Behavioural and Cognitive Psychotherapy, 1993, **21**, 219–238

Interactions Between Self-Exposure and Alprazolam in the Treatment of Agoraphobia Without Current Panic: An Exploratory Study

Enrique Echeburúa, Paz De Corral, Elvira García Bajos and Mercedes Borda

Universidad del País Vasco, España

The aim of this work was to test the comparative efficacy of four therapeutic modalities (self-exposure, self-exposure + Alprazolam, Alprazolam, and self-exposure + placebo) and also to determine the combined effects of self-exposure with Alprazolam and self-exposure with placebo in the treatment of agoraphobia without current panic. The sample consisted of 31 patients selected according to DSM-III-R criteria. A multigroup experimental design with repeated measures of assessment (pre-treatment, post-treatment and 1, 3 and 6-month follow-up) was used. The results indicated that there was a similar therapeutic improvement (in about 75% of the cases) between pre- and post-treatment in all therapeutic modalities, except for the Alprazolam group, where improvement did not take place, was rather weak or tended to fade as time passed. This improvement increased at the follow-ups in the self-exposure + placebo group, remained stable in the self-exposure group, and was irregular or fairly unpredictable in the self-exposure + Alprazolam group. There was a positive combined action between self-exposure and placebo and a negative interaction between self-exposure and Alprazolam. The highest relapse rate appeared in the therapeutic modalities where the active drug was administered. The intratreatment evolution was faster in the self-exposure group than in the others, but it tended to remain stable in the second part of the therapy. It is therefore concluded that the efficacy of self-exposure therapy may be the same if reduced to half the number of sessions. Finally, several topics that may contribute to future research in this field are commented upon.

Acknowledgments: This research was supported by UPV 230.12–41/86 Research Grant from the University of the Basque Country. The authors would like to acknowledge the assistance of Mercedes Borda, Lourdes Echeverría, Míkel Elizondo, Juan F. Ezpeleta, Diana Sauca and José Luis Arrese. Dr Marks gave valuable comments on the manuscript, which is gratefully acknowledged.

Reprint requests to Enrique Echeburúa, Departamento de Personalidad, Evaluación y Tratamientos Psicológicos, Universidad del País Vasco. Apartado 1249, 20080 San Sebastián, España.

Introduction

It is only recently that the combined action between drugs and psychological therapies has begun to be studied systematically. This combined action is still quite unfamiliar to us. From the perspective of behaviour therapy, agoraphobia, together with depression and obsessive-compulsive disorders, are the major fields where such combined treatments have been carried out (Marks, 1987).

Patients referred to in this research have been agoraphobic without current panic according to DSM-III-R criteria (American Psychiatric Association, 1987) (cf. Mavissakalian, 1988). In other studies, combined behavioural and psychopharmacological (particularly with antidepressants) treatments in the management of agoraphobia have proved to be highly efficient (Aronson, 1987; Telch, Agras, Taylor, Roth and Gallen, 1985). But drop-out rates in these programmes are too high (about 30–35%) and indeed they are over the average drop-out figures (about 10%, according to Mavissakalian and Barlow, 1981, or 16% according to Marks *et al.*, 1983) in non-pharmacological programmes. This is partly due to the slow rate of improvement and partly to undesirable side effects.

The interaction under test in this study, therefore, was that between a benzodiazepine, which has less side effects than tricyclic antidepressants, and spouse-assisted exposure, which has proved to be the best therapeutic option in the treatment of agoraphobia (Jannoun, Munby, Catalan and Gelder, 1980; Marks and O'Sullivan, 1988, 1989) (see Table 1). The aim of this choice was to take advantage of combined therapeutic treatments and to avoid the high drop-out rate that appears in treatments using antidepressants.

TABLE 1. Long term follow-up of self-exposure in the treatment of agoraphobia

Country	Authors	Follow-up (years)	N	Results
Germany	Hand (1986)	6	75	Improvement
Great Britain	Marks (1971)	4	65	Improvement
Great Britain	Munby and Johnston (1981)	7	65	Improvement
Great Britain	McPherson *et al.* (1980)	4	56	Improvement
Great Britain	Burns *et al.* (1986)	8	18	Improvement
Great Britain	Lelliott *et al.* (1987)	5	40	Improvement
Holland	Emmelkamp and Kuipers (1979)	4	70	Improvement
Spain	Echeburúa *et al.* (1991)	1	31	Improvement

This research focused on the differential efficacy of four therapeutic modalities (self-exposure, self-exposure + Alprazolam, Alprazolam, and

self-exposure + placebo), which have been assessed at five different times (pre-treatment, post-treatment, 1-month, 3-months and 6-month follow-up).[1]

Method

Subjects

Thirty-one individuals were identified on the basis of the following criteria: a) that they fulfil the requirements of agoraphobia without current panic in the structured clinical interview according to DSM-III-R criteria (Spitzer and Williams, 1987), and answer a minimum of 5 motor responses in the Inventory of Agoraphobia (Echeburúa and Corral, 1990b) with a mark of 3 or more; b) that they should be between 16 and 65 years old; c) that they had suffered from the agoraphobic disorder for at least one year before the treatment; d) in the case of female patients, that they be unable to become pregnant due to proper contraception methods, to sterility or to the absence of sexual relations; e) that they should not suffer from any kind of physical incompatibility regarding psychopharmacological drugs; f) that they should be ready to abandon any other psychological or psychopharmacological treatment for at least 1 week (or 2 weeks if the drug is a MAOI) before starting the treatment; g) that they had not been treated with an *in vivo* exposure treatment before; h) that they be available during the whole study period and ready to attend weekly meetings as decided in the programme; i) that they should not be alcoholic or addicted to drugs, nor suffer from a current major depressive episode or serious organic illness; and j) that they consent to the study once they had been duly informed.

