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Depersonalization disorder and anxiety: A special relationship?

Mauricio Sierra [a,*], Nick Medford [b], Geddes Wyatt [a], Anthony S. David [a]

[a] Depersonalization Research Unit, Institute of Psychiatry, King's College London
[b] Brighton and Sussex Medical School, Brighton, UK

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ABSTRACT

A significant association between anxiety and depersonalization has been found in healthy controls and psychiatric patients irrespective of underlying conditions. Although patients with depersonalization disorder (DPD) often have a history of severe anxiety symptoms, clinical observations suggest that the relation between anxiety and depersonalization is complex and poorly understood. Using relevant rating scales, levels of anxiety and depersonalization were assessed in 291 consecutive DPD cases. 'High' and 'low' depersonalization groups, were compared according to anxiety severity. Correlation and multivariate regression analyses were also used to assessed the contribution of anxiety to the phenomenology and natural course of depersonalization. A low but significant association between depersonalization and anxiety (as measured by Beck's Anxiety Inventory) was only apparent in those patients with low intensity depersonalization, but not in those with severe depersonalization. Levels of anxiety did not seem to make specific contributions to the clinical features of depersonalization itself, although DPD patients with high anxiety seem characterised by additional non-specific perceptual symptoms. The presence of a 'statistical dissociation' between depersonalization and anxiety adds further evidence in favour of depersonalization disorder being an independent condition and suggests that its association with anxiety has been overemphasized.

1. Introduction

It has been known for more than a century that depersonalization and anxiety states are often closely associated. Indeed, most patients complaining of 'feelings of unreality', originally described by Krishaber (1873), also suffered from episodes of paroxysmal anxiety, reminiscent of panic attacks. Echoing those early observations, Roth (1959) emphasised the presence of anxiety symptoms in patients with chronic depersonalization and coined the term 'phobic-anxiety depersonalization syndrome', to define a specific anxiety disorder, which had depersonalization and agoraphobia as its central manifestations.

Subsequent studies have also documented a significant association between anxiety and depersonalization across the severity spectrum of depersonalization. Thus, significant correlations have been found in non-clinical populations (Trueman, 1984); in psychiatric in-patients regardless of primary diagnosis (Noyes et al., 1977), and in patients with depersonalization disorder (Baker et al., 2003). In fact, of all emotional states, anxiety has been found to be the strongest predictor of depersonalization (Simeon et al., 2003). Of all anxiety manifestations accompanying depersonalization, studies have emphasised social anxiety and panic attacks (Noyes et al., 1992; Toni et al., 1996; Michal et al., 2005). Indeed, depersonalization (including derealization) has always been considered one of the constituent symptoms of a panic attack, occurring in up to 60% of patients (Swinson and Kuch, 1990). While in most such patients, the experience of depersonalization is limited to the duration of the attack, in others it outlasts its duration and can become persistent (Hollander et al., 1989). A recent study on 104 patients with panic disorder found that 20% met criteria for depersonalization disorder (Mendoza et al., 2011). In fact, a common clinical observation in patients with depersonalization disorder is the clustering of panic attacks around the time of onset of depersonalization, subsequently becoming less frequent or absent as depersonalization becomes chronic and predominant. A similar inverse association has also been found in psychophysiological studies. Thus, as compared with anxiety disorder patients, DPD patients reporting similarly high levels of subjective anxiety, show attenuation of autonomic sympathetic responses (Kelly and Walter, 1968; Sierra et al., 2002, 2006). The above observations suggest that the relation between anxiety and depersonalization is complex and poorly understood. The following is a systematic analysis of the relationship between the two conditions in a large series of patients with DPD. In particular we addressed two related questions: 1-Does the presence of comorbid anxiety impose a qualitative or quantitative change on the depersonalization experience? 2- Can anxiety account for the presence of adjunct symptoms, which often accompany depersonalization such as tinnitus, dizziness, or hallucinatory-like experiences?

2. Patients and Methods

This study was carried out on 291 consecutive cases with DPD assessed in the Depersonalization Disorder Clinic at the Maudsley Hospital, London (Baker et al., 2003). All patients underwent a semi-structured psychiatric interview which incorporated

* Corresponding author at: Box PO68, De Crespigny Park, Denmark Hill, London SE5 8AF. Tel.: +44 20 7848 0138; fax: +44 20 7848 0572.
E-mail address: mauricio.sierra-siegert@kcl.ac.uk (M. Sierra).

