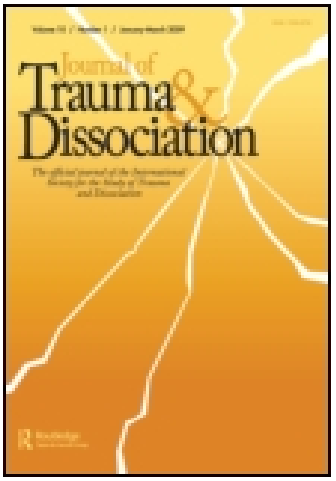

Journal of Trauma & Dissociation
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/wjtd20

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Accepted author version posted online: 27 Jul 2011.Published online: 30 Apr 2012.

To cite this article: Poppy L. A. Schoenberg PhD, Mauricio Sierra MD & Anthony S. David MD (2012) Psychophysiological Investigations in Depersonalization Disorder and Effects of Electrodermal Biofeedback, Journal of Trauma & Dissociation, 13:3, 311-329, DOI: 10.1080/15299732.2011.606742

To link to this article: http://dx.doi.org/10.1080/15299732.2011.606742

Journal of Trauma & Dissociation, 13:311–329, 2012

ISSN: 1529-9732 print/1529-9740 online
DOI: 10.1080/15299732.2011.606742

Routledge
Taylor & Francis Group

Psychophysiological Investigations in Depersonalization Disorder and Effects of Electrodermal Biofeedback

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Previous studies investigating depersonalization disorder (DPD) report a lower baseline skin conductance level (SCL) and attenuated skin conductance response (SCR) to emotive stimuli. We hypothesized that increasing physiological arousal levels via electrodermal biofeedback may ameliorate disembodiment and emotional numbing symptomatology. Real-time versus sham biofeedback yielded a significant SCL increase after just 3 real–time biofeedback sessions in healthy volunteers. Subsequently, a randomized controlled biofeedback trial was administered with DPD patients. Findings were not replicated as SCL tended to fall, curiously more substantially in the real-time condition, concomitant with increased low- and high-frequency heart rate variability. To further investigate abnormal autonomic regulation in DPD, we compared basal autonomic activity between patients and healthy volunteers and found the former to be significantly more labile, indexed by greater nonspecific SCRs and higher resting SCLs. Rather than low sympathetic arousal, DPD might be better characterized by abnormal autonomic regulation affecting emotional and physiological responsivity.

KEYWORDS depersonalization disorder, skin conductance, heart rate variability, biofeedback

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Received 9 September 2010; accepted 27 June 2011.

This study was supported by a Medical Research Council studentship and by A. P. Pilkington Pilozzo Charitable Trusts. The authors would like to thank all of the participants.

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INTRODUCTION

Depersonalization disorder (DPD) remains a poorly understood condition characterized by a chronic and distressing dissociation altering the perception and experience of the self (American Psychiatric Association, 2000). Symptoms are egodystonic and nondelusional in nature, often including emotional blunting, disembodiment, cognitive detachment, and derealization, a pervasive feeling of "unreality." It is frequently intractable, affecting between 1% and 2% of the population, although its comorbidity with depression and anxiety is in the region of 20%–40%. DPD remains unjustifiably neglected within mainstream psychiatry and the rate of misdiagnosis high (Hunter, Sierra, & David, 2004).

Extant neurobiological models (Noyes & Kletti, 1977; Sierra & Berrios, 1998) propose that depersonalization is mediated by a fronto-limbic inhibitory mechanism (Phillips et al., 2001), frequently triggered by threat appraisals and "no-control" feelings, which suppresses emotional experiencing while maintaining hypervigilance. Thus, the process that infuses emotional composition to one's perceptual/cognitive activity diverges, inducing subjective feelings of "unreality" and a lack of emotional ownership. In DPD this state becomes dysfunctional, leading to a constant and distressing sense of detachment and alienation from oneself and one's environment. Sympathetic response has been proposed to be instrumental in feelings of familiarity (Morris, Cleary, & Still, 2008). Therefore, abnormally low skin conductance response (SCR) in DPD may have explanatory power in accounting for particular symptomatology.

Early observations in anxiety showed that the onset of depersonalization frequently coincided with an attenuation in sympathetic activity (Lader & Wing, 1966). Forearm blood flow, a measure of sympathetic autonomic function, showed that DPD patients had significantly lower basal recordings compared to healthy controls and other clinical groups (Kelly & Walter, 1968). Sierra et al. (2002) found that DPD patients had significantly lower basal skin conductance levels (SCLs) compared to clinically anxious controls, despite both groups reporting similarly high anxiety scores. Patients also showed selective attenuation in SCRs to unpleasant pictorial stimuli. Research comparing SCL in DPD and healthy controls concomitant with the presentation of a physiologically arousing scene from a horror movie found that patients exhibited an earlier peak in SCL followed by subsequent flattening that failed to return to baseline levels after termination of the stimulus (Giesbrecht, Merckelbach, van Oorsouw, & Simeon, 2010). Consistent with a dampening mechanism on sympathetic autonomic activity, Simeon, Guralnik, Knutelska, Yehuda, and Schmeidler (2003) found a highly significant inverse correlation between urinary norepinephrine and depersonalization severity ($r = -.88$) in DPD patients.

