Physiological Correlates of Emotion Regulation in Depersonalization Disorder

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by

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Abstract

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by

Kai-Mosadi Monde

Advisor: Professor Victoria Luine

Depersonalization disorder (DPD), is an often debilitating DSM V psychiatric disorder characterized by feelings of detachment from the self or others as well as emotional blunting or numbness. Subjective and physiological evidence of decreased emotional arousal may suggest impaired emotion regulation abilities. Deficits in emotional processing of DPD may be the result of dysregulated cortisol and oxytocin levels, however oxytocin levels have never been assessed in DPD. In this series of studies, we aimed to investigate the physiological correlates of emotion regulation in depersonalization disorder. In experiment 1, DPD patients and a normal control group subjectively enhanced and suppressed emotion to affective pictures. Compared to the control group, the DPD group tended to be better at suppressing emotion to unpleasant pictures and tended to modulate subjective arousal less effectively. In experiment 2, we measured heart rate and skin conductance response while DPD patients and a healthy control group enhanced and suppressed emotion to affective stimuli. DPD patients were better able to suppress and less able to enhance emotion (heart rate). In experiment 3, we investigated the relationship between cortisol and oxytocin responsivity during the Trier Social Stress Test (TSST) in DPD. The TSST induced subjective stress in the normal control group but not in the DPD group. The control
group also demonstrated a positive association between post-stress cortisol and decrease in oxytocin during the 20 minute stress recovery period, an association not found for the DPD group. However, the DPD group had higher overall cortisol levels and tended toward higher oxytocin levels. In experiment 4, we explored the relationship between cortisol, oxytocin, and depersonalization during recall of a personally relevant stressful event by Psychology 100 course students. Consistent with experiment 4, post-stress cortisol was associated with a decrease in oxytocin during stress recovery. However, depersonalization was associated with less decrease in oxytocin during stress recovery. Taken together, these results suggest emotional blunting in DPD is accompanied by a superior ability to suppress emotion and dysregulated hormonal responses. DPD patients may benefit from pharmacological interventions that regulate cortisol and oxytocin levels and therapeutic interventions that support enhancing emotion subjectively and physiologically.
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Introduction

The aim of these studies is to investigate the neurobiological underpinnings of emotion regulation in depersonalization disorder. Further elucidation of the neural and chemical mechanisms which underlie detachment and emotional blunting in DPD will improve our ability to develop therapeutic treatments that ameliorate these symptoms.

Overview of Depersonalization Disorder

Symptomology

Dissociative disorders are DSM IV psychiatric disorders which comprise disruptions in memory, awareness/consciousness, identity, or perception, all of which are psychological functions that are typically integrated in healthy individuals (American Psychiatric Association, DSM IV-TR, 2000). However, persons diagnosed with these disorders have intact reality testing. The DSM IV classifies five dissociative disorders which include dissociative identity disorder, dissociative fugue, dissociative amnesia, depersonalization disorder (DPD) and dissociative disorder, not otherwise specified. DPD represents a disruption in the integration of self-perceptions with the sense of self (Simeon, 2004). Depersonalized individuals feel detachment from themselves or others, and describe feeling as if they are outsiders in their own mental processes or bodies. Persons with depersonalization disorder feel as if they are in a dream, movie, or fog, or feel disconnected from their body, and/or feel like they are on autopilot. Other components of the depersonalization experience include a sense of emotional numbing or bluntness as well as somatosensory distortions (Sierra and Berrios, 2001). Depersonalization disorder is often accompanied by derealization—feeling detached from one’s surroundings (people and objects) or feeling that known surroundings are actually unfamiliar (Simeon, 2004). DPD
patients also present with high incidence of alexithymia, specifically difficulty identifying feelings (Simeon, Giesbrecht, Knutelska, Smith, & Smith, 2009). Brief experiences of depersonalization and transient depersonalization in response to severe trauma (e.g., accidents or assault) are common in the general population. However, persistent or recurrent depersonalization in conjunction with significant distress or impairment would be classified as DPD barring the concurrent presentation of other conditions such as epilepsy, head trauma, hallucinogen persisting perception disorder, schizophrenia, etc.

DPD is often accompanied by difficulty in focusing. Neuropsychological testing has demonstrated impairments in attention, short-term visual and verbal memory, and spatial reasoning while long term memory appears intact (Guralnik, Schmeidler, & Simeon, 2000). Somatosensory distortions often reported by DPD patients include such symptoms as subjective flattening of the 3 dimensional visual-perceptual world into two dimensions (Sierra and Berrios, 2001) which may contribute to the disruptions in attention and memory (Simeon, 2004).

Depersonalization disorder is underdiagnosed for the following reasons: 1. DPD is often comorbid with anxiety and mood disorders and treatment often focuses on ameliorating those symptoms without addressing the depersonalization and derealization. 2. Many clinicians are unfamiliar with the symptomology of the disorder; the average length of time a patient seeks treatment before receiving a diagnosis of DPD is 8 years (Simeon, Knutelska, Nelson, & Guralnik, 2003). 3. Many patients do not disclose of their symptoms of depersonalization for fear of being considered crazy or misunderstood (Simeon, 2004). However, consistent with other well-known disorders, prevalence of DPD ranges from 40% to 80% of psychiatric inpatient population (Brauer, Hauer, & Tucker, 1970; Hunter, Sierra, & David, 2004) and 1% to 2.4% in the general population (Ross, Joshi, & Currie, 1991; Hunter, Sierra, & David, 2004), rates
comparable to those of schizophrenia and bipolar disorder. Although often comorbid with mood and anxiety disorders, unlike these disorders which affect more women than men, the gender ratio for DPD is about 1:1 (Simeon et al, 2003; Baker, Hunter, Lawrence, et al., 2003). There is also high comorbidity of depersonalization disorder with personality disorders like borderline, avoidant, and obsessive-compulsive personality disorders (Simeon et al., 2003).

Etiology

As early as the 1800’s and 1900’s, theorists like Charcot and Janet had hypothesized that individuals with a predisposition for dissociation who were exposed to trauma could develop a dissociative disorder (Hart & Worst, 1989). Later, Bowins (2004) described dissociative states as evolutionarily adaptive, beneficial to the organism in milder states, but maladaptive when they begin to interfere with daily function. Still others have theorized that dissociation is a defense mechanism employed to deal with overwhelming stress and trauma. In fact, trauma, and specifically, childhood trauma may be one risk factor for the development of depersonalization disorder (DPD). DPD patients report a high incidence of childhood interpersonal trauma with emotional abuse and neglect being most prevalent, however, physical and sexual abuse and physical neglect have also been reported (Simeon et al., 2001). However, later-life traumatic events and interpersonal stressors can also trigger DPD or further exacerbate milder forms of the disorder (Simeon et al., 2004) Hence, Sierra (2008) hypothesized that depersonalization may be a pervasive inhibitory cognitive and physiological response to chronic stress.

Onset of DPD may be acute or deliberate with typical DPD onset occurring in adolescence (Simeon et al, 2003), and early onset associated with greater symptom severity (Baker et al., 2003). Acute onset may be in response to a severe stressor or trauma, in
conjunction with onset of another disorder such as panic disorder or depression (when the other disorder subsides but depersonalization persists, a diagnosis of DPD is considered), in conjunction with consumption of a controlled substance, or with no apparent precipitating factor. However, for deliberate onset, clear memory of precipitating factors or incidents may not be available often because onset was too early in development to recall the antecedents (Simeon, 2004). Acute onset of DPD with a temporal association of chemical use like marijuana, hallucinogens and ecstasy suggest that drug use may trigger depersonalization disorder in some cases (Simeon et al., 2003). Simeon (2004) proposed that the effects of these substances which alter self-perception are interpreted as a trauma by the predisposed individual and trigger depersonalization. Simeon also posited that these drugs may interfere with neurochemical systems of individuals with a predisposition for depersonalization, and specifically trigger the disorder biologically. Notably, ketamine and cannabinoids like marijuana are NMDA receptor antagonists and have been shown to induce symptoms of depersonalization in laboratory settings (Curran & Morgan, 2000; Szymanski, 1981).

In about one-third of patients, DPD is episodic and can last hours, days or months, however the disorder can eventually become continuous, possibly with varying intensities over time (Simeon et al, 2003; Baker, Hunter, Lawrence, et al., 2003). DPD can be accompanied by severe distress and impairment. The difficulty in focusing, the feelings of being detached from the self or others, and the emotional blunting and numbness complicate, and in severe cases, impede work and interpersonal relationships (Simeon, 2004).

*Emotion Regulation in DPD*

*Emotions and Emotion Regulation Defined*
Emotions arise in response to salient cues in the environment. Emotional responses can occur immediately or only after meaning has been deducted from a situation (Gross, 2002). Humans have evolved to utilize emotions to appraise physical and psychological threat and then devise a response to the threat that is deemed most advantageous (e.g., fight, flight, or freeze). Although, our emotional responses are typically appropriate given our life circumstances, there are instances when our emotionality does not coincide with the situation. Dysfunctional emotional responsivity occurs when our emotions are inappropriate for a situation and evidenced by how we experience them internally (subjective emotionality) or how and when we are display them (projective emotionality, which may include observed physical behavior as well as physiological responses). However, subjective and projective emotionality are not mutually exclusive; how we feel often corresponds with or even dictates what we do. Extreme examples of displayed dysfunctional emotionality are demonstrated by psychiatric disorders such as schizophrenia: positive symptoms of schizophrenia like hallucinations can present with inappropriate laughter while negative symptoms like flat affect may present in response to sad news. An example of experienced dysfunctional emotionality is evident in persons who experience alexithymia, which encompasses an inability to identify or describe emotions. Other psychiatric conditions are marked by variations in the magnitude of emotional responsivity. While borderline personality disorder is known for extreme and abrupt shifts in and exasperated presentation of both projective and subjective emotionality, symptoms of schizoid personality disorder include emotional coldness or apathy (see American Psychiatric Association, DSM IV-TR, 2000). These differences in emotional responsivity and emotional intensity have been documented with physiological correlates both centrally (e.g., brain activity) and peripherally (e.g., skin conductance response, heart rate measures, plasma and salivary hormone levels).
The limbic brain comprising the emotion centers of the brain was theorized to be one of the earliest clusters of brain structures to evolve in humans. Its purpose is to manage fight, flight, or freeze circuitry which is an evolutionary necessity for organisms in the presence of threatening stimuli (Newman & Harris, 2009). In humans, the structures of the limbic system include the hippocampus (associated with memory formation), the amygdala (associated with fear and pleasure) the insula (associated with disgust), the cingulate gyrus (associated with autonomic functions), the nucleus accumbens, associated with pleasure and reward, the hypothalamus (associated with hormone regulation), and the fornix, which connects the hippocampus to the hypothalamus, the thalamus (relays signals between brain structures as well as the spinal cord). Limbic structures are innervated by cortical structures which in turn regulate limbic activation and facilitate sensory integration. The complex interplay of neurochemical changes in these brain structures is perceived cognitively by the individual as emotion, often eliciting specific behaviors.

When our emotions are inappropriate for a given situation, we try to regulate them, curtailing our emotional responses so that they better fit the current setting (e.g., we suppress laughing at a funny incident that occurs spontaneously during a funeral, we enhance our excitement while watching our child’s favorite cartoon with them, and we try to maintain enthusiasm for an interesting lecture that goes too long). The ability to accurately perceive, name, and regulate emotions so that they are appropriate given the situation is key to mental wellbeing. Gross (2002, p. 282) defines emotion regulation as “changes in the latency, rise time, magnitude, duration, and offset of responses in behavioral, experiential, or physiological domains.” Emotion regulation strategies can be conscious or unconscious, and no strategy works for all people in all situations.
Particular emotion regulation strategies may be utilized throughout the emotion generative process. Gross (2002) distinguishes between antecedent-focused and response-focused strategies. Antecedent-focused strategies are those employed prior to full activation of the emotional response. They include situation selection (approaching or avoiding people or situations in order to regulate emotions), situation modification (also known as problem-focused coping: tailoring the situation in order to regulate emotions), attentional deployment (focusing on or distracting oneself from specific aspects of the situation in order to regulate emotion), and cognitive change (also known as reappraisal: deciding the meaning of a situation or changing one’s outlook prior to full onset of the emotion). Response-focused strategies involve response modulation: changing the emotional response after an emotion has been elicited. Response modulation can affect experiential (subjective), behavioral, and physiological components of emotion.