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Present State Examination (PSE; Wing et al., 1974) probing questions for depersonalization and derealisation, as follows:

'Derealization: Have you ever had the feeling recently that things around you were unreal? '. 'Depersonalization : Have you yourself felt unreal, that you were not a person, not living in the real world? ' If the subject answered yes to either of these probes, the examiner went on to rate severity: 1 = moderately intense or transient ('definitely occurring during the past month and persisted for hours at a time'); 2 = very intense and persistent form. Our case definition required a total score of 2 (range 0–4). In accordance with DSM-IV criteria (APA, 1994), it was required that in addition to persistent or recurrent experiences of depersonalization, reality testing remained intact; and that the depersonalization caused clinically significant distress or impairment in social, occupational or other important areas of functioning. Lastly, it was required that the depersonalization was not secondary to a neurological condition, drug abuse and did not occur exclusively in the presence of another psychiatric condition (i.e. if there is a co-morbid condition, it is necessary to establish that depersonalization is clinically independent). As part of the assessment, all participants also filled in a 'purpose-built' extensive questionnaire intended to obtain information regarding current anxiety symptoms, history of or current co-morbid disorders including drug and alcohol abuse, or any history of medical and neurological illness etc. (for previous studies using this questionnaire see Baker et al., 2003; Medford et al., 2003). Probing questions typically include a Yes or No reply format, followed (in case of a 'yes' answer) by a likert scale to indicate their frequency. Some examples are: Have you ever seen flashes of light in front of your eyes? How often do you have these experiences (1-rarely, 2-frequently, 3- all the time). Have you ever had persistent and distressing thoughts which you cannot control or get rid of? Have you ever had 'visions' (hallucinations) whilst being awake?

The severity and phenomenology of depersonalization was determined by means of the Cambridge Depersonalization Scale (CDS), a 29-item self-rating scale designed to explore in detail the phenomenology of depersonalization within the last 6 months (Sierra and Berrios, 2000). The scale has been used in different cultures and consistently found to have a good psychometric profile (Michal et al., 2004; Molina Castillo et al., 2006; Sugiura et al., 2009).

We used the Beck Anxiety Inventory (BAI) as a primary measure of anxiety (Beck et al., 1988) given that it is a widely validated scale, which comprehensively explores somatic and cognitive anxiety symptoms. It was also thought that being a 'state' scale (it has a time-frame of one week), it was more useful indication of current anxiety levels, given clinical evidence that anxiety can change significantly against the backdrop of constant depersonalization. We also used the trait and state Spielberger scales (Spielberger et al., 1977) as secondary anxiety measures (they are less comprehensive than the BAI) to further disentangle potential differential contributions of trait vs. state anxiety. Given that patients with DPD frequently complain of low mood, Beck's depression inventory (BDI) was also administered as a measure of depression (Beck et al., 1961).

In order to contrast 'high' and 'low' depersonalization groups, we divided the sample using the CDS median score. The designation 'low' should be seen in the clinical context of DPD: all patients reported at least moderate depersonalization, so 'high' and 'low' here represent milder and more severe depersonalization groups within the category of those diagnosed with DPD. For each of these two groups, in turn, 'high' and 'low' anxiety groups were determined as the upper and lower thirds on the respective BAI score range. Although this procedure diminished the sample size, it was done with the intention of creating a high contrast between extreme high and low anxiety scorers, with the aim of uncovering potential differential interactions between anxiety and DP symptoms, which could be missed with techniques making use of the whole score continuum.

2.1. Statistical Analysis

Statistical analysis was carried out with SPSS version 12. Nonparametric statistical methods were used throughout (Mann-Whitney *U* test) given that most variables with the exception of CDS scores, had a right-skewed distribution. Differences were considered to be significant at a $p<0.05$, and all significance tests were two-tailed.

In order to explore the predictive effect of depersonalization, and anxiety on symptomatology and course of illness, a stepwise multiple regression analysis was carried out using variables extracted from the structured interview questionnaire as the dependent variables and global scale scores on the CDS, BAI, BDI and Spielberger (state and trait) as the independent ones. Since multiple regression assumes a normal distribution, right skewed variables (BAI, BDI, Spielberg) were 'normalised' by means of square-root transformation. Variable correlations were also examined by means of scatter-plots to ensure they met linearity assumptions.

