Autonomic Response in Depersonalization Disorder

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Background: Emotional-processing inhibition has been suggested as a mechanism underlying some of the clinical features of depersonalization and/or derealization. In this study, we tested the prediction that autonomic response to emotional stimuli would be reduced in patients with depersonalization disorder.

Methods: The skin conductance responses of 15 patients with chronic depersonalization disorder according to *DSM-IV*, 15 controls, and 11 individuals with anxiety disorders according to *DSM-IV,* were recorded in response to nonspecific elicitors (an unexpected clap and taking a sigh) and in response to 15 randomized pictures with different emotional valences: 5 unpleasant, 5 pleasant, and 5 neutral.

Results: The skin conductance response to unpleasant pictures was significantly reduced in patients with depersonalization disorder (magnitude of 0.017 μsiemens in controls and 0.103 μsiemens in patients with anxiety disorders; *P* = .01). Also, the latency of response to these stimuli was significantly prolonged in the group with depersonalization disorder (3.01 seconds compared with 2.5 and 2.1 seconds in the control and anxiety groups, respectively; *P* = .02). In contrast, latency to nonspecific stimuli (clap and sigh) was significantly shorter in the depersonalization and anxiety groups (1.6 seconds) than in controls (2.3 seconds) (*P* = .03).

Conclusions: In depersonalization disorder, autonomic response to unpleasant stimuli is reduced. The fact that patients with depersonalization disorder respond earlier to a startling noise suggests that they are in a heightened state of alertness and that the reduced response to unpleasant stimuli is caused by a selective inhibitory mechanism on emotional processing.

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DEPERSONALIZATION disorder is characterized by persistent or recurrent episodes of "detachment or estrangement from one's self."[1] The individual may feel like an automaton, or there may be the sensation of being an outside observer of one's own mental processes.[1] Many patients have a subjective absence of emotional feelings despite apparently normal emotional expression.[2]

In contrast to the subjective nature of depersonalization, some early work[3] suggested that patients with depersonalization may have an underactive sympathetic nervous system. For example, while measuring the skin conductance (SC) of a patient with anxiety, Lader and Wing[4] reported a dramatic change in the SC tracing from the typical low-resistance, fluctuating pattern usually associated with anxiety to a high-resistance, nonfluctuating pattern at the onset of a depersonalization episode. These changes were also accompanied by a decline in pulse rate.[4] A similar pattern was later reported by Lader[5] in a second patient with ongoing depersonalization. When the patient reverted to her previous anxious state, the SC changed to extreme activity.

Using forearm blood flow as an index of sympathetic autonomic function, Kelly and Walter[6] found that 8 "depersonalized patients" had the lowest basal recordings compared with patients with a range of psychiatric disorders and controls. The finding that a high proportion of patients with depersonalization disorder have high levels of anxiety[7] renders the previous studies counterintuitive. Other conditions accompanied by high levels of anxiety, such as posttraumatic stress disorder, panic disorder, and obsessive-compulsive disorder (OCD), have hyperactive skin conductance responses (SCRs).[8-11]

A recent model of depersonalization proposed that emotional numbing and reduced autonomic responses might be accounted for by inhibition of the amyg-

dala and related limbic structures by the prefrontal cortex.[2] This putative inhibitory mechanism could be a component of a hard-wired protective response in the brain. The evolutionary benefits of such a mechanism would be to enhance chances of survival during life-threatening situations by suppressing disorganizing levels of fear while maintaining vigilant alertness.[2,12] A prediction stemming from this model is that people with depersonalization disorder will have attenuated SCRs to emotionally unpleasant stimuli. This model also predicts that the state of heightened alertness will generate normal or heightened SCRs to nonspecific stimuli ("physical stimuli") in patients with depersonalization disorder.

To test these predictions, we compared SCRs to neutral and emotional visual stimuli in 15 patients with chronic depersonalization disorder, 15 controls, and 11 patients with anxiety disorders. The study was approved by the ethics committee of the Institute of Psychiatry and Maudsley Hospital, London, England.