The screening was carried out with 88 individuals. The number of patients selected according to required criteria was 47. Only 36 started the treatment, 33 finished it, and 31 completed the study with the appropriate follow-ups. The reasons why 11 of those fulfilling the inclusion criteria did not start the treatment were as follows: a) incapacity to give up the psychopharmacological treatment before starting the clinical trial (3); b) clinical improvement between the screening and the start of treatment (3): c) disagreement with the pharmacological treatment group assigned (3); d) incapacity to go out to the place of treatment due to agoraphobia (1); and e) loss of contact with the patient (1).

Therapists

There were six therapists (four clinical psychologists and two psychiatrists) responsible for the treatment. The clinical psychologists were trained in behaviour therapy and had about 4 years clinical experience; the psy-

chiatrists had been trained in psychopharmacology and had the same amount of clinical experience.

Patients belonging to the four therapeutic modalities were distributed at random among the four clinical psychologists at the screening stage. Patients included in the self-exposure, self-exposure + Alprazolam and self-exposure + placebo groups were assessed and treated by the clinical psychologists. Patients assigned to the Alprazolam group were also assessed by the clinical psychologists, but treated by one of the two psychiatrists.

Independent assessor

The independent assessor in this research was a clinical psychologist with one year therapeutic experience. She was "blind" regarding the therapeutic modalities to which patients were assigned.

Experimental design

A multigroup experimental design with multiple and repeated measures of assessment (pre-treatment, post-treatment and 1, 3 and 6-month follow-ups) was used in this study. The patients were assigned to the different groups at random, after a preliminary stratification on the following variables: age, sex, duration and seriousness of the problem. The final groups and therapeutic modalities, as well as some demographic features corresponding to the patients, are shown in Table 2.

It was a "double blind" study, where neither therapists nor patients knew whether they were administering or taking, respectively, an active drug or an inert substance. In addition, at the end of the treatment, when therapists and patients were asked to guess if they had been administering or taking, respectively, drug or placebo, they were not able to discriminate between both of them in a significant way.

In this study, a no-treatment control group was not used, firstly because of ethical problems and secondly, because non-treated agoraphobic patients suffering from this disorder for at least one year (the only kind of patients selected for this research) do not tend to show spontaneous remissions (Agras, Chapin and Oliveau, 1972).

Assessment measures

The specific measures used were the Fear Questionnaire (Marks and Mathews, 1979), the Inventory of Agoraphobia (Echeburúa and Corral, 1990b), the Adaptation Scale (Echeburúa and Corral, 1990a) and the Self-Records (Mathews, Gelder and Johnston, 1981). Adequate reliability and validity data have been reported for these instruments by their respective authors.

TABLE 2. Groups, therapeutic conditions and demographic characteristics of research sample

Groups	Therapeutic conditions	Number of subjects	Age mean	Sex		Marital status		Number of subjects with previous psychopharmacological treatments
				M	F	S	M	
1	Self-exposure	8	38.11	1	7	2	6	5
2	Self-exposure + Alprazolam	9	36.11	3	6	2	7	6
3	Alprazolam	7	36	2	5	0	7	5
4	Self-exposure + placebo	7	36.28	1	6	2	5	6
	Total	31	36.62	7	24	6	25	22

Procedure

Psychological treatment. The psychological treatment chosen for this research was that of gradual *in vivo* self-exposure, which is related to the programmed practice method (Mathews *et al.*, 1981). The therapeutic programme consisted of seven individual weekly sessions (except for the first two sessions, which took place in the same week), so that the whole treatment lasted six weeks. The average total time therapist and patient spent together, apart from the assessment (of variable duration), was 4 hours and 15 minutes.

The self-exposure programme was based on patients' daily records, on the self-help booklet by Mathews *et al.* (1981), and also on the collaboration of a spouse (or a friend, in cases where there was no spouse or where there was a serious marital conflict) as co-therapist, being provided with a help booklet for the patient (Mathews *et al.*, 1981). Each individual had a tailor-made self-exposure treatment, which was related to the target-problems designed together between the therapist and the patient. The patient had to keep an exposure-homework diary (Marks, 1986) and accomplish the self-exposure tasks six days a week, two hours a day, according to the therapist's instructions.

Pharmacological treatment. The drug used in this research was Alprazolam in three daily 0.5 mg. doses at fixed times. Compared to other studies with Alprazolam in panic disorder and agoraphobia (Ballenger, Burrows and Dupont, 1988), the dose used in this research is lower, but adequate for the kind of patients studied (agoraphobics without current panic) (Echeburúa, Corral, García and Borda, 1991). The patient had to take the drug throughout seven sessions, organized in the same way as in the psychological treatment.

The treatment started at least one week (or two in the case of treatment with MAOIs) after patients had stopped taking any other drug. It was planned that withdrawal syndrome should be avoided by administering a moderate but therapeutic dose of Alprazolam (1.5 mg./day) to the patients and by withdrawing the drug gradually from the 6th week in the following way: a reduction of 0.5 mg./day the first four days of the 7th week, and of 0.5 mg./day the remaining three days. At the end of the 7th week, the treatment was totally over.

Individuals belonging to the self-exposure + placebo group were administered with placebo pills, apparently identical and with the same dosage rules as to Alprazolam.

Independent assessment. The independent assessment was carried out before the treatment, after the 4th session, after the treatment, and during

the three follow-up controls (1, 3 and 6 months). In this research, it is of note that the independent assessment also took place in the middle of the therapy (not usually the case in other studies), owing to our desire for a reliable evaluation of the intratreatment progress.