Antecedent-focused and response-focused strategies can affect subjective and projective emotionality differently. Gross (1998) found that while the antecedent-focused strategy of cognitive reappraisal to down-regulate emotions decreases subjective emotion, emotion-expressive behavior, and physiological responsivity (heart rate, temperature, and skin conductance), using the response-focused strategy of suppression (controlling ones outer appearance so that others cannot detect your emotion) decreases emotion-expressive behavior but increases subjectively experienced emotion and physiological responsivity. Additionally, compared to reappraisal, emotional suppression was associated with decreased memory for situation details and was generally associated with reported poorer social support, social support coping, and social likability (Gross, 2002).
There may be sex differences in emotion regulation ability. For instance, McRae et al. (2008) administered a cognitive reappraisal task to participants while they underwent functional magnetic resonance. The authors found that compared to women, men showed less increases in prefrontal regions that are associated with reappraisal, greater decreases in the amygdala activation and less ventral striatal activity (an area associated with reward processing). The authors posited that results may indicate that for men, cognitive regulation requires less effort due to greater autonomic emotion regulation or that women use more positive emotions for reappraising negative emotions which, in turn, require more cortical resources.

**Emotional processing in DPD**

Evidence suggests impairment in emotional processing for DPD patients. DPD patients show high levels of alexithymia and may experience emotional blunting (a dampening of the emotional experience) or numbness as well as an emotional disconnection from their loved ones (Sierra and Berrios, 2001), both delineating a dysfunctional experience of emotion. DPD patients have also expressed feeling less aroused by unpleasant pictures (Sierra, Senior, Dalton, McDonough, Bond, et al., 2002) and have rated emotional pictures as less intense (Sierra, Senior, Phillips, & David, 2006; Phillips, Medford, Senior, Bullmore, Suckling, et al., 2001) than healthy controls and anxiety groups indicating a decreased magnitude of emotions. Correspondingly physiological measures assessed in these studies indicate a decrease in neural response while viewing emotional stimuli: lower amplitudes in skin conductance response were found for unpleasant pictures and disgusted faces in the DPD groups compared to controls and an anxiety group (Sierra et al., 2002; 2006). Early case studies have also indicated decreases in skin
conductance that corresponded to symptoms of depersonalization (Lader and Wing, 1966; Lader, 1975).

In functional Magnetic Resonance Imaging studies, DPD patients have shown differences compared to controls in the activity of brain areas associated with emotional processing. DPD patients exhibit increased right ventral prefrontal cortex (PFC) and decreased insula activation in response to aversive pictures (Phillips, et al., 2001). Additionally, Lemche, Anilkumar, Giampietro, Brammer, Surguladze, et al. (2008) found that when presented with faces consisting of happy and sad expressions of varying intensities, DPD patients showed decreased activity in the right hypothalamus/semilunar gyrus in response to happy faces and in the right amygdala/uncinate gyrus in response to sad faces, activity which negatively correlated with expression intensity. PFC activation was also associated with decreased autonomic response in this study. While the insula is a limbic area associated with the neural response to disgust, negative mood, and unpleasant visceral sensations like pain, the PFC has been associated with emotion regulation (Phan, Fitzgerald, Nathan, Moore, Uhde et al., 2005; Dolcos, Kragel, Wang, L., & McCarthy, 2006). Taken together, these studies suggest the PFC is playing an active role in the inhibition of the emotional response of limbic areas in the DPD group and may underlie the blunting of both positive and negative emotions found in DPD.

Active regulation of the emotional response has never been investigated in DPD patients. However, the decreased subjective and projective arousal to affective stimuli found in the disorder may suggest a greater ability to suppress but a lesser ability to enhance emotion as evidenced by subjective report and physiological measures like heart rate and skin conductance response.
Stress

Stress and the hypothalamo-pituitary adrenocortical (HPA) axis

The literature well documents the negative effects of chronic stress on both physical and mental health. Thus, stress influences physical disorders like heart disease, diabetes and stroke. It may also be a precipitating factor for mental disorders like schizophrenia and depressive and anxiety disorders. Stress has been defined as any situation where demands are perceived to exceed personal resources (Lazarus, 2006). Thus, stress is a subjective experience, relevant to each individual, and a given stressor may affect two individuals differently. The perception of stress facilitates a cascade of cognitive and neuroendocrine changes in the body for purposes of adapting to the stressor.

Cortisol (hydrocortisone) is one hormone released in response to stress (see Buckingham, 2006 for review). It is a lipid based steroid hormone, specifically a glucocorticoid that impacts all bodily systems. Cortisol is synthesized from cholesterol in the zona fasciculate of the adrenal glands. Two corticosteroid receptors have been identified: the mineralocorticoid receptor and glucocorticoid receptor. While mineralocorticoid receptors are localized primarily in the kidneys and other tissues involved with sodium/potassium balance, glucocorticoid receptors are widely distributed throughout the body with receptor concentrations fluctuating depending on cell cycle stage and environmental factors (like stress). While for humans, the predominant glucocorticoid produced is cortisol, rats produce corticosterone while pigs and dogs produce both.

A major function of cortisol is to foster release of amino acids and fats from cells in order for them to be used as energy and to be synthesized into new compounds, fostering gluconeogenesis: the generation of glucose from non-carbohydrate carbon substrates such as
lactate and glycerol (Levine, Zagoory-Sharon, Feldman, Lewis, & Weller, 2007). Cortisol also plays a role in suppressing the immune system which includes its anti-inflammatory effects.

There is a diurnal pattern of pulsatile cortisol release which is associated with normal development (e.g., lung development) and homeostasis. In the diurnal clock of humans, cortisol levels peak early prior to waking, spike by 50 – 100% within the first 30 to 45 minutes of waking (the awakening cortisol response) and gradually decrease throughout the day. These changes in cortisol levels correspond to the pulsatile release of CRH and ACTH which also decreases throughout the day (see Levine et al, 2007 for review).

The stress response release of cortisol governed by the hypothalamo-pituitary adrenocortical (HPA) axis overlaps the pulsatile diurnal clock of cortisol (Buckingham, 2006). The HPA axis functions thusly: in response to a stressor, the cells in the periventricular hypothalamic nucleus (PVN) of the hypothalamus secrete corticotrophin releasing hormone (CRH) which travels via the hypophyseal portal blood vessels to the anterior pituitary prompting secretion of adrenocorticotropic hormone (ACTH). ACTH then stimulates the release of cortisol from the zona fasciculate of the adrenal glands. The HPA axis functions with a negative feedback loop: elevated cortisol levels suppress CRH and ACTH release which inevitably suppresses the release of cortisol. Activation of the HPA axis is influenced by projections to the medial PVN which typically arrive from first and second order inputs of somatic nociceptors (pain perception), visceral afferents (neurons of the autonomic nervous system), or humoral sensory pathways (concerning immunity) suggesting a reflexive function of the PVN in the HPA axis (Herman et al, 2003).

Release of other neuropeptides work in conjunction to the HPA axis in regulating cortisol (see Herman et al., 2003 for review). The nucleus of the solitary tract in the brainstem also
projects to the PVN, releasing norepinephrine (NE) and epinephrine. However, evidence suggests that the effects of norepinephrine on the PVN may be mediated by glutaminergic interneurons, and high levels of NE may have inhibitory effects on the release of ACTH and thus, on cortisol release. Arginine Vasopressin (AVP) is produced by the hypothalamic supraoptic nuclei (SON) and paraventricular nuclei (PVN) and released by the posterior pituitary gland and also works in conjunction with CRH to enhance the effects of ACTH (AVP also inhibits release of oxytocin). Serotonin in the PVN also stimulates production of cortisol, although few projections originating from the raphe nucleus are found in the PVN. Dopaminergic cells originating from the thalamus also innervate the PVN and dopamine is also known to activate the HPA axis. Projections emanating from other regions of the hypothalamus innervate the PVN as well and are primarily GABAergic although some glutamatergic innervations are also found, indicating the complexities of regulation of the HPA axis as well as highlight the specificity of the stress response as different cells centers of the HPA axis are activated depending on the stressor. For instance, in rodents NMDA and AMPA/kainate receptor antagonists inhibit ACTH responses to immobilization, but not footshock or ether. The PVN also receives innervations from the posterior hypothalamus which in turn receives inputs from the limbic forebrain which may indicate the role of the limbic system in initiating and regulating the stress response. Other limbic structures such as the hippocampus, the prefrontal cortex, and the amygdala influence the stress response indirectly via intermediate innervations to the medial PVN.

Jankord & Herman (2009) describe two ways in which the HPA axis is activated. A reactive stress response is a reflexive response to a physical challenge and results from direct innervations of the PVN by peripheral neurons like nociceptors, Conversely, in the absence of
tangible threat activation of the HPA axis can be an anticipatory response initiated by innate organismic programing like instinctual fear or by psychogenic stressors like memories. Anticipatory responses result from innervations emanating from the limbic system. Chronic stress enhances both basal HPA function and stress reactivity indicating that there are mechanisms to bypass negative feedback inhibition. Limbic structures such as the hippocampus, the prefrontal cortex, and the amygdala influence the anticipatory stress response indirectly via intermediate innervations to the medial PVN, while the hippocampus and prefrontal cortex inhibit response to anticipatory stressors, the amygdala facilitates the stress response (Herman et al, 2003).

Cortisol is found in the bloodstream in both free and bound forms and has a half life of about 80 minutes. In plasma, cortisol is primarily bound to corticosteroid-binding globulin (CBG) but also to albumin while the remainder is free. The molecular weight of free cortisol is low (about 362 Da), allowing for passive diffusion of cortisol across capillary walls. The free hormone hypothesis posits that only free cortisol is biologically active. However, Tait and Burstein (1964) argue that since cortisol has a weak affinity for albumin, cortisol loosely bound to albumin should also be considered as free. The amount of free cortisol catabolized by the liver via hepatic uptake is three times that of free cortisol found in plasma. Plasma cortisol levels less than 80nM at 9:00 AM may indicate inadequate adrenal function while levels greater than 300nM at that time may exclude such deficiency (see Levine et al. 2007 for review). However, the awakening cortisol response as measured in saliva is not always reliable.

In contrast to plasma, salivary cortisol is primarily free cortisol that has passively diffused from the blood into saliva glands. Salivary cortisol represents 50-70% of serum free cortisol levels. However, correlations between salivary cortisol and total plasma cortisol levels
range between $r=0.71$ and $r=0.96$, thus lending salivary cortisol an effective substitute for free plasma cortisol, despite diurnal differences between the two. (See Levine et al., 2007 for review).

There are sex differences in cortisol levels and stress. Cortisol is generally found in higher levels in women than in men and females show greater HPA reactivity particularly during the proestrus day of the estrus cycle compared to males while testosterone inhibits HPA response to stress. (Herman et al. 2003). Dedovic et al. (2009) document greater deactivation of the prefrontal cortex and hippocampus for men compared to women in response to a social stressor. For the task, cerebral blood flow in the hippocampus and perceived stress for the task were positively correlated for women but negatively correlated for men. However, in these studies, stage of menstrual cycle for the women was not recorded. Cortisol has been shown to be lowest during the follicular phase, highest during ovulation, and then decrease but still remain higher during the luteal phase compared to the follicular phase (Gennazzi et al., 1975; Walder, Statucka, Daly, Axen, Haber, 2012). Basal cortisol levels in women in the early follicular phase have been shown to be lower than men (Walder et al., 2012). Additionally, in response to the TSST, while there is no difference in stress reactivity between women in the luteal phase of their cycle and men, men have greater cortisol reactivity than women in the follicular phase of their cycle, and there is no difference between women in the follicular stage and women using oral contraception (Kirschbaum et al., 1999).

**The HPA Axis and Depersonalization Disorder**

Research findings are inconsistent with regard to cortisol levels in DPD patients. In a pilot study, Simeon et al (2001) found that when they controlled for depression, the DPD group had higher basal plasma cortisol levels than a control group. In another study, Simeon et al.
(2007) found higher basal urinary cortisol levels in dissociative patients compared to controls. In the same study, the DPD group with comorbid lifetime major depression had significantly higher urinary cortisol levels than healthy controls and a tendency toward higher urinary cortisol levels compared to non-depressed DPD participants. The study of Stanton et al. (2001) diverges from these findings: they indicated salivary cortisol levels of DPD patients were lower over a 24 hour period than those of patients with major depressive disorder but did not differ from healthy controls. However, taken together, the results of these studies are consistent with previous research that found higher cortisol levels in depressed patients than controls (Hein et al, 2001) and may suggest that depression is a mediating factor of potentially elevated cortisol levels in DPD patients.