PARTICIPANTS AND METHODS

PARTICIPANTS

Fifteen patients with a *DSM-IV* diagnosis of depersonalization disorder were recruited from the Depersonalization Disorder Clinic at Maudsley Hospital.[13] The diagnosis of depersonalization disorder was ascertained by means of a semistructured interview using the Present State Examination[14] by an experienced psychiatrist (M.S.) and by scores above the cutoff point of 70 on the Cambridge Depersonalization Scale.[15] All patients had chronic and continuous (as opposed to intermittent) depersonalization disorder of durations ranging from 2 to 15 years. No patients were taking any medication at the time of the study, and they were all medication free for 2 months or longer. Patients with comorbid psychiatric or neurologic conditions or substance or alcohol abuse were excluded by means of a thorough standard psychiatric interview.

Eleven patients meeting *DSM-IV* criteria for anxiety disorders (5 with OCD; 6 with panic disorder with agoraphobia) were recruited from the Behavioral Psychotherapy Unit at Maudsley Hospital. Patients were diagnosed by experienced clinicians by means of a thorough standard clinical interview. In addition to the exclusion criteria applied to patients with depersonalization disorder, care was taken to exclude "washers" in the OCD sample, as frequent washing could affect SCRs. Two patients with OCD were receiving medication (40 mg of fluoxetine hydrochloride and 50 mg of sertraline hydrochloride). These 2 were not outliers on any of the psychophysiologic measurements and, hence, were retained for the data analysis.

Fifteen controls were selected from staff members and students at the Institute of Psychiatry, King's College. All controls denied a personal history of mental illness and scored below the cutoff points on the administered scales. No controls were taking any medication.

The 3 groups were matched for sex and age because these 2 variables affect electrodermal activity.[16] All participants were paid for their participation in the study and provided written informed consent.

STIMULI

Fifteen pictures selected from the International Affective Picture System (IAPS)[17] were used. Three groups of 5 pictures were selected by valence: neutral (IAPS numbers 1670, 7160, 7150, 7100, and 7830) pleasant (IAPS numbers 1463, 1610, 1710, 1352, and 2530), and unpleasant (IAPS numbers 3060, 9320, 6570, 6370, and 1930).

The pictures were randomized and arranged in counterbalanced order in 2 blocks. Each block was allocated randomly to roughly half of each group. Pictures were presented on a color television placed 1.5 m from the participant. Each picture was shown for 30 seconds, followed by a 30-second interstimulus interval when the monitor screen was blank. Before presentation of the stimuli, 2 neutral pictures (IAPS numbers 7170 and 7050) were presented to facilitate habituation to the projection system.

During the 30-second interval between pictures, participants were asked to rate the picture they had just seen on the dimensions of valence (positive to negative) and arousal (excited to calm) using the Self-Assessment Manikin, an affective rating system devised by Lang.[18] Ratings of valence on the Self-Assessment Manikin are indicated by 5 graphic depictions of the manikin with facial expressions ranging from a severe frown (most negative) to a broad smile (most positive). For arousal, the manikin varies from a state of low to high agitation. The participant can select any of the 5 figures, or boxes in between, on a 9-point rating scale for each dimension. Ratings are scored such that 9 represents a high rating on each dimension (ie, high pleasure or high arousal) and 1 represents a low rating on each dimension.[18]

PROCEDURE

Skin conductance was recorded using standard silver–silver chloride electrodes 0.5 cm in diameter. Electrodes were attached to the distal phalanges of the first and second digits of the nondominant hand. Skin conductance was measured using a constant voltage (0.6 V) SC module (SC4; Contact Precision Instruments, Cambridge, Mass) attached to a personal computer. Water soluble jelly (KY Jelly; Johnson & Johnson, Slough, England) was used as an electrolyte. The SC signal was sampled at 100-millisecond intervals. Only deflections greater than or equal to 0.04 µsiemens were computed. The timing of the stimuli presentation was synchronized to the SC recording program.

Before the galvanic skin resistance (response) measurements, all participants completed the following self-rating scales: the Beck Depression Inventory,[19] the Spielberger trait and state scales,[20] and the Cambridge Depersonalization Scale.[15]