Results[2]

All the analyses were carried out using non-parametric statistics, due to the fact that the data referred to small groups. Firstly, the ANOVA Kruskal-Wallis was used at each assessment in order to test the distribution of the

TABLE 3. Means and standard deviations for each outcome measure at the pre-treatment, intratreatment, post-treatment, and 1 month, 3 month and 6 month assessments

	Self-exposure (N = 8)		Self-exposure + Alprazolam (N = 9)		Alprazolam (N = 7)		Self-exposure + placebo (N = 7)	
	Mean	(*SD*)	Mean	(*SD*)	Mean	(*SD*)	Mean	(*SD*)
Fear Questionnaire (FQ) Subscale of Agoraphobia (0–40)								
Pre-treatment	24.62	(11.73)	22.22	(12.87)	24.43	(9.83)	25.29	(9.65)
Post-treatment	12.12	(13.00)	6.67	(5.11)	16.86	(8.15)	8.71	(5.09)
1 month	9.25	(12.00)	12.11	(11.56)	19.71	(10.67)	8.57	(5.41)
3 months	9.25	(11.91)	9.22	(8.36)	16.28	(13.15)	6.57	(5.26)
6 months	8.14	(10.65)	13.55	(12.51)	15.71	(13.79)	5.29	(4.99)
Adaptation scale Global Subscale (0–5)								
Pre-treatment	3.50	(1.30)	3.88	(0.92)	3.57	(1.51)	4.00	(1.00)
Post-treatment	1.62	(1.30)	2.44	(0.88)	3.14	(0.90)	2.28	(0.95)
1 month	1.75	(1.48)	2.44	(1.01)	2.71	(1.11)	2.00	(1.29)
3 months	2.00	(1.77)	2.00	(1.11)	2.57	(1.27)	2.00	(1.15)
6 months	1.57	(1.71)	1.88	(1.26)	2.71	(1.11)	1.57	(0.97)
Independent assessment Global Subscale (0–5)								
Pre-treatment	3.75	(1.16)	3.88	(0.60)	3.28	(1.97)	4.42	(0.97)
Intratreatment (3 weeks)	2.50	(1.55)	2.66	(0.70)	1.85	(1.67)	3.14	(0.69)
Post-treatment	2.37	(1.59)	1.66	(0.70)	2.57	(1.51)	2.00	(1.00)
1 month	2.50	(2.00)	1.88	(1.45)	2.14	(1.34)	1.42	(0.78)
3 months	2.12	(1.95)	1.88	(1.05)	2.17	(1.11)	1.00	(0.81)
6 months	2.12	(1.88)	1.55	(1.01)	2.00	(1.29)	0.85	(0.89)

groups assigned to the different therapeutic modalities. Secondly, the Mann-Whitney test was used to compare the groups by pairs. And finally, in order to follow the groups throughout the different assessments, we used the Wilcoxon test, which enabled us to compare by pairs the repeated measures within the groups.

Means and standard deviations for each measure at the pre-treatment, intra-treatment (3 weeks), post-treatment and 1-, 3- and 6-month assessments are presented in Table 3. A summary of the statistical findings referred to between-group and within-group comparisons at all assessments is shown in Table 4.

Agoraphobia subscale in the fear questionnaire

This consists of five items, assessed in terms of the intensity at which people avoid the situation expressed by the questionnaire, on a 0–8 scale, 0 corresponding to "I do not avoid it" and 8 "I always avoid it". Means corresponding to each therapeutic modality and assessment are presented in Figure 1.

In the ANOVA Kruskal-Wallis on therapeutic modalities at each assessment, no significant results were shown. However, in the Mann-Whitney analysis between pairs of groups there were statistically significant differences between self-exposure + Alprazolam and Alprazolam ($U=7.5$; $p<.01$) at the post-treatment assessment; and between self-exposure and Alprazolam ($U=12$; $n<.05$) at the 1-month follow-up assessment; and between self-exposure + placebo and Alprazolam at the post-treatment ($U=19$; $p<.05$), the 1-month ($U=8$; $n<.05$) and 6-month ($U=10.5$; $p<.05$) follow-up assessments. These results showed that the level of avoidance under the self-exposure, under the self-exposure + Alprazolam and under the self-exposure + placebo conditions was much lower than the level observed in the Alprazolam group for those periods of time.

The results and significances of comparisons between assessments for each therapeutic modality according to the analysis of Wilcoxon are summarized in Table 4. These results showed significant pre- to post-treatment differences in all therapeutic modalities. These differences tended to remain stable at follow-up assessments, except for the Alprazolam group, whose therapeutic effects tended to fade over time. In the self-exposure + placebo group, the results showed that the improvement continued over time.

Global subscale of the adaptation scale

This consists of one item, where the individuals have to evaluate from 0 "nothing" to 5 "very much" the degree to which their normal life can be