Few studies have documented the effects of acute neurochemical stressors in DPD. However, two studies used dexamethasone administration to investigate suppression of the physiological stress response in DPD. Dexamethasone is a glucocorticoid receptor antagonist with a higher affinity for the glucocorticoid receptor than cortisol. The binding of dexamethasone to the glucocorticoid receptor instigates suppression of the Hypothalamus-Pituitary-Adrenal (HPA) axis. DPD patients have demonstrated higher plasma cortisol levels following dexamethasone administration (Simeon et al, 2001) as well as significant resistance to and faster escape from dexamethasone suppression (Simeon et al., 2007), suggesting that depersonalized individuals are more resistant to HPA axis suppression than healthy controls.

There are also few studies investigating the response of depersonalized individuals to acute social stressors. In one study, although DPD patients rated the Trier Social Stress Test (TSST) as significantly more stressful than a control group but less stressful than a Posttraumatic stress disorder (PTSD) patient group, plasma cortisol reactivity in response to the TSST did not
differ between the groups (Simeon et al., 2007). However, in another study utilizing undergraduate students, both subjective stress following the TSST and cortisol reactivity were positively related to dissociation severity (Giesbrecht et al, 2007).

Norepinephrine (NE) is also important in the regulation of the HPA axis. DPD patients have been shown to have altered levels of NE. Simeon et al. (2003) found elevated levels of urinary NE in DPD patients compared to controls when they controlled for anxiety. However, there was an inverse relationship between NE levels and depersonalization severity which suggests that some mechanism involved in DPD also results in some inhibition of NE. While low levels of NE are associated with depressed mood, increased levels of NE are associated with anxiety as well as an inability to recognize negative emotion (Harrison, Morgan, & Critchley, 2010). Thus, in addition to increased cortisol levels, elevated NE levels in DPD patients may correspond with elevated levels of anxiety and alexithymia typically seen with the disorder, however more severe cases of depersonalization may show less elevated NE levels, corresponding with often comorbid symptoms of depression.

Oxytocin and the HPA axis

Oxytocin (OT) is a neurohypophysial peptide hormone closely related in structure to arginine vasopressin. It is produced in the magnocellular neurons of the hypothalamic supraoptic nuclei (SON) and paraventricular nuclei (PVN) of the brain, and stored in the neurohypophylys of the posterior pituitary where it may be released into the bloodstream, or released from OT fibers of the hypothalamus that project to a multitude of brain areas including limbic structures where it acts as a neurotransmitter or neuromodulator (Gimpl & Fahrenholz, 2001). OT is also produced in other parts of the body such as the gastrointestinal tract, heart, testes and uterus.
(Kiss and Mikkelsen, 2005) and is found in elevated concentration in the adrenal glands (Gimpl & Fahrenholz, 2001) suggesting that oxytocin may play a direct role in regulation of cortisol levels.

OT receptors are well distributed throughout the human brain with highest concentrations found in the substantia nigra and globus pallidus, the anterior cingulate, and the medial insula, but not in the hippocampus, amygdala, entorinal cortex, or olfactory bulb (Marazziti and Dell’Osso, 2008), suggesting a targeted role of OT in emotion. Estradiol, progesterone, and testosterone facilitate OT receptor binding while castration reduces it (Gimpl & Fahrenholz, 2001), and in women, OT levels are higher during the follicular and ovulatory phases compared to the luteal phase (Salonia, Nappi, Pontillo, Daverio, Smeraldi, Briganti, et al., 2005; Shukovski, Healy, & Findlay, 1989). Hence, gonadal hormone levels may greatly influence OT action. OT release follows a circadian rhythm with cerebral spinal fluid levels peaking at midday (McCarthy & Altemus, 1997). Although salivary and plasma OT levels have been shown to be correlated (Grewen, Davenport, & Light, 2010), OT levels in the CSF are not related to plasma OT levels (Kagenbauer, Martin, Schuster, Blobner, Kochs, & Landgraf, 2013), and OT cannot readily traverse the blood-brain barrier (Gimpl & Fahrenholz, 2001).

Oxytocin influences a multitude of systems within the body. It is released in response to nipple and genital stimulation, suckling, estrogen administration, oral contraceptive use, and pregnancy (McCarthy and Altemus, 1997), and the effects of OT on sexual and reproductive behavior have been well documented. OT release is also associated with decreased blood pressure, and corticosterone levels in rats, as well as increased insulin, all actions which are counter to the HPA stress response (Gimpl & Fahrenholz, 2001). Notably, intravenous infusion of OT shows a suppressive effect on the HPA axis in humans (Legros, 1984; Chiodera, & Coiro,
187), and OT has also been shown to attenuate the cortisol surge in response to physical stress (Cardoso, Ellenbogen, Orlando, Bacon, & Joober, 2012). As well, subchronic intranasal administration of OT has also been shown to attenuate the HPA axis response to social isolation in monkeys (Parker, Buckmaster, Schatzberg, & Lyons, 2005). Additionally, cortisol inhibits both the hypothalamus and the pituitary gland leading to reduced secretion of AVP. Conversely, cortisol administration in humans has also been shown to increase oxytocin (Tops, van Peer, & Korf, 2007) which has been related to decreased recall of unpleasant stimuli (Tops, Bursman-Piglman, Boksem, Wijers, & Korf, 2012). These findings indicate that cortisol and oxytocin work in tandem in regulating the stress response.

Cognitive effects of OT have also been shown. Oxytocin is known to decrease learning and memory (Gimpl & Fahrenholz, 2001) but facilitate social bonding (see McCarthy & Altemus, 1997 for review). Increased OT levels are associated with generosity (Morhenn et al., 2008) and trust (Kosfeld, Heinrichs, Zak, Fischbacker, & Fehr, 2005). OT also induces satiety, reducing feeding in rats (Gimpl & Fahrenholz, 2001). However, oxytocin administration seems to decrease emotionality in some subjects. OT reduces anxiety and shows anti-depressive effects on rats (Arletti & Bertolini, 1987). OT administration and social support individually reduce anxiety, and in conjunction decrease cortisol levels during the TSST (Heinrichs, Baumgartner, Kirschbaum, & Ehlert, 2003). Intranasal OT administration has also been shown to attenuate the increased cortisol response to a social stressor in persons with impaired emotion regulation abilities (Quirin et al., 2011) and borderline personality disorder (Simeon, Bartz, Hamilton, Crystal, Braun, Ketay, et al., 2011). OT administration has also been shown to impede trust in Borderline Personality Disorder patients (Bartz, Simeon, Hamilton, Kim, Crystal, Braun, et al., 2011). Correspondingly, activation of the right amygdala to positive and negative stimuli has
also been shown to decrease with intranasal oxytocin (Domes, Heinrichs, Gläscher, Büchel, Braus, & Herpert, 2007).

Dysregulated OT levels have been found in several psychiatric disorders but findings are conflicting. Although lower OT levels during pregnancy have been associated with post-partum depression (Skrundz, Bolten, Nast, Hellhammer & Meinlschmidt, 2011), increased OT levels may be associated with depression (Parker, Kenna, Zeitzer, Keller, Blasey, Amico, et al., 2010; Cyranowski, Hofkens, Frank, Seltman, Cai, & Amico, 2008). Elevated OT levels in cerebrospinal fluid have been associated with obsessive compulsive disorder in one study (Leckman, Goodman, North, Chappell, Price, Pauls, et al., 1994) but not another (Altemus, Jacobson, Debelles, Kling, Pigott, Murphy, et al. 1999), and may be equated to increased grooming behavior found in animals with OT microinjection since excessive grooming in animals is considered a model for compulsion (Marazziti and Dell’Osso, 2008). Consistent with the effects of OT on feeding in rats, decreased levels of OT in cerebrospinal fluid of eating disorder patients have been observed (Demitrack, Lesem, Listwak, Brandt, Jimerson, & Gold PW, 1990). OT levels return to normal when eating disorder patients return to normal body weight. An inverse relationship between OT levels in cerebrospinal fluid and negative symptoms of schizophrenia has also been found (Sasayama, Hattori, Teraishi, Hori, Ota, Yoshida, et al., 2012). Decreased OT levels have also been found in autistic individuals, and long term administration increases social cognition in autism (Anagnostou, Soorya, Chaplin, Bartz, Halpern, Wasserman, et al., 2012). Plasma OT levels are also decreased in women with borderline personality disorder (Bertsch, Schmidinger, Neumann, Herpertz, 2013). A recent study has indicated that increased levels of OT may be associated with dissociation (Seng,
Miller, Sperlich, van de Ven, Brown, Carter, et al., 2013), however OT levels have never been measured in DPD.

Although OT has been shown to suppress ACTH and cortisol release, OT secretion in response to psychosocial stress is not as clear. Two studies have found that psychosocial stress increases oxytocin in humans. Sanders et al. (1990) showed that uncontrollable noise elicited increased OT in emotional women but not men. Pierrehumbert et al. (2010) found a tendential increase in plasma OT in response to the Trier Social Stress Test (TSST) and an inverse relationship between OT and salivary cortisol levels. However, others have failed to find a significant OT response to the TSST or modified versions thereof (Altemus, Redwine, Leong, Frye, Porges, & Carter, 2001; Heinrichs, Meinlschmidt, Neumann, Wagner, Kirschbaum, Ehlert, et al., 2001; Cyranowski et al, 2008). These results suggest that the relationship between OT and psychosocial stress should be further investigated.

**Oxytocin in DPD**

Although oxytocin levels have never been measured in DPD patients, several factors suggest oxytocin levels may be elevated in depersonalization disorder patients:

1. OT administration has inhibited amygdala activity suggesting that the decreased amygdala activity found in DPD patients may be due to elevated OT levels.

2. Elevated cortisol levels in DPD may be associated with elevated OT levels since cortisol administration has been shown to increase oxytocin levels.
3. Elevated levels of OT are found in depressed and anxious patients suggesting that DPD patients may also have elevated OT levels given high comorbidity with mood and anxiety disorders.

4. A recent study found that persons with higher levels of dissociation also have elevated OT levels.

Thus, OT levels should be investigated in DPD patients. If DPD patients have increased OT levels, effective regulation of OT may help ameliorate symptoms of emotional numbness, anxiety, and depression and facilitate better social cohesiveness in DPD individuals.

Conclusions

Depersonalization disorder (DPD), is an often debilitating psychiatric disorder characterized both by feelings of detachment from the self or others as well as emotional blunting or numbness. Subjective and physiological evidence of decreased emotional arousal may suggest impaired emotion regulation abilities. Deficits in emotional processing of DPD have been associated with dysregulated cortisol levels and may also involve dysregulated oxytocin levels. In this series of studies, we aimed to investigate the physiological correlates of emotion regulation in depersonalization disorder. To that end, we used self-report and physiological measures to assess how effective DPD patients are at regulating their emotions. We also investigated the relationship between changes in oxytocin and cortisol in the stress response of DPD patients. Further elucidation of the neural and chemical mechanisms which underlie detachment and emotional blunting in DPD will improve our ability to develop therapeutic treatments that ameliorate these symptoms.
CHAPTER ONE

Aim I: Investigation of ability of DPD patients to subjectively down-regulate and up-regulate pleasant and unpleasant emotions.

Evidence suggests impairment in emotional processing for DPD patients. DPD patients show high levels of alexithymia and often experience emotional blunting (a dampening of the emotional experience) or numbness as well as an emotional disconnection from their loved ones (Sierra and Berrios, 2001), both delineating a dysfunctional experience of emotion. DPD patients have also expressed feeling less aroused by unpleasant pictures (Sierra, Senior, Dalton, McDonough, Bond, et al., 2002) and have rated emotional pictures as less intense (Sierra, Senior, Phillips, & David, 2006; Phillips, Medford, Senior, Bullmore, Suckling, et al., 2001) than healthy controls and anxiety groups, indicating a decreased magnitude of emotions. This propensity for decreased emotionality and arousal in DPD may suggest a relative inability to up-regulate emotion but an enhanced capacity to down-regulate emotion. However to date, no studies in the literature have investigated the ability of DPD patients to modulate their response to emotional stimuli. In this study, DPD patients and a normal control group used reappraisal, an antecedent-focused emotion regulation strategy, to up-regulate or down-regulate their emotional response to pleasant and unpleasant pictures. Participants then reported the emotional salience (how pleasant or unpleasant the picture was), emotional arousal, and dominance (how controlled by or in control of the situation in the picture the person felt) of each picture.

