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Memory processes and the course of anxiety and depression in cancer patients

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ABSTRACT

Background. Intrusive memories of stressful events, many involving illness and death, are found in a minority of depressed cancer patients, and may predict the course of anxiety and depression.

Method. Matched samples of mild to moderately depressed and non-depressed cancer patients were followed up after 6 months. Anxiety and depression at follow-up were related to measures of intrusive memories of stressful life events and autobiographical memory functioning that had been assessed at baseline.

Results. Levels of anxiety and depression remained fairly constant over time in the two groups, and the depressed group continued to experience high levels of intrusive memories. The presence of intrusive memories at baseline, and the extent to which these memories were consciously avoided, predicted greater anxiety at follow-up, even after controlling for initial severity of physical and psychiatric symptoms. None of the measures of memory functioning predicted levels of depression at follow-up.

Conclusions. Intrusive memories appear to be a marker of more prolonged psychopathology in cancer patients and may respond to direct therapeutic intervention.

INTRODUCTION

Cancer, it has often been reported, is associated with elevated levels of psychopathology, particularly anxiety and depression (Derogatis *et al.* 1983; Spiegel, 1996). Little is known, however, about the course of anxiety and depression in cohorts of cancer patients, and what predicts better and worse outcomes. In this article we report a 6-month follow-up of matched samples of mild to moderately depressed and non-depressed cancer patients. We investigate the stability of psychopathology in the depressed group over the 6 months, and examine whether anxiety and depression at follow-up can be predicted by a variety of baseline measures of memory processes.

In a previous report (Brewin *et al.* 1996*a*) we investigated the occurrence of spontaneous intrusive memories of negative events in depressed and non-depressed cancer patients. We found that a substantial minority of patients, and significantly more depressed than non-depressed individuals, reported memories of specific negative events coming spontaneously to mind in the week prior to interview. These memories most frequently involved the death or illness of friends and relatives, often related to cancer. Where such memories were present, the amount of intrusion and avoidance associated with them was comparable to that shown by psychiatric patients diagnosed as having post-traumatic stress disorder. These findings are consistent with other studies of depressed psychiatric patients, all of which have found high levels of spontaneous intrusive memories of a small number of specific negative experiences (Kuyken & Brewin, 1994; Brewin *et al.* 1996*b*; Spenceley & Jerrom, 1997). Drawing on more general information-processing theories of

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psychopathology (Ingram, 1984; Teasdale, 1988), and on longitudinal studies of post-traumatic stress disorder (Joseph *et al.* 1996; McFarlane, 1992), it seems likely that the activation of such memories could exacerbate or prolong anxiety and depression.

Our previous work indicated that the avoidance of intrusive memories is related to a more global difficulty in retrieving specific autobiographical memories to positive and negative cues (Kuyken & Brewin, 1995; Brewin *et al.* 1996*a*). Following Williams & Broadbent (1986), participants were given cue words such as 'clumsy' or 'lonely' and were asked to retrieve a memory of an autobiographical episode that occurred at a particular time and place. Over-general recall was rated when the participant produced a memory relating to a series of incidents or to a whole period in their life. This problem of over-general recall is frequently found in depressed and suicidal patients (Williams & Scott, 1988; Williams, 1992). Moreover, in one study over-general recall has itself been found to predict the course of a depressive episode even when controlling for initial symptom severity (Brittlebank *et al.* 1993). Based on the prior research summarized above, we hypothesized that, after controlling for initial levels of psychopathology and physical pathology, psychopathology at follow-up would be predicted by the following baseline measures: presence of spontaneous intrusive memories of negative experiences, the degree of intrusion and avoidance associated with them, and the tendency to produce over-general memories on an autobiographical memory test.

METHOD

Patients

A consecutive series of 740 out-patients diagnosed with cancer attending the Royal Marsden Hospital, London and Sutton branches, was screened for depression using the Hospital Anxiety and Depression Scale. Following previous research (Greer *et al.* 1992), patients who scored $\geqslant 8$ on the depression subscale were categorized as depressed and selected for the second, interview stage of the study. For each depressed patient interviewed, a control patient was selected from among other attenders at the same clinic. Controls were individually matched on age, sex, type of cancer, and stage of disease with the depressed group, but scored $\leqslant 4$ on the depression subscale. Where more than one patient was suitable as a control, one patient was selected at random (see Brewin *et al.* 1996*a*, for further details of sample selection and matching). Sixty-five depressed patients (of whom 28 met DSM-III-R criteria for major depressive episode: American Psychiatric Association, 1987) and 65 controls were interviewed; 96 were female (73·8%); and 34 male (26·2%). Patients ranged in age from 24 to 81 years, with a mean age of 54 years (S.D. = 13·3 years). Patients were categorized into three groups depending upon the size and spread of their cancer: 38 patients had localized disease confined to one primary site (29·23%); 20 patients had loco-regional disease (15·38%); and 72 patients had metastatic disease (55·38%). This provided a 3-point scale representing the stage of the illness.