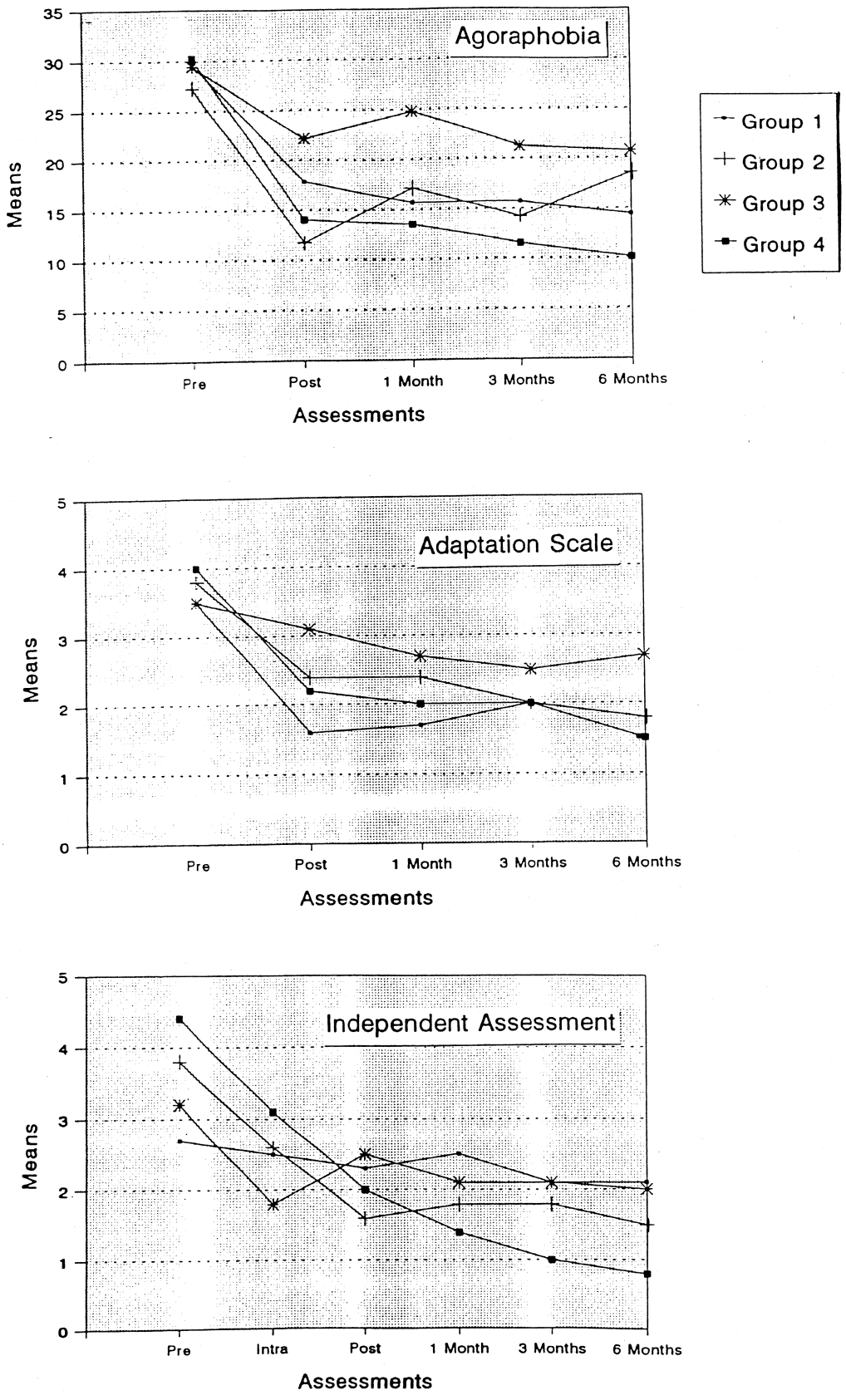
TABLE 4. Significance of overall treatment effects, between-group comparisons and within-group changes for each measure at the pre-treatment, intratreatment, post-treatment, and 1 month, 3 month and 6 month assessments

Variable	Treatment effects	Between-group comparisons							Within-group comparisons			
		Group 1 vs Group 2	Group 1 vs Group 3	Group 1 vs Group 4	Group 2 vs Group 3	Group 2 vs Group 4	Group 3 vs Group 4		Group 1 ($N = 8$)	Group 2 ($N = 9$)	Group 3 ($N = 7$)	Group 4 ($N = 7$)
	(U-test)				(U-test)						(T-test)	
Fear questionnaire (FQ)												
Subscale of Agoraphobia												
Pre-treatment (a)	0.387	31	25.5	27.5	28	26	24.5	—				
Post-treatment (b)	6.182	31	17.5	27	7.5***	25	9*	(a-b)	0***	2***	0**	0**
1 month (c)	4.936	43	12*	22	18	33.5	8*	(b-c)	13	13.5	13	9
3 months (d)	2.754	40.5	15	26.5	21	33	14	(b-d)	5	23.5	12	3
6 months (e)	3.660	41	14.5	23	27	42	10.5*	(b-e)	3	30	11.5	2*
Adaptation scale												
Global Subscale												
Pre-treatment (a)	0.446	39	30	21	35.5	29.5	20	—				
Post-treatment (b)	5.293	48	10*	20.5	27.5	33	13	(a-b)	0***	3**	4	0**
1 month (c)	2.001	46.5	17	23.5	27	35.5	18.5	(b-c)	14	22	0**	5.5
3 months (d)	0.974	34.5	22.5	29.5	23	31.5	18	(b-d)	19	22	0**	0**
6 months (e)	3.223	34.5	14.5	23.5	20.5	38	11*	(b-e)	6	19	0**	0**
Independent assessment												
Global Subscale												
Pre-treatment (a)	2.521	33	29	19	30	18.5	16	(a-a^1)	0***	0***	0**	2*
Intratreatment (3 weeks) (a^1)	2.655	33.5	37	23	40	21.5	13.5	(a^1-b)	7.5	0***	6	0**
Post-treatment (b)	3.600	23	25	37	18	24	13	(a-b)	0***	0***	4	0**
1 month (c)	1.690	29.5	30.5	33	26.5	36	15.5	(b-c)	13.5	21	5	0**
3 months (d)	5.664	31.5	26.5	37	24	46	4***	(b-d)	11	28.5	13	0**
6 months (e)	6.263	28	32.5	39	29	40	6***	(b-e)	5.5	14	4.5	0**

Group 1 – Self-exposure Group 2 = Self-exposure + Alprazolam Group 3 = Alprazolam Group 4 = Self-exposure + placebo

*$p<0.05$

**$p<0.02$



Group 1: Self-exposure; Group 2: Self-exposure + Alprazolam
Group 3: Alprazolam Group 4: Self-exposure + Placebo

FIGURE 1. Graphic representations of means in the different therapeutic conditions and assessments

globally affected by their present problems. Means are graphically presented in Figure 1.