**Hypothesis**: Given their propensity for decreased emotional responsivity, we hypothesized that DPD patients would be better at down-regulating and worse at up-regulating emotion to both unpleasant and pleasant stimuli than the control group.
**Main finding:** Compared to the control group, the DPD group was better at down-regulating emotional salience and dominance for unpleasant pictures. However, for arousal ratings, DPD patients were less aroused by the pictures overall, and less able to modulate arousal levels.

**Methods**

*Participants*

Participants were 16 dissociative disorder patients recruited via self-referral and 15 age and gender-matched normal controls. Diagnosis of dissociative disorders was established using the Structured Clinical Interview for Dissociative Disorders (SCID-D-R; Steinberg, 1994). Participants with diagnoses of substance abuse, schizophrenia, eating disorders, severe depression, suicidality, as well as history of head trauma were excluded. Fifteen dissociative disorder patients met diagnostic criteria for DPD while one participant met criteria for Dissociative Disorder NOS (not otherwise specified). DPD participants taking psychotropic medications were not excluded. The control group was recruited from the undergraduate Psychology 100 course population at Hunter College of the City University of New York and via craigslist.com advertising. Participants in the control group were prescreened using the Dissociative Experiences Scale (DES; Carlson & Putnam, 1993), Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977), and the State/Trait Anxiety Inventory-Y2 (STAI; Spielberger, 1983). Control participants with total scores above 12 on the DES depersonalization subscale (DES_DPS) and DES amnesia subscale (DES_AMN), 14 on the CES-D, and 44 on the STAI-Y2 were excluded.
The study was conducted at Hunter College and approved by the Institutional Review Boards of Beth Israel Medical Center, New York and City University of New York Hunter College. All participants gave written informed consent prior to study participation. Participants in the control group received $30 compensation.

**Measures**

The Dissociative Experiences Scale (DES; Carlson & Putnam, 1993) is a 28-item questionnaire used to measure the frequency of dissociative experiences on a 0% to 100% scale in 10% increments. Sound psychometric properties of the DES have been established (van IJzendoorn and Schuengel, 1996). A factor analysis extracted a 3 factor solution comprising of Amnesia: associated with dissociative identity disorder; Absorption: associated with the propensity to daydream or fantasize; and Depersonalization/derealization (Ross et al., 1991). The items of these 3 factors have since been classified as the DES subscales: Amnesia (DES-AMN), Absorption (DES-ABS) and Depersonalization/derealization (DES-DPS). These subscales are purported to represent, not only the 3 factors of dissociation, but have been proposed to represent 3 distinct constructs themselves.

The Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977) is a 20-item self-report questionnaire commonly used to screen for symptoms of depression in the general population. Respondents report the incidence of items on a 4-point scale from 0, rarely or none of the time (less than 1 day” to 3, most or all of the time (5-7 days). The measure has high internal consistency and adequate test-retest reliability given it measures state levels of depression. Although a cut-off score of 16 is standardly used to delineate a depressive syndrome,
in the current study, a more conservative cut-off score of 14 was used to screen control participants.

The State/Trait Anxiety Inventory-Y2 (STAI; Spielberger, 1983) is a 40-item questionnaire that assesses state (STAI-Y1) and trait (STAI-Y2) levels of nervousness and anxiety. The STAI-Y1 and STAI-Y2 versions comprise of 20 items each and have been demonstrated to have good test-retest reliability and internal consistency. Given that Spielberger found a mean score of 34.89 for working adults with a standard deviation of 9.19, we used a cut off score of 44 to screen control participants.

The Cambridge Depersonalization Scale (CDS: Sierra & Berrios, 1996) is a 29-item self-report questionnaire which assesses frequency and duration of symptoms of depersonalization experienced in the last 6 months. Frequency is reported on a 5-point scale (anchors: 0 = never; 4 = all the time), and duration is reported on a 6 point scale (anchors: 1 = few seconds; 6 = more than a week). The test has very good internal consistency (Cronbach’s alpha = 0.89) and is able to differentiate DPD patients from other patient groups and healthy controls.

The Childhood Trauma Questionnaire-Short Form (CTQ: Bernstein & Fink, 1997) is a 28-item self-report scale used to gage childhood and adolescent experiences of interpersonal trauma. Items are rated on a 5-point, Likert-type scale ranging from Never True to Very Often True. Clinical subscales of the CTQ include physical abuse, sexual abuse, emotional abuse, physical neglect, and emotional neglect.

The Toronto Alexithymia Scale (TAS: Bagby, Parker, & Taylor, 1994) -20 is a 20-item self-report scale which measures alexithymia. Respondents indicate on a 5-point scale the degree to which each item applies to them (anchors: 1 = strongly disagree; 5 = strongly agree). Three subscales have been derived from the TAS-20: Difficulty Describing Feelings, Difficulty
Identifying Feelings, and Externally Oriented Thinking, The TAS-20 has demonstrated good internal consistency (Cronbach’s alpha = .81) and test-retest reliability (.77).

The Emotion Regulation Questionnaire (ERQ; Gross & John, 2003) asks respondents to report their use of reappraisal and suppression strategies to regulate positive and negative emotion. The scale is comprised of 10 items which are each rated on a scale from 1 (strongly disagree) to 7 (strongly agree). Results of exploratory factor analysis indicate the measure comprises of two factors: a suppression factor and a reappraisal factor. Items of these factors form the suppression and reappraisal subscales of the ERQ. Cronbach’s alpha for the Reappraisal and Suppression subscales is .79 and .73 respectively and the test-retest reliability is .69.

The Peritraumatic Dissociative Experiences Questionnaire (PDEQ: Marmar, Weiss, & Metzler, 1997) is an 8-item questionnaire used to measure immediate dissociation at the time an event is occurring. Respondents indicate the degree to which they experienced each item on a Likert scale (1 = not at all true, 2 = somewhat true, 3 = definitely true). The PDEQ has demonstrated adequate test–retest reliability and internal consistency (Birmes, Brunet, Benoit, Defer, Hatton, Sztulman, et al., 2005). In the current study, instructions were modified to read “Please rate the following statements based on your experience right now, at this moment” for the version given just prior to administration of the emotion regulation task, and “during the task you just completed” for versions given during and directly following the emotion regulation task.

The Positive and Negative Affect Scale (PANAS; Watson, Clark, & Tellegen, 1998) is a 20-item self-report measure that assesses subjective distress and unpleasurable engagement (negative affect) and pleasurable engagement (positive affect) on a 5-point likert scale from 1 (very slightly or not at all) to 5 (extremely). The positive affect and negative affect subscales comprise 10-items each and have shown high internal consistency and good test-retest reliability.
Two versions of the PANAS were administered: the PANAS-now asked respondents to indicate ‘to what extent you feel this way right now, that is, at the present moment’ while the PANAS-past week asked respondents to indicate ‘to what extent you felt this way during the past week.’

Beck Depression Inventory-II (BDI-II; Beck et al., 1996) is a 21-item self-report scale that assesses severity depression symptomology. Each item contains four possible statements related to a given emotion (e.g., sadness, guilty feelings, and agitation) that are rated from 0 to 3. The questionnaire asks respondents to choose the statement that most accurately describes how they have been feeling over the past two weeks. Item responses are summed yielding a total score from 0 to 63.

The Self-Assessment Manikin (SAM; Lang et al., 1999) is a self-report measure assessing subjective valence, arousal, and dominance. The SAM comprises 9 graphical figures for each of 3 scales: emotional salience (ranging from 1, extremely unpleasant to 9, extremely pleasant), arousal (ranging from 1, extremely calm to 9, extremely aroused), and dominance (ranging from 1, completely controlled to 9, completely in control). Respondents choose the figure that best represents their response.

**Stimulus.** Stimuli consisted of 280 pictures from the International Affective Picture System (IAPS, Lang, Bradley, & Cuthbert, 2009; 120 pleasant, 120 unpleasant, 40 neutral). Results of analyses of variance (ANOVA) using ratings assessed by Lang et al. indicated all picture types differed significantly in ratings of valence (emotional salience; $F_{2,277} = 10523.96, p < .001$; pleasant pictures: $M = 7.34$, $SD = 0.26$; unpleasant pictures: $M = 2.34$, $SD = 0.26$; neutral pictures: $M = 5.00$, $SD = 0.30$), arousal ($F_{2,277} = 115.44, p < .001$; pleasant pictures: $M = 4.98$, $SD = 0.97$; unpleasant pictures: $M = 5.77$, $SD = 0.70$; neutral pictures: $M = 3.42$, $SD = 0.89$), and dominance ($F_{2,277} = 655.29, p < .001$; pleasant pictures: $M = 6.03$, $SD = 0.53$; unpleasant pictures:
M = 3.63; SD = 0.55; neutral pictures: M= 5.78; SD = 0.51) Pictures were presented on a 17” computer monitor.

Emotion regulation task. Instructions for the emotion regulation task were the same as for Moser et al. (2006). Briefly, participants were instructed to either enhance (increase the intensity of the emotion felt in response to the picture), suppress (decrease the intensity of the emotion felt in response to the picture) or view the picture as they normally would. To avoid confusion of enhancing or suppressing a nonexistent emotion, participants were only instructed to view neutral pictures. The instruction (“Enhance,” “Suppress,” or “View”) was presented on screen for 2000 ms. Then a blank screen appeared for 500 ms followed by 5 pictures for 2000 ms each with an interstimulus interval of 1500 ms that also consisted of a blank screen. Each condition contained 40 pictures. Half of the pictures were presented before a questionnaire break and the other half after the questionnaire break. All pictures of a condition were presented in succession. Presentation of conditions was randomized.

Ratings. Following the emotion regulation task, participants were interviewed and asked to indicate the strategies they used during the task to regulate their emotions to pleasant and unpleasant pictures on a 5-point scale (0, “never,” 1, “rarely,” 2, “50/50,” 3, “mostly,” and 4, “always”). Strategies were “shifting attention to another part of the picture,” “focusing on physical experience,” “increasing or decreasing breathing,” “tightening muscles,” “moving the face,” “closing eyes or looking away,” and “thinking of other things not in the picture.” All pictures were then re-presented for 2000 ms in random order and participants rated their emotional salience, arousal, and dominance using the SAM directly following each picture presentation.
Procedure

Participants signed a consent form and completed the demographic questionnaire, BDI, STAI-Y2, PANAS-past week, DES, CDS, CTQ, TAS, and ERQ. Participants then completed the PDEQ, STAI-Y1, and PANAS-now. They then began the first half of the emotion regulation task which included the 7 conditions with 20 pictures each. Participants then completed the PDEQ, STAI-Y1, and the PANAS-now in order to assess changes in state levels of emotion and dissociation during the task. They then underwent the second half of the emotion regulation task consisting of the 7 conditions with different pictures. Participants again completed the PDEQ, STAI-Y1, and the PANAS-now. At the end, an interview was conducted to assess the emotion regulation strategies they used. Finally, participants were re-presented the pictures and rated them using the SAM.

Statistical Analyses

Independent t-test and chi square statistics were used to analyze group differences in demographic and clinical characteristics. For the emotion regulation conditions, an ability score was calculated to indicate each individual’s ability to regulate emotion to pleasant and unpleasant pictures. Ability to enhance was calculated by subtracting mean values of the view conditions from mean values of the enhance conditions. Ability to suppress was calculated by subtracting mean values of the suppress condition from mean values of the view conditions. Thus, greater positive scores represent a greater ability to enhance or suppress emotion respectively.

For picture ratings irrespective of emotion regulation instruction, an RM-ANOVA was calculated for valence (pleasant, unpleasant, neutral) X rating type (emotion, arousal,
dominance) X group (DPD, control). For picture ratings of each SAM subcategory during the view condition, RM-ANOVA was also calculated for valence (pleasant, unpleasant, neutral) X presentation (1, 2) X group. For picture ratings of each SAM subcategory of ability scores, RM-ANOVA was calculated for valence (pleasant, unpleasant) X presentation (1, 2) X instruction (enhance, suppress) X group. For state questionnaires completed before, during, and after the emotion regulation task, a RM ANOVA for time (before, during, after) X group (DPD, control) for each questionnaire. Greenhouse-Geisser correction was used for P-values associated with multiple degrees of freedom RM ANOVAs. Post-hoc analyses included RM-ANOVAs, Bonferroni correction, 2-way ANOVA’s, independent and paired t-tests.