Twenty patients declined to participate in screening, and eight at the initial interview stage. Seven patients died between screening and first interview, and a further 21 before the follow-up interview. All remaining patients were reinterviewed by telephone and were requested to return questionnaires, except for three depressed patients who could not be contacted. Follow-up data were obtained from 43 depressed and 57 control patients.

Measures

Hospital Anxiety and Depression Scale (HADS: Zigmond & Snaith, 1983)

The HADS is a 14-item self-report scale which was developed specifically for the measurement of depression and anxiety in physically ill populations. The subscale scores of depression and anxiety have been validated in cancer patients (Razavi *et al.* 1990; Moorey *et al.* 1991).

Life Events and Memories Interview

As explained in detail in Brewin *et al.* (1996*a*), patients were administered a semi-structured interview enquiring about the occurrence of a series of life events and stressors commonly associated with the onset of depression. The interview also covered the occurrence of deaths or illnesses of family and friends, and childhood adversity, including physical and sexual abuse. In the final section of the interview patients were asked if they had noticed memories of any of these deaths, life events, or childhood experiences, or of any other negative event, spontaneously coming into their minds during the past week. To qualify, memories had to consist of a visual image of a specific scene that had actually taken place. General thoughts or worries were not included. Patients were asked to identify up to two intrusive memories, selecting the most intrusive if there were more than two. Patients rated each memory on the Impact of Event Scale.

Impact of Event Scale (IES: Horowitz *et al.* 1979)

The IES is a 15-item self-report scale which examines subjective distress as a result of a specific event. The intrusion subscale measures the intrusiveness of the memories and the avoidance subscale measures the extent to which memories are consciously suppressed. Each item is rated on a four point scale, from not at all, rarely, sometimes to often.

Autobiographical Memory Test (Williams & Broadbent, 1986)

Subjects were given 1 min to retrieve a specific personal memory to cue words describing five positive and five negative emotions. Words were presented in a pseudo-random order: the five negative and five positive cue words were shuffled and then presented with positive and negative words alternating. If subjects did not give a specific memory they were prompted to do so ('Can you think of a specific time – one particular event?'). Inter-rater agreement on whether a sample of 200 memories were specific or general was 91%.

Procedure

Full details of the initial wave of data collection are given in Brewin *et al.* (1996*a*). Six months after their first interview patients were recontacted by telephone and, if relevant, were asked if they were still experiencing the specific intrusive memories they had reported earlier. They were also asked if they had noticed any new intrusive memories during the intervening period. They were then asked to complete both the HADS and a copy of the IES in respect of each continuing or new intrusive memory, and to return these by post.

RESULTS

Stability of psychopathology

Mean scores on the anxiety and depression subscales of the HADS, broken down by group and time of administration, are given in Table 1. A 2 (Group) × 2 (Time) mixed model ANOVA on the anxiety scores revealed a significant effect of Group, $F(1,98) = 44{\cdot}7, P < 0{\cdot}001$, but no effect of time and no interaction, largest $F(1,98) = 3{\cdot}86, P > 0{\cdot}05$. A similar ANOVA on the depression scores revealed a significant Group effect, $F(1,98) = 269{\cdot}0, P < 0{\cdot}001$, but again no Time effect, $F(1,98) = 1{\cdot}78, P > 0{\cdot}05$. There was a significant interaction, $F(1,98) = 18{\cdot}52, P < 0{\cdot}001$, indicating a slight reduction in depression among the depressed group and a slight increase in depression among the controls.

In general, therefore, the groups showed little change in psychopathology over the 6-month follow-up period. Within the depressed group, individual patients' levels of anxiety showed temporal stability, $r(43) = 0{\cdot}63, P < 0{\cdot}001$, but individuals' levels of depression were unstable, $r(43) = 0{\cdot}05$. Twenty patients were referred for psychological treatment over this period, and received an average of six sessions each. Once baseline symptoms and stage of illness were controlled, referral for treatment did not predict either anxiety or depression at follow-up (largest beta $= 0{\cdot}20, P > 0{\cdot}10$).