In the ANOVA Kruskal-Wallis on therapeutic modalities at each assessment, no significant results were shown. However, in the Mann-Whitney analysis between pairs of groups there were statistically significant differences between self-exposure and Alprazolam ($U=10$; $p<.05$) at the post-treatment assessment, and between self-exposure + placebo and Alprazolam ($U=11$; $p<.05$) at the 6-month follow-up assessment. These results showed a therapeutic superiority of the self-exposure and the self-exposure + placebo over Alprazolam in the variable considered for those periods of time.

The results and significances of comparisons between assessments for each therapeutic modality according to the analysis of Wilcoxon are summarized in Table 4. These results showed significant pre- to post-treatment differences in all therapeutic modalities, except for the Alprazolam group. These differences tended to remain stable at follow-up assessments, but in the self-exposure + placebo group the results showed that the improvement continued over time.

Global scale of the independent assessment

In this scale, individuals have to assess the degree of global disability they experience in daily life because of the agoraphobia. This scale, going from 0 "nothing" to 5 "very much", was completed in the third week of therapy in order to assess the rate of change during the treatment. Means are presented in Figure 1.

In the ANOVA Kruskal-Wallis on therapeutic modalities at each assessment, no significant results were shown. However, in the Mann-Whitney analysis between pairs of groups there were statistically significant differences between self-exposure + placebo and Alprazolam at the 3-month ($U=4$; $p<.01$) and 6-month ($U=6$; $p<.01$) follow-up assessments. These results showed a therapeutic superiority of self-exposure + placebo over Alprazolam in the follow-ups considered.

The results and significances of comparisons between assessments for each therapeutic modality according to the analysis of Wilcoxon are summarized in Table 4. These results showed significant pre- to post-treatment differences in all therapeutic modalities, except for the Alprazolam group. These differences tended to remain stable at follow-up assessments. However, in the self-exposure + placebo group, the results showed that the improvement continued over time.

From the perspective of the intratreatment assessment, there was a fast therapeutic improvement in all the groups. In the Alprazolam group, however, this improvement tended to diminish and was not present at the end

of the treatment. The self-exposure + Alprazolam and self-exposure + placebo groups went on improving in the second part of the treatment, but improvement in the self-exposure group was simply maintained.

Interobservers reliability

The results of the Independent Assessment (Global Scale) were compared to the ones obtained in the Adaptation Scale (Global Subscale). Once the comparisons of both tests by pairs of measures according to the Wilcoxon analysis for large samples had been carried out, no z value was found to be significant. These results indicated that the information obtained by the independent assessor corresponded to the one obtained by the therapists.

On the other hand, the interobserver agreement between the Independent Assessment (Global Scale) and the Adaptation Scale (Global Subscale) assessed by the Kendall and Pearson correlation coefficients has been significant ($\tau=.63$ and $r=.68$, $p<.05$). In addition, the scores of the therapist and the independent assessor have concurrent validity with the Inventory of Agoraphobia ($r=.78$, $p<.05$).

Refusals and drop-outs of the treatment

As shown in Table 5, there was a small number of refusals. These refusals affected the groups in which the patient was going to take (or thought he was going to take) Alprazolam. There was also a small number of drop-outs which was quite similar among the different therapeutic modalities.

TABLE 5. Number of treatment refusals and drop-outs according to the therapeutic condition

Groups	Therapeutic conditions	Refusals	Drop-outs
1	Self-exposure	0	1
2	Self-exposure + Alprazolam	0	0
3	Alprazolam	2	1
4	Self-exposure + placebo	1	1
	Total	3	3

Improvements and relapses

The results shown in Table 6 suggest therapeutic superiority using self-exposure (on its own or combined with Alprazolam or placebo) over Alprazolam, but what was particularly noteworthy was the improvement obtained in the self-exposure + placebo group. From the perspective of sustained improvement, the therapeutic successes remained stable in the self-exposure and self-exposure + placebo groups; on the other hand, progress was more unpredictable in the self-exposure + Alprazolam group,

since there was a greater relapse rate. Patients were considered to have a relapse if they had improved at the post-treatment assessment, but their score in the FQ (Subscale of Agoraphobia) was greater than 17 at 6-month follow-up.

TABLE 6. Improvement and relapse rate according to the therapeutic condition in the fear questionnaire (Subscale of Agoraphobia)

Groups	Therapeutic conditions	*N*	Improvements*	Maintenance or increase of improvement**	Relapses**
1	Self-exposure	8	6 (75%)	5 (62.5%)	1 (17.5%)
2	Self-exposure + Alprazolam	9	9 (100%)	6 (66.5%)	3 (33.5%)
3	Alprazolam	7	4 (57%)	3 (43%)	1 (15%)
4	Self-exposure + placebo	7	7 (100%)	7 (100%)	0 (0%)

*Pre-posttreatment
**Post-treatment–6 Month follow-up

Discussion

The validity of this research arises from the intergroup homogeneity of all the assessment measures at pre-treatment; also from the interobserver reliability between the therapists and the independent assessor, and from the coherence of the results in the different variables measured. However, the small sample size is a problem which limits the generalization of the results.

The therapeutic improvement between pre- and post-treatment was found in all the therapeutic modalities, except in the Alprazolam group, where improvement either did not take place, was rather weak or diminished as time passed. On the other hand, no significant differences were noticed among the successful therapeutic modalities at this assessment stage.

The therapeutic improvement remained stable at follow-up, but with some differences among the groups. The self-exposure + placebo group tended to improve as time went on. The self-exposure group tended only to maintain the therapeutic results. Finally, the self-exposure + Alprazolam group tended to undergo an irregular and not very predictable progress.