Results

Demographics and clinical characteristics

Table 1 presents the demographic and clinical characteristics of the sample. There were no significant differences between the groups for age, gender, income, marital status, or education. The control group was more ethnically diverse ($t_{29} = 3.050, p < 0.05$), comprising of 6 African Americans, 2 Asians, 4 Hispanics, and 3 Caucasians compared to the DPD group, who were all Caucasian except one participant who identified as multi-racial. The DPD group scored higher on the DES-total, DES-AMN, DES-DPS, DES-ABS, CDS, BDI, STAI-Y2, PANAS-past week (positive & negative), TAS-total, TAS-difficulty describing feelings, and TAS-difficulty identifying feelings (all p’s < 0.05). Although the groups did not differ in total score on the CTQ, the DPD group scored higher on the emotional neglect subscale but lower on the physical abuse subscale of the questionnaire (p’s < .05). There was a trend difference for the
ERQ Reappraisal and Suppression scales with the DPD group endorsing less reappraisal strategies and more suppression strategies (p’s < .10).

*Emotion Regulation Task Questionnaires*

Figure 1 presents results of the questionnaires completed before, during, and after the emotion regulation task. For the PDEQ, there was an overall group difference in dissociation throughout the task (F_{1,29} = 26.510, p < .001). *T*-tests indicated that the DPD group was more dissociated before (t_{22.844} = -5.177, p < .001), during (t_{29} = -2.984, p < .01), and after (t_{22.230} = -4.361, p < .001) the task. For the STAI-Y1, there was a main effect for time (F_{2,58} = 5.295, p < .01). Pairwise comparisons indicated anxiety before the task (M = 33.94, SD = 11.59) was lower than during (M = 37.97, SD = 12.77) and after (M = 38.45, SD = 12.84) the task. There was also a main effect for group (F_{1,29} = 12.804, p < .005). The DPD group was more anxious before (t_{19.919} = -4.459, p < .001), during (t_{29} = -2.597, p < .05), and after the task (t_{29} = -2.901, p < .01). For the PANAS-positive now questionnaire, there was a main effect for group (F_{1,28} = 294.190, p < .001). Compared to the control group, the DPD group reported less positive affect before, and after the task. During the task, the groups differed in positive affect at the level of a trend. There was also group X PANAS-positive now interaction at the level of a trend (F_{1.56,43.67} = 2.697, p = .09; Greenhouse Geisser Epsilon=.78). For the PANAS-negative now questionnaire, there was a main effect for group (F_{1,28} = 7.774, p < .01). The DPD group reported more negative affect before and during the task.

*Picture Ratings*

*View Condition*
**Emotional Salience.** For the view condition of emotional salience, there was a main effect for valence (\( F_{1.15,32.08} = 136.98, p < .001, \text{Greenhouse Geisser Epsilon} = .57 \)). Unpleasant pictures (M = 2.89, SD = 0.96) were rated less pleasant than neutral (M = 5.09, SD = 0.44) pictures and pleasant (M = 6.43, SD = 0.85) pictures were rated more pleasantly than neutral pictures. There was also a valence X group interaction (\( F_{1.15,32.08} = 4.643, p < .05, \text{Greenhouse Geisser Epsilon} = .57 \)); the control group rated pleasant pictures more pleasantly (M = 6.86, SD = .86) than the DPD group (M = 6.01, SD = .83), \( t_{27.975} = 2.739, p < .05 \).

**Arousal.** For arousal, there was a main effect for valence (\( F_{1.42,39.80} = 10.021, p < .005, \text{Greenhouse Geisser Epsilon} = .71 \)). Neutral (M = 3.60, SD = 1.45) pictures were less arousing than pleasant (M = 4.47, SD = 1.79) and unpleasant (M = 4.81, SD = 1.70) pictures. There was also a trend toward a group effect (\( F_{1,28} = 3.37, p = .08 \)). Overall, the DPD group rated pictures as less arousing (M = 3.83, SD = 1.97) than the control group (M = 4.76, SD = 1.97). Exploratory tests revealed that compared to the control group, DPD patients tended toward rating neutral and pleasant pictures as less arousing (neutral pictures: \( t_{28} = 1.78, p = .09 \); pleasant pictures: \( t_{28} = 1.91, p = .07 \)).

**Dominance.** For Dominance, there was a main effect for valence \( F_{1.43,40.01} = 36.10, p < .001, \text{Greenhouse Geisser Epsilon} = .72 \) Participants indicated feeling less in control for unpleasant (M = 4.28, SD = 1.85) pictures than neutral (M = 5.83, SD = 1.63) and pleasant (M = 6.20, SD = 1.40) pictures. There was a also a valence X group interaction at the level of a trend (\( F_{1.43,40.01} = 3.12, p = .07, \text{Greenhouse Geisser Epsilon} = .72 \)). The DPD group tended toward rating pleasant pictures as less dominant (M = 5.62, SD = 1.44) compared to the control group (M = 6.77, SD = 1.36) \( t_{28} = 2.24, p < .05 \).
Emotion Regulation Conditions

Emotional Salience. For ability to modulate emotional salience, there was a main effect for group (F_{1,28} = 4.471, p < .05). Overall, the DPD group was better at regulating emotion (M = .043, SD = 0.13) than control group (M = -.023, SD = 0.11). There was also a valence X instruction X group effect (F_{1,28} = 4.377, p < .05), reflecting that the DPD group tended to better suppress emotion to unpleasant pictures (M = .12, SD = .33) compared to the control group (M = -.08, SD = .25), t_{28} = -1.929, p = .06 (see Figure 2A).

Arousal. For ability to modulate arousal, there was a trend toward a main effect for group (F_{1,28} = 3.35, p = .08). The DPD group was less able to modulate arousal levels (M = -0.05, SD = .14) than controls (M = .04, SD = .21; see Figure 2B). There were no interaction effects.

Dominance. For ability to modulate subjective dominance, there was a trend toward an instruction X group effect (F_{1,28} = 3.07, p < .10), reflecting that the DPD group tended to be better able to suppress loss of control during unpleasant pictures (M = .10, SD = .28) compared to the control group (M = -.11, SD = .36), t_{28} = -1.78, p = .09 (see Figure 2C).

Emotion Regulation Strategies

The groups showed differences in emotion regulation strategies used during the task. Compared to the control group, the DPD group reported they focused more on their physical experience during pleasant (X^2_4 = 14.29, p < .01) and unpleasant (X^2_3 = 10.19, p < .05) pictures, and varied their breathing less during unpleasant pictures at the level of a trend (X^2_3 = 6.92, p = .08).
Discussion

In this experiment, we investigated the ability of DPD patients to subjectively regulate emotion. During the task, DPD patients presented with more anxiety and had less positive affect and more negative affect than the control group. For the view condition, the DPD group rated pleasant pictures as less pleasant, tended to feel less in control during pleasant scenes, and tended to rate neutral and pleasant pictures as less arousing than the control group.

For pictures that were emotionally regulated, overall, DPD patients were better than the control group at regulating emotional salience, a result which was driven by the DPD group’s tendency to be better at suppressing unpleasant emotion. Compared to the control group, the DPD group tended to modulate arousal less effectively. The DPD group also tended toward a better ability to suppress feeling less in control of unpleasant scenes than the control group.

Differences in emotion regulation strategies were also found. Compared to control group, DPD patients reported a tendency toward less use of reappraisal strategies and more use of suppression in emotional situations. For the Regulation task, DPD patients focused on their physical experience more for both pleasant and unpleasant pictures and tended to alter their breathing less than the control group.

The tendency of DPD patients to rate pictures as less arousing during the view condition is consistent with previous findings (Sierra et al., 2002). Correspondingly, DPD patients also have decreased skin conductance (Sierra et al., 2002; 2006) and limbic activity (Phillips et al., 2001; Lemche et al., 2008) in response to viewing emotional stimuli. Decreased subjective arousal may, therefore, be due to dysfunction of the limbic system in DPD.

The tendency of DPD patients to rate pleasant pictures as less pleasant is also consistent with previous findings in which DPD patients rated unpleasant stimuli as less intense (Sierra et
al., 2006; Phillips et al., 2001). However, we did not find differences between the groups in emotional salience for unpleasant pictures. Discrepancies between findings for pleasant and unpleasant pictures may be related to differences in stimuli arousal levels. Sierra hypothesized that evaluation of emotional intensity may be, in part, dependent upon a stimulus’ representation of autonomic arousal, and therefore, evaluation of emotional intensity may also be dysfunctional in DPD due to decreased limbic activity. It should be noted that the current study employed pleasant pictures with lower standardized arousal ratings than unpleasant pictures as assessed by Lang et al. (2009). Thus, under high arousal circumstances, DPD patients may experience sufficient arousal levels and can accurately discern emotional salience. However, when stimuli are less arousing, DPD patients may find emotional stimuli less intense (i.e., interpret pleasant pictures as less pleasurable).

A superior ability to regulate emotion in DPD was driven by a trend significant ability of DPD patients to suppress emotion to unpleasant pictures. DPD patients also tended toward a better ability to suppress feelings of loss of control when viewing unpleasant pictures. Correspondingly, DPD patients reported a tendency to use more emotional suppression and less reappraisal.

Taken together, these results suggest that at the heart of depersonalization is pervasive emotional suppression. DPD patients report higher rates of childhood interpersonal trauma (Simeon et al., 2001). Frequent exposure to negative events in childhood may lead young DPD individuals to develop a pattern of withdraw from negative emotion or emotional avoidance. A depersonalized child may, therefore, not feel associated feelings of helplessness and loss of control that a highly traumatized child may feel. Hence, as adults, DPD patients generally feel less. This constant pattern of withdrawal and avoidance may also make it difficult for DPD
patients to modulate arousal, as demonstrated. Already low arousal levels would be difficult to lower further while a persistent pattern of emotional suppression would impede arousal enhancement. Thus, DPD patients might feel stuck in a pattern of emotional numbness.

Conclusion

Consistent with previous findings, we found that DPD patients rated emotional pictures as less arousing and less emotionally salient. However, to our knowledge, intentional modulation of emotion has never been investigated in DPD. We found that during active emotion regulation, DPD patients demonstrate a pattern of decreased positive emotionality and arousal as well as a pervasive suppression of negative emotion. Study 2 will investigate the relationship between subjective suppression during emotion regulation in depersonalization and corresponding physiological responsivity.
CHAPTER TWO

Aim II. Physiological Evidence for Impaired Emotion Regulation in Depersonalization Disorder

Corresponding with reports of hypoemotionality and hypoarousal in DPD, physiological measures indicate a decrease in neural response while viewing emotional stimuli: lower amplitudes in skin conductance response were found for unpleasant pictures and disgusted faces in DPD groups compared to control and anxiety groups (Sierra et al., 2002; 2006). Early case studies have also indicated decreases in skin conductance that corresponded to symptoms of depersonalization (Lader and Wing, 1966; Lader, 1975). Experiment 1 demonstrated that consistent with subjective reports of decreased emotionality in previous studies, DPD patients also demonstrate difficulties in subjectively enhancing emotion but a superior ability to suppress emotion. In this study, we aim to determine if impaired emotion regulation in DPD corresponds with physiological responses. In this study, DPD patients and a normal control group used a response-focused emotion regulation strategy, to up-regulate, or down-regulate their emotional response to pleasant and unpleasant pictures while skin conductance response and heart rate were measured. Participants then reported the valence (emotional salience, arousal, and dominance of each picture.

**Hypothesis:** We expected increased ability to suppress emotion subjectively would correspond with better ability to suppress emotion physiologically as measured by heart rate and skin conductance.

**Main finding:** For emotional salience, while control participants were better at subjectively modulating unpleasant emotion than pleasant emotion, the DPD group
showed no differences. However, heart rate measures indicated that compared to the control group, DPD patients were better at suppressing but worse at enhancing emotion (see below publication: Monde, Ketay, Giesbrecht, Braun, & Simeon, 2013 Reprinted with permission from Elsevier Inc).

Introduction

Depersonalization Disorder (DPD) is characterized by feelings of detachment from one’s mental processes or body (American Psychiatric Association, DSM IV-TR, 2000) and associated childhood interpersonal trauma, most notably emotional maltreatment (Simeon et al., 2001), alexithymia (Simeon et al., 2009), and emotional numbing (Simeon et al., 2008). DPD patients exhibit decreased skin conductance responses (SCR) to viewing emotional pictures (Sierra et al., 2002) and a differential time course of SCR during an emotional video viewing (Giesbrecht et al., 2010) compared to healthy controls. The hypoemotionality of DPD is associated with prefrontal cortex hyperactivation and limbic hypoactivation on fMRI (Lemche et al., 2007). This altered emotional responsiveness suggests that depersonalization may involve an impaired ability to upregulate emotion, a hypothesis previously untested. In the present study, physiologic and subjective ratings were recorded while DPD participants and controls modulated their response to emotional pictures. We hypothesized that individuals with depersonalization would have difficulty enhancing, but would be better at suppressing, emotion irrespective of stimulus valence.