Similar attenuation of autonomic response has been exhibited in trauma survivors with posttraumatic stress disorder (PTSD) and high peritraumatic

dissociation, who show low physiological reactivity at baseline and during trauma recall compared to those PTSD sufferers with low dissociative comorbidity (Griffin, Resick, & Mechanic, 1997).

Considering these findings suggestive of attenuated sympathetic tone, we tested the hypothesis that electrodermal training aimed at increasing sympathetic tone would have alleviating effects on DPD symptomatology, specifically experiences of emotional blunting and disembodiment. What is interesting is that a study using electromyographic (EMG) biofeedback inducing states of relaxation and hypoarousal reported depersonalization as an unexpected side effect in some participants (LeBoeuf, 1977). Biofeedback aids awareness and control, via visual/auditory real-time feedback, of one's physiology. Its therapeutic efficacy has been demonstrated in a range of psychiatric conditions, including PTSD (Peniston, 1991) and anxiety (D'Amato, 1996). To our knowledge there are no reports of its application in DPD. A secondary aim of this study was to explore a physiological profile of the disorder to investigate further the hypothesis that DPD reflects dysfunction in autonomic arousal.

EXPERIMENT I: PROOF OF CONCEPT STUDY

The few skin conductance (SC) biofeedback studies carried out with psychiatric populations decreased autonomic activity (Denney, Rupert, & Burish, 1983; Pop-Jordanova, 2000; Steinberg & Schwartz, 1976). Thus, a proof of concept study with healthy volunteers was implemented, aimed at establishing whether an increment of increased electrodermal activity was a viable target that could then be implemented in patients with DPD. A secondary outcome measure of this initial study was to ascertain whether increasing SCL would adversely affect anxiety levels.

Method

Sixteen healthy volunteers (6 male, 10 female) took part in a randomized single (participant) blind design. Eight participants (4 male, 4 female) were allocated (via random number tables) to real-time biofeedback, and eight (2 male, 6 female) were allocated to sham (noncontingent). Participants received 3 × 20 min of biofeedback training over 3 weeks. The mean ages of the real and sham groups were 28.3 ± 6.1 and 26.6 ± 5.5 years, respectively (range = 22–42 years).

Biofeedback setup. Biofeedback training was administered using the Nexus-10 physiological monitoring and feedback system (www.mindmedia.nl), detecting changes less than 0.0001 μs (1/1000th resolution). Carbon-coated sensor cables reduced recording artifacts. The apparatus setup consisted of an experimenter laptop connected to a secondary

monitor screen that presented biofeedback. The wireless Nexus system was comported to the experimenter laptop.

Biofeedback consisted of an arcade game interface whereby increases in SCL moved an onscreen Pacman character along a maze. Real-time feedback was directly displayed on the presentation monitor. Sham feedback consisted of a prerecorded sequence, simulating natural fluctuating SC activity, transferred to the presentation monitor while the real-time recording remained on the experimenter laptop. Real-time and sham sessions were conducted using standardized procedures, and the presentation interface was identical for both. The experimenter was very cautious not to disclose any cues pertaining to condition allocation.

Procedure. During sessions, participants were seated in a temperature-regulated room (23 ± 1.0°C) approximately 60 cm from a 15-in LCD computer screen. Two dry Ag/AgCl electrodes were strapped around the distal phalanges of the palmar surface on the index and middle digits of the nondominant hand. Active electrodes were used; thus, no electrolyte or skin preparation was necessary. Blood volume pulse was also recorded by a clip sensor fastened to the middle digit of the opposite hand from the SC electrodes, monitoring relative blood flow via infrared photoplethysmography. Participants were informed that increasing SCL above an indicated threshold would make the character move on the screen.

A baseline phase (5 min) in which participants were instructed to relax with their eyes open was recorded before biofeedback training. During biofeedback a gauge on the screen indicated how far SCL was from a regulated threshold. Initially, this threshold was set by the experimenter on an individual basis, at 0.05 μs above patients' natural settled SCL post-baseline phase. The threshold was then changed manually by the experimenter throughout the biofeedback using the following rules: (a) 30 s above threshold = threshold level increased by 0.05 μs, (b) 30 s below threshold = threshold level decreased by 0.05 μs.

Results

Real-time and sham groups were well matched for age ($F = 0.315$, $p = .58$), sex ($\chi^2 = 9.0$, $p = .34$), and pretrial baseline physiological measures ($F = 0.014$, $p = .91$). All participants completed three biofeedback sessions.

Raw data were divided into baseline (Minutes 2–5), whole (Minutes 5–20), and end (Minutes 17–20) epochs of the 20-min recording for analyses. Within session increment change for each session (end epoch – baseline epoch) showed that participants in the real-time condition appeared to improve performance (increasing SCL) from Session 1 to Sessions 2 and 3. A decline in performance after Session 1 was evident in the sham condition. One-way analyses of variance (ANOVAs) revealed a significantly lower increment change in the sham condition compared to the real-time condition

during Session 2, $F(1, 14) = 12.7$, $p = .003$, and Session 3, $F(1, 14) = 6.40$, $p = .02$. When within-session SCL was converted into percent increment change to account for differences in individual baseline ([end epoch – baseline epoch/baseline epoch] × 100), repeated measures ANOVA (r-ANOVA) revealed a significant main effect of condition over the three sessions, $F(1, 14) = 10.2$, $p = .007$. Post hoc tests showed a significantly lower mean percent increment change during Session 2, $F(1, 14) = 4.99$, $p = .04$, and Session 3, $F(1, 14) = 6.10$, $p = .03$, in the sham compared to real-time condition.