As regards progress during therapy, all groups reacted quickly, with therapeutic improvement occurring during the first part of the treatment. In the second part, however, this improvement appears to have been lost

in the Alprazolam group, but was sustained in the self-exposure group, and actually continued to develop in the self-exposure + placebo and self-exposure + Alprazolam groups.

Considering the pre- to post-treatment period, the therapeutic efficacy of Alprazolam tended to be less than the other modalities. The improvement of the three groups (with no significant differences between them) where the self-exposure (on its own or combined) was used, enable us to conclude that this therapeutic approach was the major factor responsible for the therapeutic change, as has been found in other studies (Ghosh and Marks, 1987; Jannoun *et al.*, 1980; Marks and O'Sullivan, 1988, 1989; McNamee, O'Sullivan, Lelliott and Marks, 1989).

The assessment of these therapeutic modalities after follow-up suggests that, although the self-exposure on its own maintained the therapeutic results at least six months after treatment, there was a positive interaction between self-exposure and placebo, and a negative interaction between self-exposure and Alprazolam. Placebo can yield positive effects on its own in the treatment of agoraphobia (Mavissakalian, 1987), but the positive interaction between self-exposure and placebo could be related, on the one hand, to the therapeutic effectiveness of the exposure and, on the other hand, to the attribution of great therapeutic effectiveness to a treatment perceived by the patients as complete and double (both pharmacological and psychological).

The relatively smaller response of the self-exposure + Alprazolam in comparison with the self-exposure and, more markedly, with the self-exposure + placebo could be related to the pharmacological dissociation; that is, to the interference of the learning process under the effects of anxiolytics (Chambless, Foa, Groves and Goldstein, 1979; Hafner and Marks, 1976; Marks, Viswanathan, Lipsedge and Gardner, 1972). That the patients pay attention to the exposure tasks is essential for the therapy (Foa and Kozak, 1986). In fact, the exposure works better if the patient experiences an increase in the heart rate or skin conductance in the first moments of the task, since these psychophysiological indicators demonstrate that a certain amount of attention is being given to the proposed tasks (Vermilyea, Boice and Barlow, 1984; Zahn, Insel and Murphy, 1984). Another possible and complementary explanation for the less successful therapeutic effects of the self-exposure + Alprazolam is related to the side effects of Alprazolam. The hypersedation consequences (sommolence, cognitive deficits related to attentiveness, concentration, memory, etc.) affect some patients more than others and could explain the irregular progress and unpredictability of this kind of treatment.

The results of the intratreatment assessment suggest that all treatments

led to an initial therapeutic improvement, but the effects of Alprazolam tended to lessen during the second part of treatment. It is also concluded that the therapeutic effectiveness of self-exposure may be the same even if the number of sessions is halved, since the improvement did not increase in the second part of the therapy (cf. Ghosh and Marks, 1987; Mathews *et al.*, 1981; McNamee *et al.* 1989). However, exposure treatment combined with Alprazolam or placebo may require the whole therapy, since the patients continued to improve in the second part.

Self-exposure + placebo (in the same format of seven treatment sessions) and self-exposure (but in a reduced format of four sessions) appear to be the most appropriate therapeutic modalities in this research, with additional advantages being a reduction in treatment duration (an average of 4 hours 15 minutes contact between patient and therapist), the non-existence of undesirable side effects, the low drop-out rate and the convenience of the treatment due to it being self-administered. From this point of view, the advantages of self-exposure are consistent with the results of other studies (Ghosh and Marks, 1987; Jannoun *et al.*, 1980; Marks, 1987; McNamee *et al.*, 1989). The therapeutic success of self-exposure and self-exposure + placebo was quite remarkable considering the fact that the patients in this research had been suffering from agoraphobia for an average of nearly 8 years.

Whether self-exposure is superior to self-exposure + placebo, or vice versa, however, cannot be clearly deduced from this study. The advantage of one option over the other may relate to individual differences, a point not addressed in this research. A subject for future research could be, for instance, to investigate whether agoraphobics with an internal locus of control would particularly profit from self-exposure, or whether patients with an external locus of control would mainly profit from self-exposure + placebo.

The refusal rate to the drug treatment before the beginning of the therapy was only 10% among those patients assigned to one of the groups where Alprazolam or placebo was going to be prescribed; however, there was no refusal among the patients assigned to the self-exposure group. From the point of view of motivation, the agoraphobics tend to accept psychological therapies, but are reticent about taking drugs, as is also proved in the Telch *et al.* (1985) study, which found a refusal rate of 20% among those patients assigned to the drug groups.

The drop-out rate from treatment in this study was 10% and was not affected by any specific modality. This percentage is usual in behavioural programmes, which range from 10% to 15% of drop-outs (Jansson and Öst, 1982; Marks *et al.*, 1981), but the percentage obtained in the drug

groups of our study was well under the 30%–35% obtained in the studies with antidepressants (Aronson, 1987; Mavissakalian and Perel, 1985; Sheehan, Ballenger and Jacobsen, 1980).

The differential figures for refusals and drop-outs depending on the type of treatment are probably related to the perception of the patient. In this way, psychological treatments (of self-exposure and cognitives) are perceived as more acceptable and effective, especially in the long run, than those based on the administration of drugs (Norton, Allen and Hilton, 1983).

The relapse rate in this research affected specifically the Alprazolam + self-exposure (33%) and the Alprazolam (25%) groups; that is to say, those kinds of treatment where the active drug had been included. These percentages correlate to the relapse rate of 33% observed after cessation of imipramine treatment in the review of Mavissakalian (1982), and also to the rate of 25%–30% observed in the behavioural treatment combined with antidepressants in the study of Zitrin, Klein, Woerner and Ross (1983).