To standardize the dermo-gel-electrode interface, participants were requested to wash their hands using a nonabrasive soap (Ivory soap) as recommended by Cacioppo and Tassinary.[21] Participants were then led into the testing room (adjacent) and sat on a comfortable chair. After the electrodes had been placed there was a 5-minute habituation period during which participants were asked to sit quietly, relax, and move as little as possible. Two minutes of baseline SC were then recorded, during which there were no stimuli and participants were instructed not to move or talk.
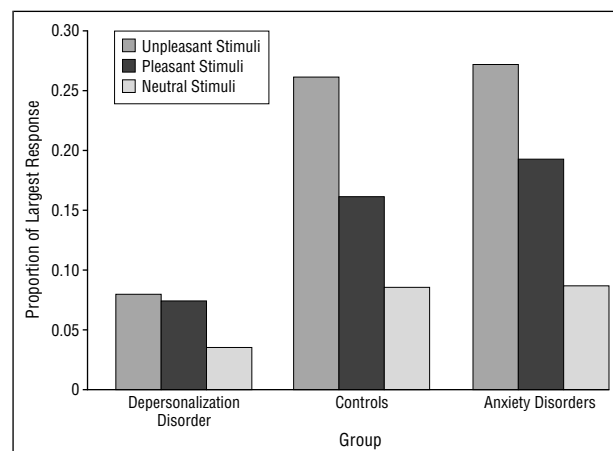
Two nonspecific elicitors of SCR, a hand clap (delivered about 30 cm from the participant's left ear without warning) and a deep inhalation by the participant, were used to assess the integrity of the dermoelectrical system. These 2 stimuli were delivered 30 and 45 seconds (clap followed by sigh) after a 2-minute baseline recording. These stimuli have been shown to reliably elicit SCRs from healthy individuals.[21,22] Participants were then told that a series of slides was going to be shown on the television screen and they were instructed to look at each of them carefully. During each interstimulus interval, participants were asked to provide verbal ratings on valence (how pleasant the picture was) and arousal (how "agitated" or moved the participant felt by the picture). For reference purposes, an enlarged Self-Assessment Manikin was placed below the television screen. All testing was restricted to afternoon hours

(2 PM–5 PM), as time of testing can be a source of confounding effects.[16]

DATA ANALYSES

Skin conductance levels and nonspecific fluctuations exceeding 0.04 µsiemens were counted during a 2-minute baseline recording. Amplitude was defined as the highest deflection (phasic increase in conductance) from baseline initiated 1 to 4 seconds after slide onset and exceeding 0.04 µsiemens. For stimulus presentation, SCR magnitude (mean value of amplitude computed across all stimulus presentations, including those without a measurable response) was obtained. A log transformation (log[SCR+1]) was used to normalize the magnitude data. Because magnitude has the potential disadvantage of confounding frequency and amplitude, which do not always covary, an SCR probability was computed as a measure of response frequency above a threshold regardless of amplitude (number of responses above 0.04 µsiemens per total number of presentations).[23] Response latencies (temporal interval between stimulus onset and SCR initiation) were computed for all responses occurring 1 to 4 seconds after onset of the stimulus. In addition to the previous measurements, baseline mean conductance level (during the initial 2 minutes) and number of nonspecific responses (ie, deflections occurring >4 seconds after stimulus onset) during each epoch were counted.

Statistical analysis was performed using a software program (SPSS version 8; SPSS Inc, Chicago, Ill). Analysis of variance was used throughout, accompanied by post-hoc analysis (Scheffé test). An $\alpha \leq .05$ was considered statistically significant, and all significance tests were 2-tailed. For the purpose of hypothesis testing, comparison of magnitudes to stimuli across groups and response latency (**Figure**) constituted the primary outcome variables. All other analyses were regarded as exploratory.

RESULTS

The 3 groups did not differ significantly by age ($F_{2,33}=0.11$; $P=.89$) or sex ($F_{2,33}=0.035$; $P=.96$). Mean global scores on the Beck Depression Inventory and the Spielberger scales (state and trait) did not differ significantly between individuals with depersonalization disorder and those with anxiety disorders; controls had significantly lower scores on these scales. Global scores on the Cambridge Depersonalization Scale were significantly higher for patients with depersonalization disorder than for controls and those with anxiety disorders (**Table 1**).

No difference was found in the ratings for valence between patients with depersonalization disorder and the other 2 groups. However, 1-way analysis of variance revealed significant differences in the arousal ratings across groups ($F_2=4.9$; $P=.01$), with depersonalized patients revealing lower scores for the unpleasant pictures than the other 2 groups (Scheffé, $P<.05$).