The change in autonomic arousal appeared to be transient as a cumulative increase over the three sessions was not apparent. Mean (*SD*) Session 1 and Session 3 comparisons showed that the real-time group increased SCL from 3.8 μs (3.2) to 5.4 μs (4.2), whereas the sham group SCL yielded a marginal decrease from 3.6 μs (2.8) to 3.4 μs (3.7). No significant main effects of condition or session were found for baseline SCL activity measures (note that baseline SCL was measured at the start of each session). Only three sessions of biofeedback were administered, which may explain the lack of a significant overall baseline change. No significant changes in anxiety were reported pre-to-post biofeedback using visual analogue scales, despite positive correlations between elevated SCL and anxiety (Jensen, Hasle, & Birket-Smith, 1996).

EXPERIMENT II: RANDOMIZED CONTROLLED TRIAL IN DPD

In view of the encouraging findings for Experiment I, an identical protocol was used with DPD patients. It was predicted that any resulting increment in sympathetic tone would have an ameliorating effect on DPD symptoms, particularly those pertaining to bodily awareness and emotional experiencing. Given the transient effects on SCL observed in Experiment I, the number of biofeedback sessions was increased to eight.

Method

Sample and design. Thirty-two patients (24 male, 8 female) with *Diagnostic and Statistical Manual of Mental Disorders* (4th ed., text rev. [*DSM–IV–TR*]; American Psychiatric Association, 2000) DPD (300.6) were recruited from the Maudsley Hospital Depersonalization Disorder Clinic. Diagnosis was ascertained using the Structured Clinical Interview for *DSM–IV* Dissociative Disorders and scores above the 70-point cutoff for the Cambridge Depersonalization Scale (CDS; Sierra & Berrios, 2000). Patients received 8 × 20 min (5 min baseline, 15 min biofeedback) sessions over a 4-week period. The mean ages of the real and sham groups were 36.8 ± 7.7 and 33.8 ± 12.0 years, respectively (range = 19–59 years). Written

informed consent to participate in a patient-blind randomized controlled trial of real versus sham biofeedback (approved by the South London and Maudsley National Health Service (NHS) Trust Ethical Committee) was obtained. Patients were briefed about SC research in DPD and the aim of testing whether increasing SCL would ameliorate symptom intensity. Patients were informed that their participation would contribute toward exploratory investigation of a possible new intervention and were reimbursed for expenses.

Patients with comorbid neurological conditions (i.e., epilepsy, learning difficulties) and current or previous substance and/or alcohol dependence were excluded. Seventeen (51.5%; 8 real, 9 sham) of the whole patient sample were medicated, 14 (42.4%; 8 real, 6 sham) were unmedicated, and 1 patient did not specify. Medications included lamotrigine (6 patients), clonazepam (6), selective serotonin reuptake inhibitor antidepressants (6), sertraline (3), and monoamine oxidase inhibitor antidepressant (1). Medication was stable at least 8 weeks prior to participation, and no changes were made during the trial.

Procedure. The biofeedback setup and experimental procedure were identical to those in Experiment I. In order to structure arousing strategies, we gave patients the following promptings (as in Experiment I): Session 1 = no suggestion; Session 2 = bodily focusing (e.g., trying to increase sensations of heat in one's hands); Session 3 = emotion focusing (e.g., emotionally reliving or imagining emotional situations). When patients could trace the onset of depersonalization symptoms to a particular trigger, we advised them *not* to use this as an emotional focus item to avoid further dissociation; Session 4 = cognitive focusing (e.g., being aware of one's thoughts in the present moment or focusing intently on the SC gauge to rise); Sessions 5–8 = free for individual choice. Patients briefly described what they did during biofeedback after each session to confirm that they were using the provided strategies and attempting to increase SCL.

Clinical measures. The following clinical scales were administered pre-to-post trial and at 3 months follow-up: (a) the CDS (Sierra & Berrios, 2000), (b) the Dissociative Experiences Scale (Bernstein & Putnam, 1986), (c) the Beck Anxiety Inventory (BAI; Beck, Epstein, Brown, & Steir, 1988), and (d) the Beck Depression Inventory (BDI; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961). The CDS State version, a modified version of the CDS whose scores reflect the depersonalization intensity experienced right now, was administered before and after every biofeedback session.