The improvement rate in the self-exposure group after the 6-month follow-up reached as high as 60%–65% of all cases (with a low relapse rate), similar to the one obtained in the self-exposure + Alprazolam group (but in this case with a higher relapse rate). The improvement rate obtained in the self-exposure + placebo group was spectacular (100%). The positive results gained in this study with self-exposure (on its own or combined) are superior to the ones obtained in other studies (about 50% in the research of Michelson, Mavissakalian and Marchione, 1988) after the follow-ups (cf. Jacobson, Wilson and Tupper, 1988). We have still, however, to find out if the results remain stable after the next programmed follow-ups (1, 3 and 5 years), as occurs, for example, in the studies of Burns, Thorpe, Cavallaro and Gossling, 1986; Lelliott *et al.*, 1987; and Munby and Johnston, 1981.

The loss of patients at the follow-ups (2 over a total of 33 patients) was low (a loss rate of 6%). This figure is consistent with a 10% loss rate at the 1 and 2 year follow-ups in other studies (Cohen, Monteiro and Marks, 1984). This very small percentage of lost patients must encourage researchers to undertake strict long-term follow-up studies in all clinical research.

Concluding comments

The results of this study raise the question of improving the scope of this kind of research in later studies by modifying some aspects, such as the use of additional assessment measures (psychophysiological records, behavioural avoidance tests or random observations) in order to evaluate the clinical relevance of the behavioural modification, the comparative assessment of the evolution in the triple system of responses (Craske,

Sanderson and Barlow, 1987), the decomposition of the treatment programme (with or without a self-help manual, for instance) in order to determine with a greater accuracy the factors responsible for the behavioural change, the measurement of drug treatment side-effects, as suggested by Marks and O'Sullivan (1988, 1989), and the control of the observance of therapeutic prescriptions. The relevance of this last issue derives from the fact that the non-observance of therapeutic prescriptions is quite frequent in the treatment of agoraphobia with drugs (Clum, 1986) and with exposure techniques (Holden, O'Brien and Barlow, 1983). A way of carrying out this control could be the surveillance of drug consumption by means of random urine analysis and, as for the exposure tasks, by means of the random control of the observance of the tasks by a relative or friend living with the patient.

Notes

1. This report shows the results observed at 3 follow-up controls (1, 3 and 6 months), but the research is still going on and the follow-up will extend to a 5-year period (with several controls after 1, 3 and 5 years) in accordance with other accurate studies (Lelliott, Marks, Monteiro and Tsakiris, 1987).

2. The results displayed in this report only refer to the Agoraphobia Subscale of the Fear Questionnaire, to the Global Subscale of the Adaptation Scale and to the Global Scale of Independent Assessment. Results referring to the remaining tests can be requested from the first author of this study.

References

AGRAS, W.S., CHAPIN, H.N. and OLIVEAU, D.C. (1972). The natural history of phobia: course and prognosis. *Archives of General Psychiatry* **26**, 315–317.

AMERICAN PSYCHIATRIC ASSOCIATION (1987). *Diagnostic and Statistical Manual of Mental Disorders* (3rd. ed. rev.). Washington: APA.

ARONSON, T.A. (1987). A naturalistic study of imipramine in panic disorder and agoraphobia. *American Journal of Psychiatry* **144**, 1014–1019.

BALLENGER, J.C., BURROWS, G.D. and DUPONT, R.L. (1988). Alprazolam in panic disorder and agoraphobia: I. Efficacy in short-term treatment. *Archives of General Psychiatry* **45**, 413–422.

BURNS, L.E., THORPE, G.L., CAVALLARO, A. and GOSSLING, J. (1986). Agoraphobia 8 years after behavioral treatment. *Behavior Therapy* **17**, 580–591.

CHAMBLESS, D., FOA, E.B., GROVES, G.A. and GOLDSTEIN, A.J. (1979). Flooding with brevital in the treatment of agoraphobia: counterreflective? *Behaviour Research and Therapy* **17**, 243–251.

CLUM, G.A. (1986). Drugs vs psychologically based interventions in the treatment

of panic disorders. Paper presented at the American Psychological Association, Washington, DC.

COHEN, S., MONTEIRO, W. and MARKS, I. (1984). Two-year follow-up of agoraphobics after exposure and imipramine. *British Journal of Psychiatry* **144**, 276–281.

CRASKE, M.G., SANDERSON, W.D. and BARLOW, D.H. (1987). How do desynchronous response systems relate to the treatment of agoraphobia: a follow-up evaluation. *Behaviour Research and Therapy* **25**, 117–122.

ECHEBURÚA, E. and CORRAL, P. (1990a). *Escala de Adaptación* (in press).

ECHEBURÚA, E. and CORRAL, P. (1990b). *Inventario de Agorafobia* (in press).

ECHEBURÚA, E., CORRAL, P., GARCÍA, E. and BORDA, M. (1991). La autoexposición y las benzodiacepinas en el tratamiento de la agorafobia sin historia de trastorno de pánico: resultados a largo plazo. *Análisis y Modificación de Conducta* **17**, 969–991.

EMMELKAMP, P.M.G. and KUIPERS, A.C.M. (1979). Agoraphobia: a follow-up study 4 years after treatment. *British Journal of Psychiatry* **134**, 352–355.

FOA, E.B. and KOZAK, M. (1986). Emotional processing of fear. *Psychological Bulletin* **99**, 20–35.

GHOSH, A. and MARKS, I. (1987). Self-treatment of agoraphobia by exposure. *Behavior Therapy* **18**, 3–17.

HAND, I. (1986). In I. Hand and H.U. Wittchen (Eds) *Panic and Phobias*. New York: Springer-Verlag.

HAFNER, H. and MARKS, I. (1976). Exposure in vivo of agoraphobics: contributions of diazepam, group exposure, and anxiety evocation. *Psychological Medicine* **6**, 71–88.

HOLDEN, A., O'BRIEN, G. and BARLOW, D. (1983). Self-help manual for agoraphobia: preliminary report of effectiveness. *Behavior Therapy* **14**, 545–556.