There was a difference in the mean [SD] resting baseline level of SC across groups ($F_2=6.468$; $P=.004$) (**Table 2**). The greatest difference (Scheffé, $P<.05$) was found between patients with depersonalization disorder (1.8 [0.89] µsiemens) and those with anxiety disorders (4.1 [1.8] µsiemens). Controls had an SC intermediate to that in the other 2 groups (2.65 [1.8] µsiemens). The mean (SD) number of nonspecific deflections during the 2-minute baseline recording showed a similar pattern, with the lowest number in the depersonalization group (1.3 [1.8]) followed by the control (1.5 [2.8]) and anxiety (4.0 [3.1]) groups. However, these differences did not reach statistical significance ($F_2=2.4$; $P=.10$).

SKIN CONDUCTANCE RESPONSE

The magnitudes of SCRs to the unpleasant, pleasant, and neutral pictures for each of the 3 groups are shown in the Figure. Because responses to the startle noise (hand

Skin conductance response (SCR) magnitude to stimuli across groups. Because the range of SCR amplitudes can vary across participants, responses are standardized as range-corrected scores (for each participant, SCR magnitudes were computed as a proportion of that participant's largest response).

Table 1. Global Scores on Administered Scales and Demographic Data*

Variable	Depersonalization Disorder (D) (n = 15)	Controls (C) (n = 15)	Anxiety Disorders (A) (n = 11)	Post Hoc Analysis (Scheffé, $P<.05$)	1-Way ANOVA
Age, y	33.8 (8.7)	34.3 (8.7)	35.6 (9.6)	NS	$F_{2,33} = 0.11$; $P = .89$
Sex, F/M No. (%)	7 (49)/8 (51)	7 (49)/8 (51)	5 (49)/6 (51)	NS	$F_{2,33} = 0.035$; $P = .96$
CDS score	141.7 (51.5)	19 (15.5)	46.42 (56.5)	D vs C, A	$F_{2,31} = 29.7$; $P<.001$
BDI score	17.57 (5.3)	2.5 (3.8)	24.2 (13.1)	D, A vs C	$F_{2,30} = 25.8$; $P<.001$
Spielberger scale score					
State	47.4 (15.2)	29.3 (10.7)	51.78 (17.88)	D, A vs C	$F_{2,32} = 7.6$; $P<.001$
Trait	53 (6.2)	35 (4.7)	57 (12.7)	C vs D, A	$F_{2,33} = 26$; $P<.001$
BAI score	20.5 (15.8)	10.5 (16.6)	24.3 (19.1)	NS	$F_{2,29} = 1.6$; $P = .28$

*Data are given as mean (SD) except where indicated otherwise. ANOVA indicates analysis of variance; NS, nonsignificant; CDS, Cambridge Depersonalization Scale; BDI, Beck Depression Inventory; and BAI, Beck Anxiety Inventory.

Table 2. Skin Conductance Responses (SCRs), Latencies, and Subjective Ratings to Administered Stimuli*