Data preparation and analyses. SC signal was recorded at 128 samples/s. Data preparation was performed using Biotrace+ software from MindMedia Corporation (www.mindmedia.nl). Raw data were segmented into baseline (Minutes 2–5), whole (Minutes 5–20), and end (Minutes 17–20) epochs. The following variables for each session were calculated for statistical analyses: (a) baseline epochs; (b) increment change: within

session change (end epoch – baseline epoch); (c) percent increment change: increment change relative to the individual baseline (end epoch – baseline epoch/baseline epoch × 100); (d) maximum biological range: maximum SCR deflection; and (e) lability: ascertained via visual inspection of the raw recording, identifying any peaks with >0.05-μs amplitude within a 0- to 3-s latency window. Mean lability score comprised nonspecific peaks per minute, derived from the 3-min baseline epoch. An overall pre- versus posttrial comparison was also done: Session 1 baseline epoch versus Session 8 end epoch.

Heart rate values below 40 beats and above 240 beats per minute, and peaks that had a difference greater than 30 beats per minute compared to the last detected beat, were defined as artifact and discarded. Heart rate was computed from the interbeat interval at 128 per second sampling rate. Heart rate variability (HRV) was analyzed by means of frequency domain spectral analysis ascertained by Fast Fourier Transform on the interbeat interval time series. *Low-frequency (LF) and high-frequency (HF) bandwidths* were defined as follows: LF = 0.04–0.15 Hz, HF = 0.15–0.4 Hz. Only whole-session epochs were used for statistical analyses (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). Data for the eight sessions were divided into temporal contrasts for statistical analyses: (a) *time* = first versus last session: used to analyze overall SC change, lability, and clinical ratings; (b) *phase* = early (mean for Sessions 1–4), late (mean of Sessions 5–8): used for all other physiological measures and CDS State scores.

Statistical analyses. Condition (real, sham) × Phase (early, late) r-ANOVAs were carried out for SCL: (a) baseline epochs, (b) increment change, (c) percent increment change, (d) maximum SCR, and (e) lability. A Condition (real, sham) × Time (pre = Session 1 baseline epoch, post = Session 8 end epoch) r-ANOVA was performed for the SCL first versus last session comparison. Main analyses for HRV data included a Condition (real, sham) × Phase (early, late) r-ANOVA for (a) HRV LF spectra, and (b) HRV HF spectra. Analyses for psychological data included a Condition (real, sham) × Time (pretrial score, posttrial score) r-ANOVA for (a) CDS Trait version, (b) Dissociative Experiences Scale, (c) BDI, and (d) BAI. The CDS State version was analyzed via Condition (real, sham) × Phase (early, late) r-ANOVA. Greenhouse-Geisser corrections were applied when the assumption of sphericity was violated for all ANOVAs. Follow-up analyses included one-way ANOVA and paired *t* tests investigating post hoc between- and within-condition effects, respectively.

Results

Real and sham groups were well matched for age ($F = 0.681$, $p = .42$), sex ($\chi^2 = 0.667$, $p = .41$), duration of illness ($F = 0.575$, $p = .39$), and medication status ($\chi^2 = 0.313$, $p = .58$). SC and HRV physiological data

are presented in Table 1. Clinical measures are presented in Table 2. Two patients (1 male, 1 female) dropped out of the sham condition.

Baseline SCL. A significant Condition × Phase interaction, $F(1, 25) = 4.47$, $p = .05$, showed decreasing baseline SCL means in the real-time condition, $t(15) = 2.79$, $p = .01$, for the latter four sessions compared to the former four (16.4 μs [$SD = 15.7$] falling to 8.4 μs [$SD = 6.9$]), which was not evident in the sham (see Table 1). Overall first versus last session SCL change across the trial reflected a significant main effect of time, $F(1, 25) = 4.49$, $p = .04$, with the real-time condition yielding a significant decrease, not increase, in SCL posttrial, $t(15) = 2.88$, $p = .01$ (see Table 1).

SC increment change. It was predicted that the ability to increase SCL would improve over the trial, as reflected by greater within-session increment change. A main effect of phase, $F(1, 27) = 9.03$, $p = .006$, indicated a general reduction in increment change from the early to the late phase of the trial. The Condition × Phase interaction was not significant, but exploratory within-condition t tests indicated that the decline in performance during the later phase, $t(12) = 2.96$, $p = .02$, was greater in the sham group. Taking percent increment change relative to baseline (end epoch – baseline epoch/baseline epoch × 100), a significant main effect of phase, $F(1, 27) = 4.24$, $p = .05$, again reflected a reduction in performance from the early to the late phase of the trial. No significant main effects of condition or Condition × Phase interactions were found (see Table 1).

Maximum SCR (biological range) and lability. No significant main effects or interactions in biological range, indexed by maximum SCR deflection, were found. However, exploratory t tests indicated a reduction from the early to the late phase of the trial, $t(15) = 2.57$, $p = .02$, in the real-time condition, supporting the declining SCL findings. A main effect of time, $F(1, 27) = 9.34$, $p = .005$, for lability (nonspecific SCRs) from pre-to-post measures (baseline epochs for Sessions 1 and 8, respectively) reflected declining nonspecific SCRs across patients but more marked in the real-time condition, $t(15) = 2.26$, $p = .04$. These findings are in line with those on maximum SCR (see Table 1).