3. Results

The whole sample ($n=291$) had the following mean scores on administered scales: CDS = 125 (SD 63.2); BAI = 20.2 (SD 12.1); Spielberger (s) = 52.8 (SD 13.7); Spielberger (t) = 55.18 (SD 12.6); BDI = 20.9 (SD 11.4).

Out of the whole sample 145 and 146 patients were allocated to the 'low' and 'High' depersonalization groups respectively (See Table 1.). Table 1. compares demographics and scale scores across these two groups.

As can be seen in Fig. 1. in both the 'high' and 'low' DP groups, those belonging to the 'high anxiety' subgroup had BAI mean scores in the range of 'severe anxiety' (26-63) while those in the 'low anxiety' subgroups had scores in the range of minimal (0-7) to mild anxiety (8-15). Those in the 'high DP' group had slight but significantly higher BAI scores than the 'low DP' group (see Table 1).

A comparison of 'High' and 'Low Anxiety' scorers within the High DP subgroup (CDS 184.7 (43.5); BAI; 36.5 (6.6) vs. CDS: 178.6 (41) BAI: 9.3 (4.3)), group did not reveal any significant differences in regards to CDS scores ($Z=-0.70$, $p=.48$); age ($Z=-0.27$, $p=.78$), gender ($Z=0.01$, $p=0.97$); age of onset ($Z=-0.98$, $p=0.32$); duration of depersonalization ($Z=-0.12$ $p=0.90$); specific event at onset ($Z=-0.006$ $p=0.99$); speed of onset ($Z=-0.05$, $p=0.95$); concomitant psychiatric symptoms ($Z=-1.7$ $p=0.088$).

As shown in Fig. 2. within the 'Low DP' group those in the 'high anxiety' subgroup scored significantly higher on the CDS than those in the 'low anxiety' subgroup ($Z=-8.5$ $p<0.0001$). There were no significant differences within the 'High DP' group between the 'low' and 'high' anxiety subgroups ($Z=-0.70$ $p=0.482$).

Whole sample Pearson correlations between normalized anxiety measures and CDS scores were as follows: BAI ($r=0.23$, $p<0.001$); Spielberger (s) = ($r=0.24$, $p<0.001$); Spielberger (t) = ($r=0.19$, $p<0.001$). Similarly, within the 'low DP' group there were significant moderate correlations between the CDS and anxiety scores on both the BAI ($r=0.31$, $p<0.001$); Spielberger trait ($r=0.27$, $p<0.001$) and state ($r=0.29$, $p<0.001$). There were however, no significant correlations within the 'high DP' group: BAI ($r=0.06$, $p=0.46$); Spielberger state ($r=0.04$, $p=0.57$); and trait ($r=0.02$, $p=0.72$) (see Fig. 3).

Table 2. shows the results of a stepwise multiple regression analysis carried out on the whole sample using global scores of administered scales as independent variables and a number of anxiety-related variables as dependent ones (See Table 2). Only those scales finally retained by the procedure are shown with their respective Beta coefficients. Scores on the different component subscales (as per Sierra et al., 2005) were also used as dependent variables. In order to avoid inflating correlations through item overlap between the subscales and the Global CDS score, those items constituting the subscale in question were subtracted from the Global CDS.

4. Discussion

In keeping with previous observations, it was found that patients with depersonalization disorder as a whole are characterized by

Table 1
Comparison of administered scale scores, demographics, and course of illness variables across 'Low' and 'High' depersonalization subgroups.