Method

Subjects

Diagnosis was established using the Structured Clinical Interview for Dissociative Disorders-Revised (Steinberg, 1994). Participants also completed the Toronto Alexithymia Scale
(TAS; Bagby et al., 1994), Childhood Trauma Questionnaire (CTQ; Bernstein et al., 2003), Beck Anxiety Inventory (BAI; Beck and Steer, 1993), Beck Depression Inventory-II (BDI; Beck et al., 1996) and Cambridge Depersonalization Scale (CDS; Sierra and Berrios, 1996). Individuals with lifetime schizophrenia or bipolar disorder, and current major depression, eating disorder, or substance use, as well as major medical conditions were excluded. The study was approved by the Mount Sinai School of Medicine and all participants gave written informed consent.

*Emotion regulation task*

Stimuli were 49 pictures from the International Affective Pictures System (IAPS; Lang et al., 1999; 21 pleasant, 21 unpleasant, 7 neutral). The IAPS characterizes pictures in terms of valence and arousal, which is in line with the circumplex model of affect (Russell and Barrett, 1999). Pleasant and unpleasant pictures were equivalent in arousal, but different in valence. Stimuli were not chosen to represent specific emotions and were presented once for 12s each on a 15-inch computer screen in randomized order. A cue was presented for 4s followed by picture onset. A verbal instruction was presented 4s post picture onset. Consistent with Jackson et al. (2000) participants were instructed to enhance (increase the intensity of the emotion they feel), suppress (decrease the intensity of the emotion they feel), or maintain their emotional response to pleasant and unpleasant pictures, while for neutral pictures only the maintain instruction was given. No specific instructions were provided for heart rate (HR) or SCR. Participants were free to choose their regulation strategy but instructed not to think about things unrelated to the scene depicted. A blank screen was displayed for 12s following picture offset. Participants then rated the picture’s valence using the 9-point Self Assessment Manikin scale (Lang et al., 1999). Finally, the word “Relax” appeared onscreen for 20s.

*Skin Conductance and Heart Rate Measurement*
SCR and HR were measured with two BioPac EL507 Disposable Electrodermal Electrodes that were filled with isotonic gel and placed on the middle phalanx of middle and ring finger of the non-dominant hand (Fowles et al., 1981). Before electrodes were attached, participants rinsed their hands with distilled water. SCR was recorded using a BioPac GSR100C with gain of 5 μS/ V and a low-pass filter at 10 Hz. HR was recorded using a BioPac PPG100C coupled to a photoelectric pulse transducer (TSD200). Signals were sampled at 200 Hz by a BIOPAC MP150 (Biopac Systems, Goleta, CA) system connected to a data-acquisition computer running the Acknowledge v3.8.2 software package. For HR and SCR, levels in the 4s preceding the emotion regulation instruction (resting level) and the 8s following the instruction were averaged for each condition. These bins were then transformed by subtracting the average resting level from the subsequent instruction.

**Calculation of Ability Scores**

We a priori operationalized that a superior ability to enhance emotion would be demonstrated by an increase in score on physiologic and subjective measures of emotion compared to the maintain condition. Conversely, a superior ability to suppress would be demonstrated by a decrease in these scores compared to the maintain condition. Therefore, we calculated an ability score reflecting each individual’s capacity to regulate emotion in response to pleasant and unpleasant pictures using mean values for each measure (Enhance Ability=Enhance - Maintain; Suppress Ability=Maintain - Suppress). Thus, negative ability values represent an inability to regulate emotion as instructed.

**Statistical Analyses**
Independent t-test and chi square statistics were used to analyze group differences in demographic and clinical characteristics. For subjective ratings, SCR, and HR separately, a 3 (valence) * 2 (group) Repeated Measures Analysis of Variance (RM-ANOVA) was conducted for the maintain condition, and a 2 (valence) * 2 (enhance/suppress instruction) * 2 (group) RM-ANOVA was calculated for ability scores. Mann-Whitney U and paired t-tests were used for post hoc analyses. Pearson’s correlations and partial correlations controlling for depression and anxiety separately were performed between descriptive and outcome variables for the combined sample and between ability scores for each group.

Results

Sample Characteristics

Demographic and clinical characteristics (mean ± SD) for the 14 DPD (4 women) and 14 healthy control (5 women) participants respectively were: Age: 30.8 ±7.2 vs. 31.3 ± 11.9; Education (years): 16.6 ±2.5 vs. 16.4 ±2.1; CDS: 144.4 ±49.9 vs. 12.6 ±13.8; BDI: 25.0 ±9.8 vs. 2.9 ±3.2; BAI: 20.3 ±13.4 vs. 2.8 ±3.0; TAS: 43.1 ±17.9 vs 33.2 ±10.7; CTQ: 43.1 ± 17.9 vs. 33.2 ± 10.7. Six DPD participants were taking psychotropic medications: sertraline, venlafaxine (n=2), quetiapine plus ramelteon, tranylcypromine, and donepezil plus lamotrigine. Three patients met current criteria for Dysthymia, 2 for Panic Disorder, 2 for Social Anxiety Disorder, 1 for Generalized AnxietyDisorder, 1 for Hypochondriasis, 1 for Body Dysmorphic Disorder, and 1 for Anxiety Disorder, NOS. Comorbidities for 3 patients were missing. Age of onset of DPD was 16.6±2.5 years, with a duration of 128.3±33.0 months. The groups did not significantly differ in age, gender, or education. The DPD group tended toward a higher score on the CTQ (P
and its emotional abuse subscale compared to controls: (10.2 ±6.2 vs 6.6 ±2.9, \( t = -1.95, P=0.07 \)). The DPD group scored significantly higher on all other questionnaires (\( P'<0.001 \)).

**Group Comparisons**

**Maintain Condition.** For subjective ratings, a significant main effect for valence was found (\( F_{1,385, 36.003} = 64.81, P < 0.001 \)): pleasant pictures were rated as more pleasant than neutral pictures, while unpleasant pictures were rated as more unpleasant than neutral pictures (\( P'<0.001 \)). There was also a trend group effect for valence (\( F_{1,26} = 3.25, P = 0.083 \)), as DPD participants tended to rate pictures more negatively than controls. For SCR, a significant main effect for valence was found (\( F_{2,50} = 4.844, P < 0.05 \)), reflecting increased SCR for emotional compared to neutral pictures (\( P < 0.025 \)). No significant effects were found for HR.

**Emotion Regulation Ability.** For subjective ratings, there was a significant main effect for valence (\( F_{1,26} = 17.30, P < 0.001 \)) indicating all participants were better able to subjectively regulate their response to unpleasant compared to pleasant pictures. There was also a significant instruction x valence interaction (\( F_{1,26} = 6.00, P = 0.02 \)), indicating all participants were more able to enhance emotion to unpleasant compared to pleasant pictures. Finally there was a marginal group x valence interaction (\( F_{1,26} = 4.21, P = 0.050 \); Figure 3A), as controls were better at modulating emotion to unpleasant than pleasant stimuli (paired \( t=3.19, P = 0.004 \)) while the DPD group showed no valence difference.

For HR, there was a significant group X instruction interaction (\( F_{1,25} = 4.56, P = 0.03 \); Figure 3B): compared to controls, DPD participants had a lesser ability to enhance (\( U = 246.00, P < 0.05 \)) and a greater ability to suppress (\( U = 234.50, P < 0.05 \)) emotion irrespective of valence. There were no significant findings for SCR.

**Correlations**
Ability to subjectively enhance unpleasant emotion was negatively correlated with depersonalization ($r=-0.42, P=0.03$) and alexithymia ($r=-0.46, P=0.01$). Ability to subjectively suppress pleasant emotion was positively correlated with childhood trauma ($r=0.55, P=0.003$). After controlling for anxiety, the above-mentioned correlations remained intact. After controlling for depression, only the positive correlation between ability to subjectively suppress pleasant emotion and childhood trauma was unaffected ($r=0.58, P=0.002$). In addition, alexithymia was negatively correlated with ability to suppress positive emotions via HR ($r=-0.44, P=0.03$).

For the DPD group, there was a positive correlation between HR and ratings for ability to enhance unpleasant emotion ($r=0.555, P=0.04$). For the control group, there was a positive correlation between HR and SCR for ability to suppress pleasant emotion ($r=0.661, P=0.01$). After controlling for anxiety and depression, the above-mentioned correlations remained intact. All other correlations were non-significant.

Discussion

To our knowledge, this is the first study examining emotion regulation in depersonalization disorder. As predicted, DPD participants exhibited an impaired ability to enhance and a heightened ability to suppress emotion (as indicated by HR). This was further supported by a positive association between HR and ratings for ability to enhance unpleasant emotion, indicating a direct and dynamic relationship between subjective emotion regulation and physiologic responsivity in DPD. Consistent with the hypoemotionality reported in the disorder, the inability to feel an emotion would make it impossible to increase the emotion whereas the act of suppression could employ a strategy of emotional withdrawal, resulting in reduced physiologic responsivity typical of depersonalization.
Additionally, the negative association between ability to enhance unpleasant emotion and depersonalization, as measured by subjective ratings appeared to be mediated by depression levels suggesting that the inability to subjectively upregulate unpleasant emotion seems to be due to heightened levels of depression in DPD. Germene to this finding is a study by Ehring et al. (2010) who found that recovered-depressed persons seem to employ emotional suppression more often than the control group. The relationship between suppressing and enhancing emotion should be further investigated.

The negative relationship between alexithymia and ability to subjectively enhance unpleasant emotion or suppress HR response to positive emotion (when controlling for depression) may imply that deficits in identifying emotion lead to impairments in regulating them. While alexithymia is itself a construct distinct from depersonalization, alexithymia, and in particular difficulties identifying emotion, are associated with depersonalization (Simeon et al, 2001) and may therefore contribute to the debilitating effects of the disorder.

Interestingly, childhood trauma was associated with suppression of positive emotion, diverging from the alexithymia and depersonalization findings in its impact on emotion regulation and warranting further assessment in future studies.

One important limitation of the study may lie in how we operationalized emotion regulation ability as an outcome variable. Documented inconsistencies in the literature regarding physiological responsivity both to emotional stimuli (see Kreibig, 2010 for review) as well as instructions to modulate emotions (see Urry, 2009) indicated this is a broader problem within the field which may be due to variations in methodology. While some studies diverge from our findings, studies using similar design paradigms to ours have found analogous trends in HR, SCR, and ratings in response to instruction to enhance and suppress emotion (Bernat et al., 2011;
Urry, 2009). Correspondingly, the positive correlations we found between ability scores for some emotion regulation conditions lend support for our operational definitions of emotion regulation abilities for the three measures.

Findings of this study may have important treatment implications, such as utilizing therapeutic interventions that emphasize experiencing, labeling, and communication of feelings in order to more adaptively regulate emotion, that is, suppress less and enhance more. Studies investigating emotion regulation strategies more comprehensively within larger non-medicated samples and including depressive control participants are needed.
CHAPTER THREE

Aim III: To Determine the Relationship between Cortisol and Oxytocin Responsivity to Acute Psychosocial Stress in DPD

DPD patients have demonstrated dysregulated basal cortisol levels (Simeon et al., 2001; Stanton et al., 2001; Simeon et al., 2007) and depersonalization has been associated with differences in the cortisol surge under psychosocial stress (Simeon et al., 2007; Giesbrecht et al., 2007). However, oxytocin levels have never been measured. Previous studies have shown that cortisol administration is associated with increased OT levels (Tops et al., 2007; Tops et al., 2012), and depression and anxiety tend to be associated with higher levels of OT (Parker et al., 2010; Cyranowski et al., 2008). Additionally, a recent study demonstrated elevated OT levels in hyperemesis gravidarum patients who presented with increased levels of dissociation (Seng et al., 2013) suggesting that OT levels may be high in depersonalized patients. We investigated emotion regulation and neurohormonal changes during acute psychosocial stress in DPD patients and a normal control group. DPD patients and normal controls performed the Trier Social Stress Test. Saliva samples were collected directly before, immediately following, and at 20 minutes and 40 minutes post stress task completion, and oxytocin and cortisol levels were assessed.