HRV. Vagal tone indexed by the HF HRV spectra during biofeedback showed a significant Condition × Phase interaction, $F(1, 27) = 6.91$, $p = .01$, reflecting an increase in HF bandwidth for the real-time condition, $t(15) = -1.77$, $p = .09$, and a significant decrease in the sham, $t(12) = 2.27$, $p = .04$. The LF spectra, mediated by both sympathetic and parasympathetic branches, also showed a significant Condition × Phase interaction, $F(1, 27) = 10.5$, $p = .003$, reflecting an increase in the LF bandwidth for the real-time condition, $t(15) = -2.34$, $p = .03$, and a decrease in the sham, $t(12) = 2.89$, $p = .01$ (see Table 1).

Depersonalization symptomatology. CDS Trait scores showed that neither the real-time nor sham condition yielded a significant change in depersonalization symptoms globally. Comparing CDS State scores, completed

TABLE 1 Patient SCL and HRV

	Real ($n = 16$) $\bar{X}$ (σ)			Sham ($n = 16$) $\bar{X}$ (σ)			
Physiological variable	Early	Late	Comparison	Early	Late	Comparison	Interaction
Mean baseline SCL (μs)	16.4 (15.7)	8.4 (6.9)	$p = .01^{**}$	16.3 (9.9)	16.6 (14.9)	$p = .90$	$p = .05^{*}$
SCL increment change (μs)	4.7 (8.3)	2.3 (2.9)	$p = .21$	7.6 (8.3)	0.9 (10.0)	$p = .02^{*}$	$p = .17$
Maximum SCR (μs)	50.0 (25.5)	33.0 (18.4)	$p = .02^{*}$	46.8 (25.8)	44.4 (33.3)	$p = .80$	$p = .19$
HRV FFT LF (ms^2)	3546 (2956)	5631 (4094)	$p = .03^{*}$	4332 (3404)	2899 (2436)	$p = .01^{**}$	$p = .003^{**}$
HRV FFT HF (ms^2)	1427 (1274)	2008 (1448)	$p = .09$	1488 (1200)	969 (951)	$p = .04^{*}$	$p = .01^{**}$
	Pre	Post	Comparison	Pre	Post	Comparison	Interaction
SCL pre vs. post comparison (μs)	20.8 (23.5)	9.7 (15.1)	$p = .01^{**}$	21.0 (20.0)	16.7 (17.4)	$p = .53$	$p = .34$
SC lability (peaks per min)	10.7 (10.0)	6.9 (8.3)	$p = .04^{*}$	10.3 (6.1)	6.7 (5.1)	$p = .06$	$p = .72$

Notes: SCL = skin conductance level; HRV = heart rate variability; SCR = skin conductance response; FFT = Fast Fourier Transform; LF = low frequency; HF = high frequency; SC = skin conductance.
$^{*}p < .05$; $^{**}p < .01$.

TABLE 2 Patient Clinical Scales

	Real ($n = 16$) $\bar{X}$ (σ)			Sham ($n = 16$) $\bar{X}$ (σ)		
Clinical scale score	Session 1	Session 8	3-month follow-up	Session 1	Session 8	3-month follow-up
CDS Trait	110.2 (39.9)	113.2 (47.4)	112.8 (51.8)	120.6 (43.8)	123.4 (37.1)	139.4 (53.4)
DES	24.6 (15.9)	23.5 (13.3)	23.4 (13.2)	27.4 (9.8)	24.0 (7.7)	29.8 (11.7)
BDI	15.1 (9.5)	14.9 (7.4)	14.3 (7.4)	20.7 (8.5)	22.2 (9.9)	23.2 (8.8)
BAI	11.1 (6.8)	13.3 (8.7)	13.9 (10.4)	17.1 (6.1)	17.4 (7.2)	18.4 (10.8)
			Comparison			Comparison
CDS State ABE	32.4 (19.3)	25.5 (21.1)	$p = .02^{*}$	32.9 (18.7)	26.3 (15.8)	$p = .05^{*}$
CDS State EN	33.6 (16.4)	26.4 (19.0)	$p = .02^{*}$	29.8 (16.4)	30.2 (16.4)	$p = .43$
	Early	Late	Comparison	Early	Late	Comparison
CDS State	36.0 (16.9)	29.9 (18.9)	$p = .01^{**}$	30.5 (14.7)	31.8 (14.9)	$p = .63$
CDS State EN	33.7 (15.8)	29.8 (20.0)	$p = .12$	28.3 (15.4)	30.1 (16.6)	$p = .73$
CDS State ABE	33.4 (20.2)	27.4 (21.5)	$p = .03^{*}$	30.3 (16.6)	31.2 (17.6)	$p = .78$

Notes: CDS = Cambridge Depersonalization Scale; DES = Dissociative Experiences Scale; BDI = Beck Depression Inventory; BAI = Beck Anxiety Inventory; ABE = anomalous body experience; EN = emotional numbing.
$^{*}p < .05$; $^{**}p < .01$.

immediately after every session of biofeedback, a main effect of time, $F(1, 27) = 6.38$, $p = .02$, and Time × Condition interaction, $F(1, 27) = 4.11$, $p = .05$, showed a significant decrease in depersonalization symptoms when analyzed by the phase contrast (36.0 [*SD* = 16.9] falling to 29.9 [*SD* = 18.9]) for the real-time condition only, $t(15) = 2.84$, $p = .01$ (see Table 2).