Stimulus	Depersonalization Disorder (D) (n = 15)	Controls (C) (n = 15)	Anxiety Disorders (A) (n = 11)	Post Hoc Analysis (Scheffé, $P<.05$)	ANOVA
Skin conductance at baseline, µsiemens	1.8 (0.89)	2.65 (1.8)	4.1 (1.8)	D vs A	$F_{2,22} = 6.4$; $P = .004$
SCR Amplitude to Stimuli, µsiemens					
Unpleasant	0.017 (0.012)	0.074 (0.062)	0.103 (0.085)	D vs C, A	$F_{2,33} = 4.13$; $P = .002$
Pleasant	0.017 (0.02)	0.051 (0.032)	0.056 (0.054)	NS	$F_{2,33} = 0.98$; $P = .38$
Pictures	0.009 (0.018)	0.032 (0.028)	0.038 (0.042)	NS	$F_{2,33} = 1.1$; $P = .34$
Physical	0.261 (0.28)	0.24 (0.22)	0.35 (0.35)	NS	$F_{2,33} = 0.21$; $P = .80$
Corrected SCR Amplitude to Stimuli, µsiemens					
Unpleasant	0.07 (0.01)	0.26 (0.07)	0.27 (0.79)	D vs C, A	$F_{2,26} = 5.1$; $P = .01$
Pleasant	0.07 (0.1)	0.16 (0.25)	0.19 (0.15)	NS	$F_{2,26} = 1.5$; $P = .23$
Neutral	0.03 (0.05)	0.08 (0.1)	0.08 (0.07)	NS	$F_{2,26} = 1.7$; $P = .18$
Probability of SCR					
Unpleasant	0.2 (0.26)	0.52 (0.37)	0.71 (0.28)	D vs C, A	$F_{2,33} = 7.4$; $P = .002$
Pleasant	0.15 (0.24)	0.31 (0.35)	0.41 (0.36)	NS	$F_{2,33} = 1.9$; $P = .16$
Neutral	0.14 (0.22)	0.18 (0.38)	0.24 (0.19)	NS	$F_{2,33} = 0.45$; $P = .63$
Physical	0.20 (0.28)	0.21 (0.42)	0.27 (0.35)	NS	$F_{2,33} = 0.52$; $P = .57$
Latency of SCR, s					
Unpleasant	3.01 (0.76)	2.5 (1.1)	2.1 (0.26)	D vs A	$F_{2,21} = 5.2$; $P = .02$
Pleasant	2.1 (0.6)	2.4 (0.53)	1.7 (0.51)	NS	$F_{2,21} = 1.7$; $P = .19$
Neutral	2.04 (0.5)	1.9 (0.6)	2.2 (0.24)	NS	$F_{2,21} = 1.5$; $P = .21$
Physical	1.6 (0.5)	2.3 (0.35)	1.6 (0.89)	D, A vs C	$F_{2,21} = 4.6$; $P = .03$
Valence Rating					
Unpleasant	7.2 (0.96)	7.8 (0.71)	7.7 (0.76)	NS	$F_{2,33} = 1.8$; $P = .17$
Pleasant	3.6 (1.3)	2.9 (0.47)	3.4 (1.10)	NS	$F_{2,33} = 1.7$; $P = .19$
Neutral	4.5 (0.58)	4.5 (0.34)	4.9 (0.27)	NS	$F_{2,33} = 2.9$; $P = .08$
Arousal Rating					
Unpleasant	3.2 (2.01)	5.8 (2.2)	7.4 (1.47)	D vs C, A	$F_{2,33} = 4.9$; $P = .01$
Pleasant	4.9 (1.6)	4.9 (1.7)	5.4 (2.1)	NS	$F_{2,33} = 0.24$; $P = .78$
Neutral	4.1 (1.3)	3.6 (1.4)	3 (1.4)	NS	$F_{2,33} = 0.43$; $P = .65$

*Data are given as mean (SD). ANOVA indicates analysis of variance; NS, not significant.

clap) did not differ significantly from those to the sigh ($F_{2,32}=0.33$; $P=.76$), both were collapsed into a single variable (physical stimulus). There were no significant differences in the responses to the physical stimuli across groups ($F_{2,33}=1.5$; $P=.36$).

Because we predicted an interaction between type of emotional stimuli and participant group (ie, a disproportionately lower response to unpleasant stimuli in depersonalized patients), a mixed 2-factor analysis of variance was used. It revealed a main effect for group ($F_{1,32}=14.6$; $P=.001$) and a main effect for valence ($F_{2,31}=8.49$; $P=.001$). There was also a significant group × valence interaction ($F_{2,32}=3.8$; $P=.03$). Simple effects analyses showed that the 3 groups differed significantly in their SCRs to unpleasant stimuli ($F_2=4.13$; $P=.02$), with patients with depersonalization disorder having significantly lower SCRs than controls and those with anxiety disorders (Scheffé, $P<.05$).

The group with depersonalization disorder also had a significantly lower probability of response to the unpleasant stimuli ($F_2=7.4$; $P=.002$), the differences being significant with controls and the anxiety group (Scheffé, $P<.05$). Although amplitude and SCR probability seemed to be lower for the pleasant and neutral pictures in the depersonalization group, the difference did not reach statistical significance ($F_2=0.03$; $P=.95$).