Hypothesis: We predicted that consistent with previous studies, DPD patients would rate the TSST as more stressful and have higher overall cortisol than a normal control group. We also expected higher oxytocin levels for DPD patients than the control group.
**Main findings:** The TSST induced subjective stress in the control group but not the DPD group. Compared to the control group, the DPD group had higher overall levels of cortisol and oxytocin.

**Methods**

*Participants*

Participants were 10 DPD patients and 15 normal controls recruited via craigslist.com. Normal controls scored below 12 on the Beck Depression Inventory and Beck Anxiety Inventory and below 10 on the Dissociative Experiences Scale. Diagnosis of dissociative disorders was established using the Structured Clinical Interview for Dissociative Disorders (SCID-D-R; Steinberg, 1994). Participants with diagnoses of substance abuse, schizophrenia, eating disorders, severe depression, suicidality, as well as history of head trauma were excluded. Nine dissociative disorder patients met diagnostic criteria for DPD while one participant met criteria for Dissociative Disorder NOS (not otherwise specified). Five DPD participants were taking wellbutrin plus trazodone; lamictal, klonopin, wellbutrin, EMSAM patch, plus topomax; synthroid plus clomid; lexapro plus wellbutrin; and lamictal, Zoloft, seroquel, plus klonopin. DPD patients were compensated $50 and normal controls were compensated $30 for study participation. Participants were instructed to refrain from eating, drinking and smoking for at least 1 hour prior to study participation and to avoid alcohol consumption for at least 12 hours prior to arrival. Two women were post-menopausal, and pre-menopausal women participated during the follicular stage of their menstrual cycle. One woman was taking birth control.

*Measures*

Beck’s Anxiety Inventory (BAI: Beck, Epstein, Brown, & Steer, 1988) is a 21 item measure that assesses severity of anxiety symptoms in the last week. Each item contains four
possible statements related to a given symptom (e.g., unsteady, terrified, and numbness or tingling) that are rated on a likert scale from 0-3. The BAI has shown high internal consistency (a = .92) and test-retest reliability over 1 week, r (81) = .75.

The Relationship Scale Questionnaire (RSQ: Griffin & Bartholomew, 1994) is a 30 item questionnaire that assesses orientation to relationships on a 7-point likert scale from 0, Not at All to 6, Very Much. The RSQ contains 4 subscales: Secure scale, Fearful scale, Preoccupied scale, and Dismissing scale.

The Difficulties in Emotion Regulation Scale (DERS; Gratz, & Roemer, 2004) is comprised of 36 self-report questions which measure multiple aspects of emotional dysregulation. The DERS yields a total score as well as scores for its 6 subscales: Non-acceptance of emotional responses (NONACCEPT), Difficulties engaging in goal directed behaviour (GOALS), Impulse control difficulties (IMPULSE), Lack of emotional awareness (AWARE), Limited access to emotion regulation strategies (STRATEGIES), and Lack of emotional clarity (CLARITY).

The Profile of Moods Scale – Short form (POMS-SF: McNair, Lorr, & Droppleman, 2003) measures state levels of various moods and is used to assess distress. The POMS-SF is comprised of 37 self-report items and includes 5 subscales: depression, anger-hostility, tension-anxiety, vigor, and fatigue subscales. Internal consistency estimates (chronbach’s alpha) for the POMS-SF subscale scores range from .76 to .95 (Curran, Andrykowski, & Studts, 1995).

Other questionnaires included the Dissociative Experiences Scale (DES), the Cambridge Depersonalization Scale (CDS), the Childhood Trauma Questionnaire (CTQ), Beck’s Depression Inventory (BDI), the Toronto Alexithymia Scale (TAS), the Emotion Regulation Questionnaire
(ERQ), the Peritraumatic Dissociative Experiences Scale (PDEQ), and the Positive and Negative Affect Scale (PANAS). See study 1 for full description of these questionnaires.

**Trier Social Stress Test**

The Trier Social Stress Test is a frequently used standardized stress task that comprises of a preparatory phase of 5 minutes, followed by a mock job interview (5 min) and a mental arithmetic task (5 min) in front of an audience (Kirschbaum et al., 1993. The TSST has been shown to reliably increase subjective stress and salivary cortisol levels in participants. For the TSST, the participant was lead to a room and introduced to the audience prior to the start of the interview. The procedure of the interview was then explained and the participant was instructed that the audience members were specially trained to monitor non-verbal behavior. The participant was led away to another room to prepare for the interview. After 5 minutes preparation period, the participant was brought back to the room of the audience to for the interview. Once 5 minutes had passed, the participant was asked to count backward from 3,081.

**Procedure**

Figure 4 presents a timeline for the procedure of experiment 3. All experiments were conducted between 12 and 5pm. Upon arrival, participants signed an informed consent and completed a demographic questionnaire, the Dissociative Experiences Scale, The Cambridge Depersonalization Scale, The Childhood Trauma Questionnaire, Beck’s Depression Inventory, Beck’s Anxiety Inventory, the Toronto Alexithymia Scale, the Emotion Regulation Questionnaire, the Difficulties in Emotion Regulation Questionnaire, and the Relationships Scale Questionnaire. After rinsing their mouth, participant rested in an empty room alone for 10 minutes. After the rest period, participants completed the Peritraumatic Experiences
Dissociative Experiences Questionnaire (PDEQ), the Positive and Negative Affect Scale (PANAS), and the Profile of Mood States-short form (POMS-SF). Saliva samples were also taken. Participants then underwent the TSST. Following the TSST, the participants completed the subjective stress scale, the PDEQ, PANAS, and POMS-SF and a second saliva sample was taken. State emotion questionnaires and saliva samples were taken again at 20 and 40 minutes post TSST cessation. Participants were then debriefed and thanked for participation and compensation was provided.

*Enzyme Immunoassays*

Saliva was vortexed and 1 mL was aliquoted. Aliquot and remaining saliva were then stored at -80 degrees F. Oxytocin assay: 1 mL aliquot was thawed, and centrifuged at 25000 rpm for 15 min. 0.8 mL was aliquoted and 0.8 mL of 0.1% trifluoroacetic acid (TFA; Fisher Scientific, Waltham, MA) in water was added. Samples were centrifuged again at 25,000 rpm for 15 minutes. Sep pak (200 mg, 3 mL; Thermo Scientific, Bellefonte, PA) columns were equilibrated with 1mL acetylnitrile (Fisher Scientific, Waltham, MA) followed by 12 mL of 0.1% TFA in water. Supernatant was then added to the column and allowed to filter through. Sep pak was then washed with 12 mL of 0.1% TFA in water. Waste was discarded. 3mL of 40% TFA/ 60% acetylnitrile concentration was added to the sep pak to elute the oxytocin which was collected in a 5mL falcon tube. Eluant was evaporated in a vacuum centrifuge and stored at -80 degrees F until assay. OT assay was performed using Enzo Life Sciences Kit (Lause, Switzerland). Cortisol was assayed using Salimetrics protocol and ELISA kit (State College, PA).
Statistical Analyses

A “stress” score was created for each time point by calculating the average of the tension-anxiety and anger-hostility subscales of the POMS-SF. We conducted a 2 (Group: DPD vs. Control) X 4 (Time: Pre-TSST, Post-TSST, TSST+20, TSST+40) repeated measures analysis of variance (RM ANOVA) for the PDEQ, PANAS positive and negative subscales, POMS-depression subscales, and stress score. We also performed a 2 (Group: DPD vs Control) X 4 (Time: Pre-TSST, Post-TSST, TSST+20, TSST+40) repeated measures analysis of covariance (RM ANCOVA) for oxytocin and cortisol levels controlling for age and gender. Post hoc tests using Bonferroni correction and Wilcoxon Signed-ranks were performed.

We calculated the following subscales for the questionnaires: DES-depersonalization (DES-DPS); DES-amnesia (DES-AMN) DES-absorption (DES-ABS), DES-taxon (DES-T), CTQ-physical abuse (CTQ-pa), CTQ-physical neglect (CTQ-pn), CTQ-emotional abuse (CTQ-ea), CTQ-emotional neglect (CTQ-en), CTQ-sexual abuse (CTQ-sa), ERQ-suppression strategies, ERQ-reappraisal strategies, DERS-non-acceptance of (the individual’s own) emotional responses (DERS-Non-accept), DERS-difficulties engaging in goal-directed behavior (DERS-Goals), DERS-impulse control difficulties (DERS-Impulse), DERS-lack of emotional (self-) awareness (DERS-Aware), DERS-limited access to emotion regulation strategies (DERS-Strategies), DERS-lack of emotional clarity (DERS-Clarity), RSQ-secure, RSQ-fearful, RSQ-preoccupied, RSQ-dismissing,. Pearson’s product moment correlations were performed between hormones, descriptive variables, and outcome variables for the combined sample.
Results

Demographic and Clinical Characteristics

Table 2 presents demographics and clinical characteristics of the groups. No significant differences were found between the groups for age, gender or marital status. The groups significantly differed in ethnicity and the DPD group tended toward higher annual income than control group. The DPD group scored higher on the DES and all subscales except for amnesia. DPD patients also scored higher on the BAI, BDI, TAS total score, TAS-difficulty describing feelings, TAS- difficulty identifying feelings, CTQ-total score, CTQ-emotional abuse subscale, and CTQ emotional neglect subscale, RSQ-preoccupied subscale, and tended toward higher scores for the DERS-goals and CTQ-sexual abuse. The control group scored higher on the BAS-fun seeking and RSQ secure relationship style.

Changes in Transient Dissociation

For the PDEQ, there was a main effect for time (F_{2.20,50.59} = 14.97, p < .001): transient dissociation increased at the post-TSST time point, decreased by the TSST+20 time point, and decreased further at TSST + 40 (Figure 5D). The DPD group showed more overall dissociation than the control group (main effect for group: F_{1,23} = 8.77, p <.01). Finally, there was a group X time interaction: F_{2.20,50.59} = 5.73, p < .01. For the control group, dissociation increased from Pre-TSST to Post-TSST (Z = -3.19, p < .01), and then decreased from Post-TSST to TSST+20 minutes (Z = 3.09, p < .01) and from Post-TSST to TSST+40 minutes (Z = -3.19, p < .01). However, no significant changes in dissociation were found in the DPD group (see Figure 5D).
Thus, transient dissociation was higher in the DPD group than normal controls, and the TSST induced dissociation in the control group but not the DPD group.

Changes in Emotion

For subjective stress (Figure 5E), there was a main effect for time (F \(2.10, 48.35 = 7.18, p < .05\)): subjective stress increased in response to the TSST and decreased between post-TSST and TSST+20min as well as between post-TSST and TSST+40min. There was also a group X time interaction (F \(2.10, 48.35 = 4.13, p < .05\)): Although the same changes in stress found in the combined group were found in the control group, the DPD group showed no changes in subjective stress in response to the TSST. There was no group effect. (see Figure 5E). Thus, the TSST induced stress in the control group but not DPD patients.

For the PANAS-positive affect (Figure 5A), there was a main effect for time (F \(2.02, 46.63 = 7.62, p < .01\)) : positive emotion decreased from Pre-TSST to TSST + 40 minutes, from Post-TSST to TSST +20 minutes and from between Post-TSST to TSST+ 40 minutes. There was also a time X group interaction: F \(2.02, 46.63 = 3.66, p < .05\). The control group showed a decrease in positive emotion from Post-TSST to TSST+20 minutes (Z = -2.03, P < .05) from Post-TSST to TSST+40 minutes (Z= -2.46, p < .05) as well as an overall decrease in positive emotion from Pre-TSST to TSST + 40 minutes (Z = -3.18, p <.01). For the DPD group, positive emotion decreased only from TSST+20 minutes to TSST+40 minutes (Z = -2.51, p < .05) and from Post-TSST to TSST + 40 minutes (Z = -2.26, p <.05; see Figure 5). No main effect for group was found for the PANAS-positive affect subscale. Hence, the TSST decreased positive emotion in both groups, but for the DPD group, decrease in positive emotion occurred later.
For the PANAS-negative affect (Figure 5B), negative emotion decreased from Post-TSST to TSST+ 40 minutes in the combined group (main effect for time: $F_{2.12, 48.65} = 3.45, p < .05$). There was also a time X group interaction. While negative mood did not change significantly for the DPD group, for the control group, there was an increase in negative mood from Pre-TSST to Post-TSST ($Z = -3.30, p < .01$) and a decrease from Post-TSST to TSST+ 20 minutes ($Z = -3.21, p < .01$), from TSST+ 20 to TSST+40 minutes ($Z = -2.02, p < .05$) and overall from Post-TSST to TSST+ 40 ($Z = -3.31, p < .01$; see Figure 5). No main effect for group was found. In sum, negative mood increased in the control group while the DPD group showed no change in negative emotion.