Exploring whether biofeedback specifically targeted disembodiment and emotional numbing symptoms, we found that the State CDS anomalous body experience (ABE) subscale scores showed a main effect of time (pre, post), $F(1, 23) = 12.5$, $p = .002$, reflecting a significant decrease in experienced ABE in both the real-time, $t(14) = 2.65$, $p = .02$, and sham, $t(9) = 2.27$, $p = .05$, conditions. No main effect of condition or Condition × Time interaction was found. The State CDS emotional numbing (EN) subscale scores also revealed a significant main effect of time, $F(1, 24) = 5.01$, $p = .04$, and no main effect of condition or Condition × Time interaction. However, within-group analysis showed that EN significantly decreased in the real-time condition, $t(14) = 2.26$, $p = .02$, and marginally increased in the sham condition pre- to posttrial (see Table 2). No significant change in ABE or EN scores were found for the Trait CDS.

Mood. BDI (depression) scores were significantly higher in the sham condition—main effect of condition, $F(1, 21) = 4.17$, $p = .05$—compared to the real-time condition, whose scores fell marginally, although the Time × Condition interaction was not significant. No significant changes in BAI (anxiety) scores were found (see Table 2).

Autonomic comparison: Patients versus controls. Patients displayed higher autonomic activity compared to healthy controls (see Figure 1).

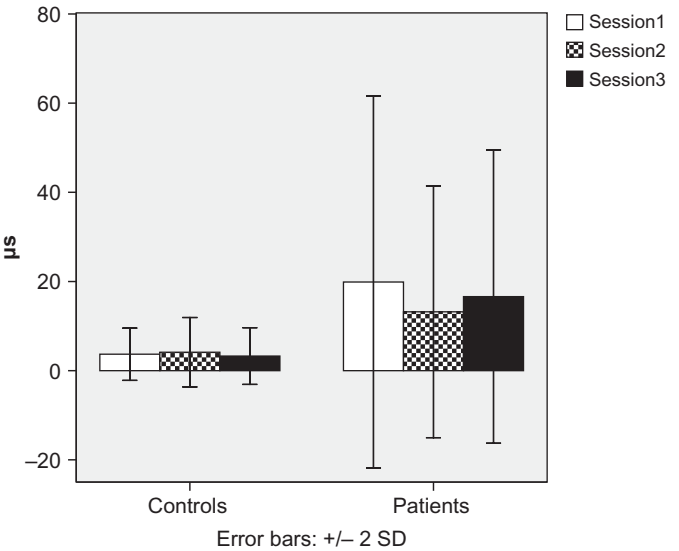

FIGURE 1 Baseline skin conductance level for the first three sessions: patients versus healthy controls.

A series of Group (patient, control) × Session (biofeedback Session 1, 2, 3) r-ANOVAs (age/sex covariates) showed significant between-group effects for baseline SCL, $F(1, 42) = 9.25$, $p = .004$; SCL during biofeedback, $F(1, 42) = 11.12$, $p = .002$; SCL increment change, $F(1, 41) = 4.93$, $p = .03$; SCL percent increment change, $F(1, 41) = 25.58$, $p < .0001$; and maximum SCR, $F(1, 42) = 28.99$, $p < .0001$; with controls yielding consistently lower SC measures. Univariate ANOVA (age/sex covariates) comparing pretrial (Session 1 baseline) lability found patients considerably more labile (greater nonspecific SCRs) than controls, $F(1, 46) = 11.5$, $p = .001$. Between-group effects were not significant for heart rate measures, suggesting that pretrial differences were specific to sympathetic autonomic nervous system activity.

DISCUSSION

This study set out to explore autonomic tone in DPD patients. To our knowledge this is the first study aiming to increase autonomic sympathetic tone in DPD via electrodermal biofeedback as a potential therapeutic intervention. The initial proof of concept study with healthy volunteers showed that those receiving real biofeedback (as opposed to sham) had an overall SCL increase of 42% during the trial. Contrary to expectations, these findings were not replicated with DPD patients. Those receiving real-time biofeedback showed a 25% reduction in SCL across the trial. DPD patients were found to have unusually high resting SCL, more typical of anxiety (Cacioppo & Tassinery, 1990), compared to healthy controls (16.1 μs [$SD = 17.0$] vs. 3.7 μs [$SD = 3.3$], respectively). A recent study also found that depersonalized patients yielded significantly higher resting SCL compared to controls (5.5 μs vs. 2.8 μs, respectively; Giesbrecht et al., 2010). Furthermore, we found that patients had significantly more nonspecific SCRs than healthy controls (10.5 [$SD = 8.3$] vs. 3.3 [$SD = 3.1$], respectively), suggesting abnormally high sympathetic lability (Jensen et al., 1996). The BAI scale scores of our patient sample were in the moderate anxiety range. The fact that patients exhibited an electrodermal profile more typical of anxiety than dissociation suggests a complex interaction between the neurobiological underpinnings of anxiety and dissociation mechanisms.

Consequently, biofeedback appeared to have a homeostatic downregulating effect on significantly high autonomic levels in DPD patients, despite efforts to increase sympathetic arousal further, perhaps explained by a ceiling effect engendering extended increment change difficult. Similarly, PTSD patients displaying autonomic hyperarousal at baseline have been found to be unable to marshal extended autonomic responses to trauma-related cues (Cohen et al., 1998).