	Low DP group $n=145$	High DP group $n=146$	Z =	Significance
CDS score	71 (SD 28.7)	177 (SD 39.8)	Z = -14.8	**$p=0.001$**
BAI Score	18.8 (SD 11.4)	22.2 (SD 12.2)	Z = -2.8	**$p=0.04$**
Spielberger (t)	53.6 (SD 11.9)	56.9 (SD 13.6)	Z = -2.7	**$p=0.005$**
Spielberger (s)	50.58 (SD 13.5)	55.8 (SD 12.8)	Z = -3.6	**$p=0.001$**
BDI Score	18.07 (SD 9.8)	25.11 (SD 10.7)	Z = -5.5	**$p=0.001$**
Age	35.7 (SD 12.2)	33.5 (SD 11.2)	Z = -1.6	$p=0.090$
Gender (female %)	70 (47.3%)	69 (43.6%)	Z = -1.7	$p=0.86$
Duration of DP	13.2 (SD 13.4)	12.8 (SD 11.6)	Z = -2.49	$p=0.803$
Age at Onset	22.3 (SD 10.7)	20.71 (SD 8.7)	Z = -1.13	$p=0.256$
Previous Diagnoses (%)				
Panic Disorder	20 (20.3)	37 (24.8)	Z = -0.845	$p=0.398$
Agoraphobia	13 (8.8)	16 (10.7)	Z = -0.113	$p=0.633$
OCD	13 (8.8)	21 (14.1)	Z = -1.300	$p=0.256$
GAD	53 (35.8)	48 (32.2)	Z = -0.701	$p=0.483$
Depression	66 (44.6)	78 (52.3)	Z = -0.878	$p=0.380$
Manic-Depressive	5 (3.4)	10 (6.7)	Z = -1.249	$p=0.212$
Schizophrenia	5 (3.4)	8 (5.4)	Z = -0.808	$p=0.419$

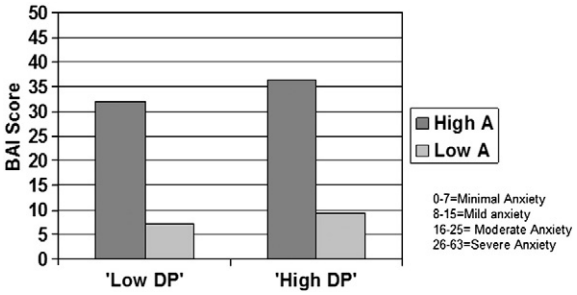

Fig. 1. Comparison of anxiety scores of 'Low' and 'High Anxiety' subgroups within the 'Low' and 'High' depersonalization groups. (BAI = Beck's Anxiety Inventory).

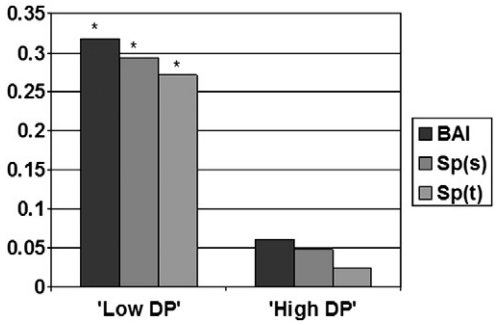

Fig. 3. Pearson correlations between CDS and the anxiety scales administered (BAI = - Beck's Anxiety Inventory; Sp = Spielberger trait and state) across 'High' and 'Low' DP groups. * $p<0.001$.

moderate levels of subjective anxiety. In addition to a moderate general correlation between depersonalization and anxiety, regression analyses revealed a predictive relationship between the latter and most components of the depersonalization syndrome. However, the finding of a subgroup of patients with severe depersonalization who score in the range of 'minimal anxiety' on the BAI, supports the view that the relationship between anxiety and depersonalization is heterogeneous and more complex than hitherto assumed. Our findings suggest that an anxiety contribution to the phenomenology and intensity of depersonalization is fairly restricted to those patients suffering from low to mild depersonalization. This might be interpreted as indicative of a ceiling effect determined by depersonalization intensity beyond which an association with anxiety becomes less apparent. In this regard a recent study looking at alexithymia and dissociation in panic disorder patients showed that those prone to depersonalization experienced difficulties in identifying and describing feelings (Majohr et al., 2011). Be it as it may, the apparent independence from anxiety in cases with severe depersonalization does not support the view that chronic depersonalization should be understood as an 'anxiety equivalent' rather than as a valid nosological category in its own right. However, we have to be cautious about this interpretation as only a longitudinal study, monitoring anxiety before and after the onset of DPD, would be able to establish cause-effect relationships between anxiety and DPD. In this respect, a recent longitudinal study on 3,275 participants of a UK population-based birth cohort, who were followed from birth to adulthood, found a DP prevalence of 0.95% at the age of 36. Not surprisingly there were strong cross-sectional relationships between DP and anxiety and depression. Interestingly, teacher-estimated childhood anxiety emerged as a strong independent predictor of adult depersonalization (Lee et al., 2012). There were no associations with socio-economic status, parental death or divorce; self-reported accidents, childhood depression, tendency to daydream or reactions to criticism.