Although our findings are consistent with the predicted lack of an SCR to unpleasant stimuli, they also show a trend suggesting generalized hyporesponsiveness. The SCRs to pleasant and neutral stimuli did not differ significantly across groups, but there was a significant main effect of group, that is, lower responses from patients with depersonalization disorder. Potentially, therefore, the interpretation of a specific effect for unpleasant stimuli might be contaminated by a floor effect arising from the reduced responses of the depersonalization group overall. Consequently, we carried out a supplementary analysis using range-corrected scores as suggested by Lykken and Venables[24]; it expresses each SCR as a proportion of that participant's largest response. These range-corrected means are shown in the Figure. With this transform, genuine differences between SCRs to unpleasant and neutral pictures were still evident as a group × valence interaction ($F_{2,32}=3.7$; $P=.046$). A valence main effect ($F_{2,64}=14.03$; $P<.001$) and a group main effect ($F_{2,32}=3.73$; $P=.043$) were still found. This shows that even when the range of responses is corrected, patients with depersonalization disorder still show a marked reduction in their SCRs to unpleasant stimuli.

The fact that in our set of pictures those with negative valence also had the highest arousability makes it difficult to know whether the reduced responses seen in the depersonalization group were arousal or valence deter-

mined. To address this problem, we compared a subset of 2 pleasant pictures (IAPS numbers 1463 and 2352) and 2 unpleasant pictures (IAPS numbers 9330 and 6570) with equivalent arousal ratings. The greatest difference between groups was with the unpleasant pictures, but the difference did not reach statistical significance ($F_2 = 1.8$; $P = .09$).

LATENCY OF SCR

Analysis of variance for latency of SCR onset to type of stimuli revealed a main effect for type of stimuli (physical and emotional: $F_{1,21} = 18.14$; $P = .001$) and for group ($F_{1,21} = 5.5$; $P = .001$). There was also an interaction between type of stimuli (physical stimuli included) and group ($F_{2,21} = 4.3$; $P = .03$). Post hoc analyses revealed that depersonalized patients had a longer latency to unpleasant pictures than did patients with anxiety disorders (Scheffé, $P < .05$). Also, depersonalized patients and those with anxiety disorders had a significantly shorter latency to physical stimuli than controls (Scheffé, $P < .05$).

COMMENT

To our knowledge, this is the first study to explore SCRs to emotional stimuli in depersonalization disorder. The study has several limitations, including the relatively small sample sizes (in particular that of the anxiety group). In addition, the anxiety group was not ideal in that it included patients with 2 different disorders (panic disorder and OCD) that may differ in physiologic response. However, because the aim of the study was to compare patients with depersonalization disorder, controls, and patients with high levels of anxiety regardless of nosologic status, this might not constitute a serious drawback. Another limitation comes from the fact that the loudness of the clap and the depth of the sigh (physical stimuli) were not rigorously controlled, and, hence, these measures might have introduced a greater source of error than the pictures.

Our findings show that, as predicted by Sierra and Berrios,[2] depersonalization disorder seems to be associated with reduced autonomic responding to aversive stimuli. In fact, there is no differential responding by patients with depersonalization disorder to unpleasant pictures compared with pleasant and neutral pictures. The absence of any differential SCR to these types of emotional stimuli is striking; higher amplitude SCRs to unpleasant stimuli were found in controls and those with anxiety disorders.

Standardizing the data to an index of response (as opposed to raw amplitude measurements) did not abolish the findings, suggesting that these are not due to a floor effect caused by a generalized dampening of SCRs. Rather, our findings suggest that the SCR abnormalities in depersonalization disorder have tonic and phasic components. Thus, the reduced baseline SC and fewer nonspecific fluctuations suggest the presence of an inhibitory mechanism, which tonically inhibits sympathetic outflow. This finding is in line with that reported by Kelly and Walter,[6] who found marked low baseline forearm blood flow in depersonalized patients.

However, the fact that patients with depersonalization disorder showed differential responses to the unpleasant stimuli suggests that phasic inhibitory mechanisms are also at play. Patients with depersonalization disorder not only had fewer measurable responses to the unpleasant pictures, but when they showed a response, it had significantly lower amplitude. Also in favor of a selective inhibitory mechanism is the finding that patients with depersonalization disorder had a longer SCR latency to unpleasant stimuli but not to pleasant, neutral, or physical stimuli. That these findings were selective to the unpleasant pictures (an effect that was still observable after controlling for arousability) implies that an adequate appraisal of valence is taking place. Indeed, subjective ratings for valence did not differ across groups; therefore, the ability to judge the emotional meaning of complex scenes is preserved in depersonalization disorder. However, these patients rated the unpleasant pictures as less arousing, thus paralleling the psychophysiologic data. In this regard, studies[25] with healthy subjects (using IAPS pictures and the Self-Assessment Manikin) have found that SCRs mainly correlate with subjective arousal as opposed to valence.