Biofeedback training showed minimal effects on trait depersonalization (CDS) symptoms, although the Trait CDS may not have been sensitive to symptom change over the 8-week period. However, a significant reduction in State CDS scores was found in the real-time condition only, specifically pertaining to disembodiment and emotional numbing, suggesting that the reduction of abnormally high SCL had a mild, self-limited ameliorating effect on dissociative experience.

Psychophysiological Profile of DPD

The majority of studies reporting abnormally low sympathetic arousal in DPD have focused on SCR as opposed to tonic measurements. The contribution of our results presents the hypothesis of a demarcation within physiological modulation in DPD whereby tonic or basal SC activity is apparently heightened while phasic response (SCRs) to specific stimuli is dampened, reflecting a separation or split in sympathetic/adrenergic functioning. Furthermore, elevated tonic SCL may explain cognitive hypervigilance, observed in biological introverts, for example, who are also autonomically labile (Cacioppo & Tassinery, 1990), whereas attenuated SCRs possibly underpin blunted emotional response in the disorder. This distinction may be important in view of the evidence suggesting that tonic (SCL) and phasic (SCR) components of autonomic electrodermal activity are mediated by differing neural networks (Nagai, Critchley, Featherstone, Trimble, & Dolan, 2004). Investigations in autonomic functioning in anxiety (Jensen et al., 1996) and depression (Mirkin & Coppen, 1980) have reported that patients' SCL and SCR corresponded to either hyperactivity or hypoactivity, respectively, supporting further a theorization of incongruence in tonic and phasic electrodermal components in DPD.

A study using event-related functional magnetic resonance imaging concomitant with SC measures compared neural responses in DPD patients versus healthy controls simultaneous with viewing varied intensities of facial expressions of happiness/sadness (Lemche et al., 2007). No significant differences were found in SCR between the two groups. However, a negative correlation was evident in the DPD patients between activity in a region (BA 9) of the dorsolateral prefrontal cortex previously implicated in emotion regulation and SCRs, suggesting an inhibitory mechanism on electrodermal response. A fronto-limbic suppressive mechanism in DPD was further supported, as patients showed decreased activity in the amygdala and hypothalamus that was greater with increased emotional expression. Healthy controls exhibited an opposite pattern. Thus, an emerging theory is that the observed attenuation on autonomic activity in depersonalization is neither generalized nor absolute but appears to be emotion specific and relative to anxiety levels. It seems plausible to hypothesize that sympathetic

autonomic activity in DPD reflects two opposing mechanisms: one excitatory and determined by anxiety and one inhibitory and determined by dissociation. PTSD studies also support the idea that anxiety and dissociation influence autonomic responses in opposing directions. PTSD patients with high comorbid dissociation display blunted autonomic physiology, whereas those with low dissociation present hyperactive physiology similar to anxiety (Griffin et al., 1997; Lanius, Bluhm, Lanius, & Pain, 2006).

Both real and sham conditions yielded declining SCL, whereas the two biofeedback conditions yielded differing parasympathetic activity patterns. Namely, increases in HF and LF components of HRV spectral analysis in the real-time condition contrasted with decreases in HF and LF in the sham condition, reflecting continued sympathetic influence on the vagus nerve and heart. These findings are interesting in light of a novel phylogenetic model of the autonomic nervous system proposed to encompass three distinct functional subsystems, each mediating differing adaptive behavioral strategies involving specific emotional and visceral responses (Porges, 2003). These subsystems are structured as a phylogenetic hierarchy. The most archaic, the dorsal-vagal complex, is a parasympathetic subsystem composed of unmyelinated, slow-conducting vagal fibers originating in the dorsal vagal motor nucleus of the brainstem, triggering "immobilization" reflected by physiological and behavioral shutdown in response to threat/stress (Porges, 2003). Relevant to depersonalization, it has been suggested that dissociative responses characterized by emotional detachment and sympathetic hypoarousal may represent predominant activation of this system (van der Hart, Nijenhuis, Steele, & Brown, 2004), although to our knowledge this proposal has yet to find empirical support. Next in phylogenetic ascendancy is the sympathetic adrenal complex, which triggers flight/fight defensive strategies upon threat appraisal. Finally, the most evolved is a vagal subsystem composed of fast-response, myelinated fibers originating in the ventral brainstem nuclei (nucleus ambiguus). This ventral-vagal complex (VVC) suppresses defensive responses, promoting social behavioral engagement via self-calming and self-soothing mechanisms. It is proposed to also be under cortical regulation with a predominant afferent component (Porges, 2003), where its major functional role is to provide fast-acting tuning of the heart rate by means of a brake-like inhibitory mechanism on both the intrinsic activity of the sinoauricular pacemaker of the heart and sympathetic adrenal activity (Grossman & Taylor, 2007). Respiratory sinus arrhythmia (RSA), captured by the HF HRV spectra, provides an index of the vagal brake, reflecting natural periodic change in heart rate synchronized with the breathing cycle. This polyvagal model proposes that the VVC mediates a social engagement system that becomes degraded in situations of perceived danger (Porges, 2003). Conversely, in situations perceived as safe, the VVC downregulates the expression of both the dorsovagal and sympathetic defensive systems. In keeping with this, it has been

found that individuals with low vagal tone, measured by RSA, are characterized by high psychological defensiveness, indexed by social desirability and self-regulation scales (Movius & Allen, 2005).