Recent findings in patients with panic disorder show that those patients suffering from more severe anxiety suffered from depersonalization, suggesting a "dosage effect" of anxiety (Mendoza et al., 2011).

A major epidemiological study looked at the relationship between depersonalization symptoms and both anxiety and depression in the general population. While DP was associated with both anxiety and depression, 'the shared variances were small and DP was clearly separated from symptoms of anxiety and depression' (Michal et al., 2011).

Other clinical studies providing evidence in the same direction have found that the use of tricyclic or SSRI antidepressants in patients with DPD does not seem to diminish the intensity of depersonalization as such but can make it more tolerable, probably by decreasing associated anxiety (Simeon et al., 1998, 2004).

It has been proposed that depersonalization is usually triggered by 'threat appraisals' characterized by fear of losing control (Sierra and Berrios, 1998). Indeed, in patients with anxiety disorders the presence of depersonalization has been specifically associated with perceived threats to feelings of being in control (Kenardy et al., 1992; Meuret et al., 2006; Sierra-Siegert and David, 2007). Although it is likely that both anxiety and a 'threat-appraisal threshold' trigger the onset of depersonalization, it is plausible that once the syndrome becomes fully-fledged, it can numb or distort any accompanying anxiety with the effect that its initial association with depersonalization becomes weakened. In this regard, clinical observations often show a significant exacerbation of anxiety symptoms coinciding with a decrease or remission of depersonalization (Ballard et al., 1992).

The undeniable but complex relationship between depersonalization and anxiety has played an important role in the uncertainties which still plague the nosological classification of chronic depersonalization. While the condition is conceptualized as a dissociative disorder by DSM-IV (American Psychiatric Organization, 1994), the ICD-10 (World Health Organization, 1992) considers it to be an independent neurotic condition. Others in turn, have emphasized the anxiety component and see the condition as being closer to an anxiety disorder than to a dissociative one (Hunter et al., 2003), or claim that depersonalization is the expression of a qualitatively distinct type of dissociation characterized by 'detachment', which differs from other dissociative conditions manifesting as compartmentalization of memory and identity (Holmes et al., 2005). As the latter proposal

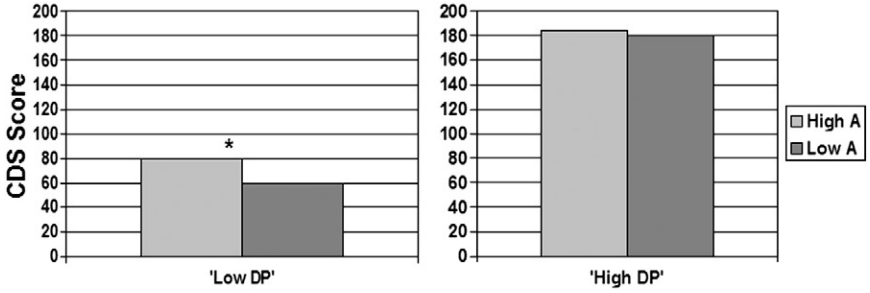

Fig. 2. Comparison of CDS scores across high and low anxiety subgroups (High A, Low A). * $p<0.001$.

Table 2
Stepwise multiple regression analysis using scores on CDS, BDI, BAI, and Spielberger trait and state. Although all administered scales were entered in the regression analysis, the table shows those which were finally retained by the procedure. For the different CDS subscales, constituent items were subtracted from the CDS when used as independent variable. De-ideation refers to subjective memory anomalies as well as alterations in the experience of time.

Dependent Variable	Frequency	Independent Variable	Beta	Significance
Desomatization	NA	CDS	0.692	0.0001
		BAI	0.160	0.0001
Emotional Numbing	NA	CDS	0.841	0.0001
		BAI	0.099	0.001
De-ideation	NA	CDS	0.824	0.0001
		BAI	0.096	0.003
Derealization	NA	CDS	0.653	0.0001
Panic Attacks	237 (54.6%)	BAI	0.300	0.001
Agoraphobia	190 (43.8%)	BAI	0.334	0.001
Obsessional thoughts	222 (51.2%)	BDI	0.225	0.001
		CDS	0.136	0.046
'Hallucinations'	69 (15.9%)	CDS	0.192	0.002
		BAI	0.151	0.014
'Flashes of Light'	132 (30.4%)	BAI	0.325	0.001
		CDS	0.189	0.002
Number of Hospitalizations	1.4 (SD 3.5)	CDS	0.266	0.001