Intrusive memories

Stability of intrusive memories

During the initial interviews 35 patients reported at least one intrusive memory. At follow-up five of these had died and two were uncontactable. Of the remaining 28, 19 reported that their most prominent original memory was still intruding. These 19 patients were used as their own controls

Table 1. *Mean HADS scores at baseline and 6 month follow-up*

HADS	Depressed group Mean (S.D.)	Controls Mean (S.D.)
Anxiety		
Baseline	10.4 (4·3)	4·8 (3·4)
Follow-up	9·4 (3·9)	5·1 (4·3)
Depression		
Baseline	10·2 (2·0)	1·8 (1·3)
Follow-up	8·2 (3·8)	2·8 (3·3)

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Table 2. *Correlations in the depressed group between baseline predictor variables and psychopathology at follow-up*

	HADS depression (follow-up)		Stage of illness		Presence of intrusive memories		Memory 1 total IES score		Over-general positive memories		Over-general negative memories	
	r	(*N*)	*r*	(*N*)	*r*	(*N*)	*r*	(*N*)	*r*	(*N*)	*r*	(*N*)
HADS anxiety (follow-up)	0·43**	(43)	−0·27	(43)	0·38*	(43)	0·47	(17)	0·08	(36)	−0·04	(36)
HADS depression (follow-up)			0·00	(43)	−0·06	(43)	0·01	(17)	0·03	(36)	0·20	(36)
Stage of illness					−0·26*	(65)	0·11	(27)	−0·00	(57)	0·21	(57)
Presence of intrusive memories							0·17	(27)	−0·20	(57)	0·01	(57)
Memory 1 total IES score									0·16	(24)	0·16	(24)
Over-general positive memories											0·33*	(57)

* $P < 0{\cdot}05$; ** $P < 0{\cdot}01$ (2-tailed).

to compare the level of intrusion and avoidance for the same memory at baseline and at follow-up (four of these had data missing). Total IES scores were very similar at both time points (baseline $\bar{x} = 41{\cdot}3$, follow-up $\bar{x} = 40{\cdot}1$, $t(14) < 1$), and were highly correlated, $r = 0{\cdot}61$, $P < 0{\cdot}001$. There were no significant differences between scores on either the intrusion or avoidance subscale, largest $t(14) = 1{\cdot}70$, $P > 0{\cdot}05$. Five patients who had reported intrusive memories at baseline, and seven who had not reported any memories, indicated that they were experiencing new intrusive memories at follow-up. The mean IES score of these new memories was 35·4 (range 22–50).

Intrusive memories and psychopathology at follow-up

For the 28 patients interviewed at follow-up who had originally reported intrusive memories, still having the memory was significantly associated with greater depression, $r(24) = 0{\cdot}51$, $P < 0{\cdot}02$, but not with anxiety, $r(24) = 0{\cdot}21$, $P > 0{\cdot}05$. Depression was significantly associated with the IES Intrusion score, $r(15) = 0{\cdot}53$, $P < 0{\cdot}05$, but not with IES Avoidance $r(15) = 0{\cdot}40$, $P > 0{\cdot}05$, and anxiety was not significantly related to either IES subscale, largest $r(15) = 0{\cdot}22$, $P > 0{\cdot}05$. Depression was not significantly related to having a new intrusive memory at follow-up, $r(79) = 0{\cdot}19$, $P > 0{\cdot}05$, but more anxious patients were significantly more likely to report such a memory, $r(78) = 0{\cdot}31$, $P < 0{\cdot}01$.

Prediction of psychopathology

The ability of baseline measures of memory to predict anxiety or depression in the depressed group at follow-up was next tested. A series of standard multiple regressions was employed, forcing baseline anxiety or depression as well as the stage of the illness to enter on the first step, and then forcing each predictor variable in turn to enter at the second step. This enabled us to test the ability of each memory variable to predict later psychopathology, while controlling for initial severity of symptoms. First-order correlations of the predictor and dependent variables are shown in Table 2.

Intrusive memories

The first predictor variable was a dichotomous variable reflecting whether or not each patient had experienced spontaneous intrusive memories either at baseline or prior to follow-up. The overall equation including baseline anxiety, stage of illness and presence of intrusive memories was significant, $F(3,39) = 11{\cdot}9$, $P < 0{\cdot}001$. After controlling for baseline anxiety and stage of illness the presence of intrusive memories made an additional significant contribution to anxiety at follow-up, beta $= 0{\cdot}29$, $P < 0{\cdot}05$. The comparable equation including baseline and follow-up depression measures was not significant, $F(3,39) < 1$.