Although previous studies exploring autonomic activity in depersonalization have focused on the sympathetic system, our results suggest consideration of the involvement of the vagal subsystems for future research. In particular, relatively low sympathetic activity in DPD may not be as primary as previously theorized, instead reflecting selective activation of an emotional disengagement strategy driven by the dorsal-vagal complex and associated with underactivation of the social engagement system (VVC). What is interesting is that PTSD and borderline personality disorder, two conditions for which research had focused primarily on the sympathetic system with equivocal findings, are more reliably characterized by poor RSA in response to emotional challenge (Austin, Riniolo, & Porges, 2007; Sahar, Shalev, & Porges, 2001). However, it should be noted that when we compared patient versus healthy control pretrial physiological data, only SC (sympathetic) measures differed significantly. In line with the polyvagal model, if DPD patients are indeed activating a defensive autonomic strategy, lower HF HRV (VVC social engagement system activity) would be expected in patients compared to healthy controls, which was not apparent in our study findings.

It is plausible that real-time biofeedback contributed to generate an implicit experience of self-efficacy and control that may have activated the VVC, accounting for significant increases in HF HRV found in the real-time group only across the trial (see Figure 2) in addition to the transient

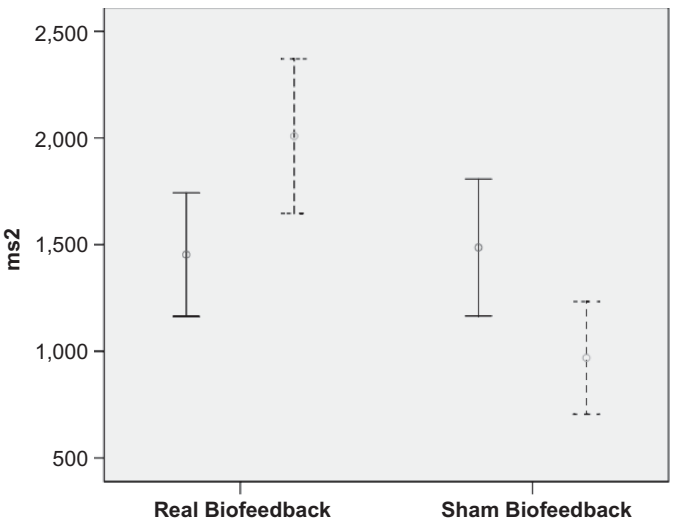

FIGURE 2 Heart rate variability high-frequency spectra in depersonalization disorder patients: early (solid) to late (dotted) phases of the trial.

therapeutic effects observed after biofeedback. In this regard, increases in RSA have been associated with focused attention and enhanced self-regulation, such as a decline in negative emotion during stress and more effective capabilities for coping with stress (Segerstrom & Solberg-Nes, 2007). A biofeedback-induced enhanced perception of control is likely to have been implicit and unconscious. For example, it has been postulated that a putative safety-monitoring mechanism is carried out constantly by unconscious, subcortical mechanisms in limbic-related regions. Furthermore, autism spectrum disorders, characterized by low RSA, show interventions aimed to implicitly generate feelings of safety (e.g., a story being read by a familiar person rather than a stranger), familiarity, and self-control (Thompson, Thompson, & Reid, 2010; Van Hecke et al., 2009) elicit significant increments in vagal tone, clinical improvement, and improved efficiency in the recognition of emotional facial expressions (Bal et al., 2010).

Study Limitations

Although half of the patients were on various medications, which can affect autonomic response, both conditions had similar proportions of medicated and nonmedicated patients, and statistical analysis did not find medication status a significant confound.

There was a preponderance of men in the patient group compared to the control group. Although differences in age/sex may have introduced biases, they do not account for the SCL discrepancies between patients and controls, given that significant between-group effects were still evident after covarying for age/sex. Furthermore, women are reported to have higher electrodermal activity (Cacioppo & Tassinery, 1990). Thus, any bias introduced by the preponderance of men would likely have been in the opposite direction (i.e., low SCL).

The experimenter was not blind to patient allocation. It is theoretically possible that non-explicit clues as to the biofeedback condition were inadvertently revealed, potentially affecting results. However, this is unlikely, as the experimenter–patient interactions were highly structured and standardized.

Summary

The driving hypothesis of this study was that apparent sympathetic underarousal in DPD may benefit from trained increases in sympathetic activity. However, our results suggest that such a mechanical view of DPD, based on a unitary concept of arousal, may be too simplistic and narrow. Our unexpected findings point to a broader autonomic involvement extending to vagal subsystems, thought to be functionally regulated by ongoing assessments of safety and control. This new physiological understanding, which

is in keeping with extant psychological views of depersonalization (Hunter et al., 2004; Sierra & Berrios, 1998), may lead to developing more effective psychophysiological interventions.

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