disorders: correlates with suicidal and impulsive aggressive behavior. Archives of General Psychiatry 46, 587–599.

Earleywine, M., Finn, P.R., Peterson, J.B., Pihl, R.O., 1992. Factor structure and correlates of the tridimensional personality questionnaire. Journal of Studies on Alcohol 53, 233–238.

Hansenne, M., Pitchot, W., Gonzalez Moreno, A., Reggers, J., Machurot, P-Y., Ansseau, M., 1997. Harm avoidance dimension of the tridimensional personality questionnaire (TPQ) and serotonin-1A activity in depressed patients. Biological Psychiatry 42, 959–961.

Limson, R., Goldman, D., Roy, A., Lamparski, D., Ravitz, B., Adinoff, B., Linnoila, M., 1991. Personality and cerebrospinal fluid monoamine metabolites in alcoholics and controls. Archives of General Psychiatry 48, 437–441.

Nelson, E.C., Cloninger, C.R., Przybeck, T.R., Csernansky, J.G., 1996. Platelet serotonergic markers and tridimensional personality questionnaire measures in a clinical sample. Biological Psychiatry 40, 271–278.

New, A.S., Tresman, R.L., Mitropoulou, V., Benishay, D.S., Coccaro, E.F., Silverman, J., Siever, L.J., 1997. Serotonin function and self-injurious behavior in personality disorder patients. Psychiatry Research 69, 17–26.

Pfohl, B., Black, D., Noyes, R., Kelley, M., Blum, N., 1990. A test of the tridimensional personality theory: association with diagnosis and platelet imipramine binding in obsessive-compulsive disorder. Biological Psychiatry 28, 41–46.

Waller, D.A., Gullion, C..M., Petty, F., Hardy, B.W., Murdock, M.V., Rush, J., 1993. Tridimensional Personality Questionnaire and serotonin in bulimia nervosa. Psychiatry Research 48, 9–15.