JACOBSON, N., WILSON, L. and TUPPER, C. (1988). The clinical significance of treatment gains resulting from exposure-based interventions for agoraphobia: a reanalysis of outcome data. *Behavior Therapy* **19**, 539–554.

JANNOUN, L., MUNBY, M., CATALAN, J. and GELDER, M. (1980). A home-based treatment program for agoraphobia: replication and controlled evaluation. *Behavior Therapy* **11**, 294–305.

JANSSON, L. and ÖST, L. (1982). Behavioral treatments for agoraphobia: an evaluative review. *Clinical Psychological Review* **2**, 311–337.

LELLIOTT, P., MARKS, I., MONTEIRO, W. and TSAKIRIS, F. (1987). Agoraphobics 5 years after imipramine and exposure: outcome and predictors. *Journal of Nervous and Mental Disease* **175**, 599–605.

MARKS, I. (1971). Phobic disorders four years after treatment. *British Journal of Psychiatry* **118**, 683–688.

MARKS, I. (1986). *Behavioural Psychotherapy. Maudsley Pocket Book of Clinical Management*. Bristol: Wright.

MARKS, I. (1987). *Fears, Phobias, and Rituals*. New York: Oxford University Press.

MARKS, I., GRAY, S., COHEN, D., HILL, R., MAWSON, D., RAMM, E. and STERN, R.

(1983). Imipramine and brief therapist-aided in agoraphobics having self-exposure homework. *Archives of General Psychiatry* **40**, 153–162.

MARKS, I. and MATHEWS, A. (1979). Brief standard self-rating for phobic patients. *Behaviour Research and Therapy* **17**, 263–267.

MARKS, I. and SULLIVAN, G. (1988). Drugs and psychological treatments for agoraphobia/panic and obsessive-compulsive disorders: a review. *British Journal of Psychiatry* **153**, 650–658.

MARKS, I. and SULLIVAN, G. (1989). Anti-anxiety drug and psychological treatment effects in agoraphobia/panic and obsessive-compulsive disorders. In P. Tyrer (Ed). *Psychopharmacology of Anxiety*. Oxford: Oxford University Press.

MARKS, I., VISWANATHAN, R., LIPSEDGE, M. and GARDNER, R. (1972). Enhanced relief of phobias by flooding during vaning diazepam effect. *British Journal of Psychiatry* **121**, 493–505.

MATHEWS, A., GELDER, M. and JOHNSTON, D. (1981). *Agoraphobia: Nature and Treatment*. New York: Guilford Press.

MAVISSAKALIAN, M. (1982). Pharmacological treatment of anxiety disorders. *Journal of Clinical Psychiatry* **43**, 487–491.

MAVISSAKALIAN, M. (1987). The placebo effect in agoraphobia. *The Journal of Nervous and Mental Disease* **175**, 95–99.

MAVISSAKALIAN, M. (1988). The relationship between panic, phobic and anticipatory anxiety in agoraphobia. *Behaviour Research and Therapy* **26**, 235–240.

MAVISSAKALIAN, M. and BARLOW, D. (1981). *Phobia: Psychological and Pharmacological Treatment*. New York: Guilford Press.

MAVISSAKALIAN, M. and PEREL, J. (1985). Imipramine in the treatment of agoraphobia: dose-response relationships. *American Journal of Psychiatry* **142**, 1032–1036.

MCNAMEE, G., O'SULLIVAN, G., LELLIOTT, P. and MARKS, I. (1989). Telephone-guided treatment for housebound agoraphobics with panic disorder: exposure vs. relaxation. *Behavior Therapy* **20**, 491–497.

MCPHERSON, F.M., BROUGHAM, L. and MCLAREN, S. (1980). Maintenance of improvement in agoraphobic patients treated by behavioural methods – a four year followup. *Behaviour Research and Therapy* **18**, 150–152.

MICHELSON, L., MAVISSAKALIAN, M. and MARCHIONE, K. (1988). Cognitive, behavioral, and psychophysiological treatments of agoraphobia: a comparative outcome investigation. *Behavior Therapy* **19**, 97–120.

MUNBY, M. and JOHNSTON, D. (1981). Agoraphobia: the long-term follow-up of behavioural treatment. *British Journal of Psychiatry* **137**, 418–427.

NORTON, G., ALLEN, G. and HILTON, J. (1983). The social validity of treatments for agoraphobia. *Behaviour Research and Therapy* **21**, 393–399.

SHEEHAN, D., BALLENGER, J. and JACOBSEN, G. (1980). Treatment of endogenous anxiety with phobic, hysterical, and hypocondriacal symptoms. *Archives of General Psychiatry* **37**, 51–59.

SPITZER, R. and WILLIAMS, J. (1987). *Structural Clinical Interview for DSM-III-R*

– *Upjohn Version*. New York: New York State Psychiatric Institute (Biometrics Research Department).

TELCH, M., AGRAS, W., TAYLOR, C., ROTH, W. and GALLEN, C. (1985). Combined pharmacological and behavioral treatment for agoraphobia. *Behaviour Research and Therapy* **23**, 325–335.

VERMILYEA, J., BOICE, R. and BARLOW, D. (1984). Rachman and Hodgson (1974) a decade later: How do desynchronous response systems relate to the treatment of agoraphobia? *Behaviour Research and Therapy* **22**, 615–621.

ZAHN, T., INSEL, T. and MURPHY, D. (1984). Psychophysiologic changes during pharmacological treatment of obsessive-compulsive disorder. *British Journal of Psychiatry* **145**, 39–44.

ZITRIN, C., KLEIN, D., WOERNER, M. and Ross, D. (1983). Treatment of phobias: I. Comparison of imipramine hydrochloride and placebo. *Archives of General Psychiatry* **40**, 124–139.