The second predictor variable was the overall IES score derived from each patient's most prominent intrusive memory at baseline. The overall equation for anxiety was significant, $F(3,13) = 24{\cdot}6, P < 0{\cdot}001$. After controlling for baseline anxiety and stage of illness, the baseline IES score made an additional significant contribution to anxiety at follow-up, beta $= 0{\cdot}33$, $P < 0{\cdot}02$. We next investigated the role in this predictive effect of the two IES subscales. Intrusion was not a predictor after controlling for baseline anxiety and stage of illness, beta $= 0{\cdot}21, P > 0{\cdot}05$, but Avoidance was a strong predictor, beta $= 0{\cdot}42, P < 0{\cdot}01$. In contrast the comparable equation including baseline and follow-up depression measures, stage of illness, and total IES score was not significant, $F(3,13) = 1{\cdot}58, P > 0{\cdot}05$.

Over-general memories

The overall equations predicting follow-up anxiety involving positive, negative and all overgeneral memories were significant, smallest $F(3,32) = 5{\cdot}46, P < 0{\cdot}01$. In each case, however, after controlling for baseline anxiety and stage of illness, the measure of over-general memories failed to make a significant additional contribution, largest beta $= 0{\cdot}18, P > 0{\cdot}05$. The overall equations predicting follow-up depression involving the three measures of overgeneral memories were uniformly non-significant, largest $F(3,32) < 1$.

DISCUSSION

Mean levels of psychopathology in the depressed and control groups remained remarkably constant over the 6 month follow-up period. This indicates that for the initially depressed (not all of whom met full diagnostic criteria for major depressive disorder) these are not problems of transient distressed mood but more serious disturbances affecting patients' quality of life. Likewise, the amount of intrusion and avoidance associated with spontaneous distressing memories remained highly stable. Although some memories disappeared over the 6 months, new memories sometimes appeared to take their place, also associated with high levels of intrusion and avoidance.

At follow-up the original intrusive memories were still related to psychopathology, greater depression being associated with higher levels of intrusion. This replicates previous findings with cross-sectional studies of depressed psychiatric patients (Kuyken & Brewin, 1994). We were additionally able to show that depression was related to the continued intrusion of the same memory after 6 months. Anxiety did not appear to be related either to the level of intrusion or avoidance of the original memories, or to their prolongation, but these findings are difficult to interpret owing to the small number of subjects involved in the analyses.

The major importance of the study was in the finding that having at least one intrusive memory was associated with greater anxiety at follow-up. One possibility is that the existence of highly accessible specific memories, many about illness and death, exacerbates existing anxieties about health outcomes, and makes negative outcomes seem more likely. There is evidence that the accessibility of examples in memory affects the perceived probability that events are likely to happen (MacLeod & Campbell, 1992). Part of this effect, however, was accounted for by anxious patients being more likely to have had new intrusive memories during the period between initial interview and follow-up. This may be explained by the second significant finding, that among those with intrusive memories at baseline, greater avoidance of the memories predicted more anxiety at follow-up. Avoidance at baseline may have been having the effect of rendering additional memories inaccessible, but by the time of follow-up this avoidance may have broken down, leading to memory intrusion and increased anxiety.

With some exceptions (Joseph *et al*. 1996), previous studies have more commonly reported that it is the extent of intrusion, rather than avoidance, that predicts future pathology (e.g. McFarlane, 1992). Another way in which our results differ is that intrusive memories predicted anxiety, but not depression. Previous studies have, however, been concerned with past traumas such as exposure to disasters, rather than with ongoing stressors that are unpredictable and that still carry future threat. It was also notable in our sample that, among individuals, levels of anxiety remained relatively stable whereas levels of depression did not. It seems likely that a sample of cancer patients differs in important ways from samples exposed to other traumatic stressors, and that the significance of intrusive memories may revolve to a greater extent around future threat than around past loss. The continued presence of this threat may also explain why avoidance appears to be more central in predicting psychopathology in this sample than in others. Avoidance may be particularly difficult to maintain in the face of an advancing disease and increasing physical symptoms.

Contrary to prediction, we did not find that overgeneral memories were predictive of future depression. Part of the reason may lie in the nature of the sample, as discussed above. We were not able to carry out a convincing test of the hypothesis, however, due to the relatively high level of mortality in the depressed sample, which resulted in insufficient power for the analyses. Replication of Brittlebank *et al.*'s (1993) findings awaits further research.

This study adds to a growing body of research identifying intrusive thoughts and memories as crucial components in health-related anxiety and depression (e.g. Kornblith *et al.* 1994; Tjemsland *et al.* 1996). More specifically, it supports previous observations that negative health-related cognitions are often anchored in past experience (Wells & Hackmann, 1993). From a clinical perspective, having a plausible hypothesis about the origin of a negative cognition may be immensely valuable in determining the most effective way of countering it. Moreover, as previously suggested (Brewin *et al.* 1996*a*), direct modification of intrusive memories may be a useful adjunct to standard psychotherapeutic treatment for these patients.

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