The fact that there were no differences across groups to the physical stimuli further suggests that SCRs are not indiscriminately reduced in depersonalization disorder. Moreover, patients with depersonalization disorder and those with anxiety disorders had quicker responses (shorter latency) to the nonspecific stimuli than controls. The SCR to an unwarned stimulus, such as a clap, is a component of the startle response, which is increased in anxiety disorders and posttraumatic stress disorder and probably reflects a heightened state of alertness.[26] Indeed, levels of anxiety as measured by self-rating scales were raised in patients with depersonalization disorder and in those with anxiety disorders.

Taken as a whole, these results suggest the simultaneous existence of inhibitory and facilitatory mechanisms on specific components of autonomic activity. Thus, patients with depersonalization disorder in common with those with anxiety disorders have similarly high anxiety ratings and SCRs (shorter latency of response) to nonspecific stimuli, suggestive of a state of heightened arousal. However, only patients with depersonalization disorder show a marked diminution and delay in response to unpleasant pictures. These findings are compatible with the model proposed by Sierra and Berrios,[2] which postulates the simultaneous existence of an inhibitory mechanism on emotional response and an excitatory mechanism leading to a state of heightened alertness.

In the face of increased arousal (as suggested by the amplitude and latency responses to the physical stimuli), a reduction in SCR amplitude and increased response latency to the unpleasant pictures lends empirical support to the notion that depersonalization is the manifestation of a protective, functional response of the nervous system intended to deal with life-threatening situations. However, the emergence and persistence of this response in a nonthreatening situation would result in an extremely strange experience, namely, the sudden onset of lack of emotional feelings, things looking devoid of emotional coloring but with improved sensory definition. Moreover, it is suggested that a state of heightened alertness in the absence of autonomic arousal might be conducive to a state of heightened self-observation,

which is a common feature of depersonalization disorder. From a nosologic standpoint, the marked psychophysiologic differences between patients with depersonalization disorder and those with anxiety disorders lend support to the view that depersonalization disorder is a valid entity in its own right. This notwithstanding, it is interesting that alexithymia and antisocial personality disorder (conditions thought to be unrelated to depersonalization) have recently been found to have similar psychophysiologic features as those found in this study. Thus, subjects with high scores on the Toronto Alexithymia Scale produce fewer specific SCRs to emotional visual stimuli regardless of category.[23] Similar findings have been reported in individuals with "developmental" antisocial personality disorder.[27] Although alexithymia and antisocial personality disorder seem to share with depersonalization disorder abnormalities in the experiencing of emotions, there are clear phenomenologic differences. For example, patients with sociopathic behavior seem to have a selective deficit in the experiencing of empathy and fail to react autonomically to pictures conveying distress but not to fearful or otherwise unpleasant pictures.[27] Moreover, unlike patients with depersonalization disorder, those with antisocial personality disorder have high levels of impulsivity and make overt displays of lack of empathy.[28] Patients with depersonalization disorder, in contrast, complain of subjective emotional deficits despite normal behavioral expression.[2] Patients with alexithymia seem to have difficulty differentiating and expressing emotions verbally, which is thought to give rise to physiologic arousal and a negative subjective state. Unlike patients with depersonalization disorder, alexithymic patients have greater tonic electrodermal activity and report more arousal and displeasure in general than controls.[29]

In conclusion, our findings support the view that depersonalization disorder is characterized by reduced emotional reactivity to emotional stimuli. Further work in this area should help in understanding this distressing disorder and the interplay between affect and cognition.