illustrates, whether depersonalization is best conceptualized as a dissociative disorder or not, is not exclusively an empirical question but very much contingent upon how 'dissociation' is defined. It is clear, however, that both the 'anxiety' and 'dissociative' views emphasize different valid observations. On the one hand, it can be hardly denied that DPD bears a close relationship with anxiety states. On the other hand, the profound disruption of self-awareness, agency and emotional experiencing, which characterizes the condition, can probably be best conceptualized along the lines of a dissociative response. This arguable distinctive nature of depersonalization is supported by our regression analysis, which showed that anxiety scores only predicted a history of anxiety symptoms such as panic attacks or agoraphobia, but contributed in small degree to the clinical components of depersonalization. Interestingly, BDI scores, and to a lesser degree depersonalization intensity, but not anxiety, predicted the occurrence of 'obsessive-like' ruminations. Patients with depersonalization often report an uncontrollable and distressing urge to ruminate about existential, philosophical questions such as the nature of 'existence' or 'reality' (Torch, 1978). Far from being a manifestation of a premorbid inquisitive personality, patients often stress the state-dependent and egodystonic nature of such ruminations.

Intriguingly, the intensity of depersonalization (as per CDS scores) but not of anxiety or depression, was associated with a history of previous psychiatric hospitalizations regardless of the diagnosis at the time. This might indicate an intensifying effect of depersonalization on the severity of comorbid conditions. For example, there is some evidence suggesting that the presence of depersonalization is associated with an earlier onset, more severe course of illness and poorer response to treatment of comorbid conditions such as anxiety and mood disorders (Mula et al., 2007, 2009).

Both depersonalization and anxiety predicted the occurrence of visual symptoms such as 'flashes of light' and 'hallucinatory-like' experiences. Although these have never been considered part of the depersonalization syndrome, their presence in some patients with DPD has been described (Baker et al., 2003). It has been proposed that complaints of 'flashes of light' might characterize a subgroup of patients with undetected atypical migraine conditions (Cahill and Murphy, 2004). This is unlikely given that most DPD patients typically experience constant, unremitting depersonalization for several years or even decades (Baker et al., 2003). Interestingly, similar visual complaints have also been reported in patients with so called 'hallucinogen visual perceptual syndrome' (Halpern and Pope, 2003). It is indeed noteworthy that in our series of cases, patients reporting hallucinatory-like phenomena are more likely to relate the onset of their depersonalization to an episode of drug usage. This subgroup of patients has been found to have a more frequent history of anxiety and/or panic attacks (Medford et al., 2003). Recent studies have found that anxiety patients often complain of visual symptoms such as a specific intolerance to fluorescent lights, which has been linked to agoraphobic symptoms (Hazell and Wilkins, 1990; Kellner et al., 1997). The significance and mechanism underpinning such non-specific symptoms is far from understood. It is worth emphasizing that unlike true hallucinatory phenomena as seen in psychotic states, hallucinatory-like symptoms in depersonalization patients are closer to being illusions or perceptual distortions experienced with full insight, and likely to be circumscribed to hypnagogic phenomena (Myers and Grant, 1972). This notwithstanding, a recent study on patients with schizophrenia suggests that the presence of depersonalization mediates an established relationship between self-focus and auditory hallucinations (Perona-Garcelán et al., 2011).

To conclude we found that there is a significant association between depersonalization and anxiety in patients with mild DPD. However, such associations become non-significant in those patients with moderate to severe DPD. It would seem that those cases manifesting more anxiety are characterised by 'noisier' clinical pictures as attested by a higher frequency of perceptual or non-specific visual symptoms.

More than three decades after coining his *'phobic anxiety depersonalization syndrome'*, at a time when 'panic disorder' was a budding new category, Martin Roth de-emphasised the role of depersonalization in the condition: "it is plain that depersonalization was given an undeserved prominence in the original description" (Roth and Argyle, 1988). Contrary to this view, our findings on patients suffering with chronic depersonalization would seem to suggest that it is perhaps the role of anxiety which has become overemphasized, at the expense of depersonalization, limiting broader understanding of the condition and possibly new avenues for treatment.

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