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REFERENCES

1. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition.* Washington, DC: American Psychiatric Press; 1994.
2. Sierra M, Berrios GE. Depersonalization. *Biol Psychiatry.* 1998;44:898-908.
3. Roth M, Argyle N. Anxiety panic and phobic disorder: an overview. *J Psychiatr Res.* 1988;22(suppl 1):33-54.
4. Lader MH, Wing L. *Physiological Measures, Sedative Drugs and Morbid Anxiety.* London, England: Oxford University Press; 1966. Maudsley Monographs No. 14.
5. Lader MH. *The Psychophysiology of Mental Illness.* London, England: Routledge & Kegan Paul; 1975.
6. Kelly DHW, Walter CJS. The relationship between clinical diagnosis and anxiety, assessed by forearm blood flow and other measurements. *Br J Psychiatry.* 1968; 114:611-626.
7. Simeon D, Gross S, Guralnik O, Stein DJ, Schmeidler J, Hollander E. Feeling unreal. *Am J Psychiatry.* 1997;154:1107-1113.
8. Pitman RK, Orr SP, Shalev AY, Metzger LJ, Mellman TA. Psychophysiological alterations in post-traumatic stress disorder. *Semin Clin Neuropsychiatry.* 1999; 4:234-241.
9. McFall ME, Murburg MM, Ko GN, Veith RC. Autonomic responses to stress in Vietnam combat veterans with posttraumatic stress disorder. *Biol Psychiatry.* 1990;15:1165-1175.
10. Roth WT, Wilhelm FH, Trabert W. Autonomic instability during relaxation in panic disorder. *Psychiatry Res.* 1998;80:155-164.
11. Hoehn-Saric R, McLeod DR, Zimmerli WD, Hipsley PA. Symptoms and physiologic manifestations in obsessive compulsive patients before and after treatment with clomipramine. *J Clin Psychiatry.* 1993;54:272-276.
12. Noyes R, Kletti R. Depersonalization in response to life-threatening danger. *Compr Psychiatry.* 1977;8:375-384.
13. Phillips ML, Sierra M, Hunter E, Lambert MV, Medford N, Senior C, David AS. A depersonalisation research unit: progress report. *Psychiatr Bull.* 2001;25: 105-108.
14. Wing JK, Cooper JE, Sartorius NT. *The Description and Classification of Psychiatric Symptoms: An Instruction Manual for the PSE and CATEGO Program.* Cambridge, England: Cambridge University Press; 1974.
15. Sierra M, Berrios GE. The Cambridge Depersonalization Scale: a new instrument for the measurement of depersonalization. *Psychiatry Res.* 2000;93:153-164.
16. Venables PH, Mitchell DA. The effects of age, sex and time of testing on skin conductance activity. *Biol Psychol.* 1996;43:87-101.
17. Lang PJ, Bradley MM, Cuthbert BN. *International Affective Picture System (IAPS): Instruction Manual and Affective Ratings: Technical Report A-4.* Gainesville: Center for Research in Psychophysiology, University of Florida; 1999.
18. Lang PJ. Behavioral treatment and bio-behavioral assessment: computer applications. In: Sidowski JB, Johnson KH, Williams EA, eds. *Technology in Mental Health Care Delivery Systems.* Norwood, NJ: Ablex; 1980:119-137.
19. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry.* 1961;4:561-571.
20. Spielberger CD, Gorsuck R, Lushene RE. *The State-Trait Anxiety Inventory-Y Form.* Palo Alto, Calif: Consultants Psychologists Press; 1977.
21. Cacioppo JT, Tassinary LG, eds. *Principles of Psychophysiology.* Cambridge, England: Cambridge University Press; 1991.
22. Schneider RE, Fowles DC. A convenient, non-hydrating measurement of electrodermal activity. *Psychophysiology.* 1978;15:483-486.
23. Roedema TM, Simons RF. Emotion-processing deficit in alexithymia. *Psychophysiology.* 1999;36:379-387.
24. Lykken DT, Venables PH. Direct measurement of skin conductance: a proposal for standardization. *Psychophysiology.* 1971;8:656-672.
25. Lang PJ, Greenwald MK, Bradley MM, Hamm AO. Looking at pictures: affective, facial, visceral, and behavioral reactions. *Psychophysiology.* 1993;30:261-273.
26. Howard R, Ford R. From the jumping Frenchmen of Maine to post-traumatic stress disorder: the startle response in neuropsychiatry. *Psychol Med.* 1992;22:695-707.
27. Blair RJ, Jones L, Clark F, Smith M. The psychopathic individual: a lack of responsiveness to distress cues? *Psychophysiology.* 1997;34:192-198.
28. Blair RJ. A cognitive developmental approach to morality: investigating the psychopath. *Cognition.* 1995;57:1-29.
29. Friedlander L, Lumley MA, Farchione T, Doyal G. Testing the alexithymia hypothesis. *J Nerv Ment Dis.* 1997;185:233-239.