For depression (see Figure 5C), although there were no main effects for group or time, we found a time X group interaction: $F_{1.65, 37.97} = 8.71, p < .01$. Depression increased from Pre-TSST to Post-TSST ($Z = -2.18, p < .05$), then decreases from Post-TSST to TSST+40 minutes in the control group ($Z = -2.11, p < .05$). However, for the DPD group, depression decreased from Pre-TSST to Post-TSST ($Z = -2.49, p < .05$) but increased from the Post-TSST to TSST+40 minute ($Z = -2.05, p < .05$). There was also an overall decrease in depression from the Pre-TSST to TSST+40 minute for the DPD group ($Z = -2.54, p < .05$; see Figure 5). Thus, while the control group showed an increase in depression in response to the TSST, the DPD group showed a decrease.

**Hormone Levels**

*Cortisol.* There was a main effect for group: $F_{1, 21} = 5.12, p = .034$. The DPD group had higher overall cortisol levels than the control group (see Figure 6A). There was also a main effect for gender: $F_{1, 21} = 9.14, p = .006$. Post-hoc Mann Whitney-U tests indicated that men had
higher cortisol levels than women at all time points (see Figure 7). Finally, there was a time X gender interaction: $F_{1.97,41.31} = 5.55$, $p = .008$. For women, there were no significant main effects or interactions. For men, there was a main effect for time ($F_{1.94, 27.11} = 11.54$, $p < .001$): Cortisol levels increased from Pre-TSST to Post-TSST and decreased from TSST+20 to TSST+40. There was also a main effect for group ($F_{1,14} = 4.81$, $p = 0.05$): Men in the DPD group had higher overall cortisol levels than men in the control group (see Figure 6B). Although there was no group X time interaction for men, exploratory Mann Whitney U test indicated that compared to men in the normal control group, men in the DPD group had higher cortisol levels at the Post-TSST time point ($Z = -2.06$, $p < .05$).

Oxytocin. Oxytocin levels showed a marginally significant main effect for group: $F_{1,19} = 4.18$, $p=.055$ with DPD patients tending toward higher OT levels than the control group (see Figure 8A). There was also a trend toward a main effect for time: $F_{3,57} = 2.25$, $P=.09$. Although there was no group X time interaction, exploratory Wilcoxon signed-rank test indicated that for the control group, Post-TSST levels of OT were significantly higher than Pre-OT levels ($Z = -2.103$ $p <.05$) and OT at TSST+20 tended toward higher levels than Pre-TSST OT ($Z = -1.92$, $p < .06$). No differences between OT levels of any time points for the DPD group were found. There was a trend toward a main effect for gender: $F_{1,19} = 3.69$, $p=.07$ (Figure 8B). Men tended toward higher OT levels than women with men demonstrating trend significant higher OT levels than women at the Post-TSST time point ($Z = -1.34$, $p = .055$; see Figure 9). As well, Post-TSST OT levels were higher than Pre-TSST OT levels in men ($Z = -2.16$, $p < .05$) but not women ($Z = -0.53$, $p > .05$).
Peak Hormone levels

When we compared OT levels between groups across the study, patients had a higher peak oxytocin level than controls (mean=11.56 pg/mL SD= 4.57) and it occurred pre-TSST while the control group had a peak oxytocin level (mean=7.64 pg/mL, SD = 3.45) which occurred at TSST+40 (Z = 2.28, p < .05). In contrast, there were no differences between the groups in peak cortisol levels.

However, we found sex differences in peak hormone levels. For women, the DPD group tended toward higher peak OT levels (mean = 9.07 pg/mL, SD = 3.33) compared to the control group (mean = 5.53 pg/mL, SD = 1.17) with peak OT levels in both groups occurring Pre-TSST (Z=1.72, p <.09). For women, peak cortisol levels occurred Post-TSST, but no differences were found between the groups for cortisol levels.

For men, the DPD group had higher peak OT levels (mean = 13.23 pg/mL, SD = 4.75) compared to the control group (mean = 8.82 pg/mL, SD = 3.78; Z = 2.12, p < .05). In both groups for men, peak OT levels occurred TSST+20. Men in the DPD group also tended toward higher peak cortisol levels (mean =.59 ug/dL, SD=.33) compared to the control group (mean = .35 ug/dL, mean = .08; Z=1.95, p=.05). In both groups for men, peak cortisol levels occurred Post-TSST.

In sum, while the groups did not differ in peak cortisol levels for men and women combined, peak oxytocin levels in DPD patients were higher and occurred earlier than the control group. For women, peak OT levels occurred before stress induction, and female DPD patients demonstrated higher peak OT levels than female control participants. For men, peak OT levels occurred at TSST + 20 min with DPD men demonstrating higher peak OT levels than
normal male controls. Peak cortisol levels in men and women occurred directly following the TSST and tended to be higher in male DPD patients than normal male controls.

**Correlations between Oxytocin and Cortisol**

Table 3 presents correlations between oxytocin and cortisol for the combined control and DPD patient group. For DPD patients and normal controls combined, cortisol decrease during early stress recovery (Post-TSST – TSST+20) was positively correlated with OT decrease during early stress recovery (r = .568, p < .01) and decrease in OT during the total stress recovery period (Post-TSST – TSST + 40; r = .573, p < .01). Oxytocin and cortisol showed no other associations for the combined group. Interestingly, correlations between oxytocin and cortisol differed between the groups. As presented in Table 4, for the control group, OT decrease during early stress recovery was positively associated with post-TSST cortisol (r = .667, p < .01), decrease in cortisol during early stress recovery (r = .607, p < .05), total cortisol stress recovery (Post-TSST – TSST+20; r = .594, p < .05), as well as cortisol stress reactivity at the level of a trend (r = .471, p = .08). In the control group, total OT stress recovery was also associated with cortisol decrease during early stress recovery (r = .617, p < .05). However, Table 5 shows that for the DPD group, only the association between decreased OT and cortisol during early stress recovery was significant (r = .683, p < .05).

**Correlations between Emotion and Hormone levels**

As shown in Table 6, there were several associations between OT and emotionality. There was a significant positive association between pre-stressor OT and lower levels of pre-stress positive affect and a trend significant positive association between pre-stressor OT and pre-stressor levels of depression. Post-stressor OT was associated with general depression levels
(BDI score), lower levels of pre-stressor positive affect, lower levels of post-stressor positive affect, less post-TSST subjective stress, less increase in subjective stress during the TSST, and less total decrease in depression and stress. There were no significant associations between emotion and OT stress reactivity. However, OT decrease during early stress recovery was associated with less decrease in depression over the total stress recovery period.

For cortisol, pre-TSST and post-TSST cortisol was associated with more decrease in positive emotion during total stress recovery. Cortisol reactivity was associated with reduction in positive emotion during the early recovery phase as well a decrease in positive emotion during total stress recovery. Decrease in cortisol during early recovery was associated with less decrease in depression during total recovery. Total cortisol recovery was associated with less decrease in positive emotion under stress but more decrease in positive emotion during total recovery. Cortisol reactivity was also positively associated with the emotion regulation strategy of suppression, however, no relationship between the emotion regulation strategy of reappraisal and hormone levels was found at any time point.

Correlations between Hormones, Dissociation and Childhood Trauma

Correlations presented in Table 7 control for general levels of depression (BDI score) and anxiety (BAI score). Results in the combined sample demonstrate that higher levels of OT and cortisol were positively related to dissociation. Specifically, pre-stressor transient dissociation was associated with pre-stressor OT and less OT increase under stress. Post-stressor transient dissociation was associated with less decrease in OT during early stress recovery as well as during total stress recovery. For depersonalization score (DES-DPD), there was a trend toward
lower decreases in OT during early stress recovery and higher cortisol levels pre- and post-TSST as well as a trend toward higher cortisol stress reactivity.

Childhood trauma was also related to elevated hormone levels (see Table 7). Emotional abuse was associated with higher pre-TSST OT levels as well as pre-TSST and post-TSST cortisol levels. Physical neglect was associated with less decrease in cortisol during early stress recovery.

Discussion

In this experiment, we investigated the relationship between salivary cortisol and oxytocin levels of DPD patients and normal controls under acute social stress. We found that in the combined group, decreases in oxytocin and cortisol were positively related during the first 20 minutes post stressor (early stress recovery). However, group differences for these hormones were evident. Consistent with previous studies (Simeon et al, 2001; Simeon et al, 2007), DPD patients showed higher cortisol levels than the control group. DPD patients also tended toward higher OT levels than normal controls. For OT, peak levels were higher and occurred earlier for the DPD group compared to normal controls. Additionally, for the control group, post-stress cortisol levels were associated with a decrease in OT during early stress recovery. There was also a trend significant positive association between cortisol reactivity and OT decrease during early stress recovery. These associations were not present for DPD patients. Given that OT administration has shown to decrease stress, these elevated levels in DPD may represent a homeostatic mechanism to decrease stress by DPD patients. We further explore this hypothesis in the final discussion section.
Group differences were also evident for dissociation and subjective emotion. For the control group, the TSST induced stress, dissociation depression, and negative emotion. Compared to the control group, DPD patients showed elevated levels of depression, negative emotion, and dissociation and tended toward higher levels of subjective stress and lower levels of positive emotion. Additionally, DPD patients showed no changes in these emotional states except for depression where instead of an increase in response to stress, DPD patients demonstrated a decrease in depression. These results further demonstrate dysregulated subjective emotion in DPD and may be related to the higher levels of alexithymia that DPD patients experience. Difficulty in identifying and describing emotion may impede the ability of DPD patients to recognize changes in emotion. As well, since elevated post-stress OT levels were associated with alexithymia, dysregulated hormone levels may also be playing a role in alexithymia in DPD.

Hormone levels were associated with dissociation in the combined group. Dissociation and depersonalization were associated with high cortisol levels, and there was a trend significant association between depersonalization severity and cortisol stress reactivity. These results are consistent with previous studies that found higher cortisol levels in DPD patients compared to controls (Simeon et al., 2001; Simeon et al.; 2007) as well as one study that demonstrated an association between depersonalization and stress reactivity in undergraduates (Giesbrecht et al., 2007). However, Simeon et al. (2007) found an inverse relationship between dissociation and cortisol stress reactivity. All studies suggest dysregulated cortisol in DPD. Higher Pre-stress OT and lower OT stress reactivity (increase in OT under stress) were related to pre-TSST levels of dissociation. These results suggest that with high levels of dissociation, basal OT is also high and that OT levels may not increase (but possibly decrease) under stress. However, we may
consider that pre-stressor measures were all collected in a stressful context: All participants were informed in the consent form that they would be speaking before a panel of judges. Thus, measures may not represent a true baseline for DPD, and elevated OT levels in DPD patients may be in anticipation of stress. Post-stress dissociation levels were associated with less OT stress recovery suggesting that unlike non-dissociated participants, individuals more susceptible to elevated dissociation under stress may present with elevated oxytocin levels after stress as well.

It should be noted that all female participants were in either the follicular phase of their menstrual cycle or post-menopausal. Consistent with previous studies (Walder et al., 2012; Kirshbaum et al., 1999), we found lower cortisol levels and a trend toward lower OT levels in female participants than males, and males showed a cortisol response to the TSST while women did not. This may suggest that higher estrogen levels during the follicular phase attenuate the stress response in women as previous studies have shown (Lindheim, Legro, Morris, Wong, Tran, Vijod, et al., 1994). As well, higher cortisol levels were found in male DPD patients compared to male normal control participants, but female DPD patients and controls showed no difference. Together, these results may indicate that DPD in men is associated with more cortisol than non-depersonalized men while DPD in the follicular phase may not differ from non-depersonalized women in the follicular phase. However, the small sample of female participants makes it difficult to draw definitive conclusions regarding hormone differences between female DPD patients and normal controls. Future studies should investigate sex differences and menstrual phase in relation to depersonalization symptomology.

For childhood trauma, emotional abuse was associated with elevated basal (pre-TSST) OT levels as well as elevated pre- and post-stressor cortisol. These findings diverge from
previous studies that demonstrated lower basal OT (Heim et al., 2009) and cortisol (Carpenter et al., 2007) in individuals with a history of child abuse. These differences may also be related to higher basal OT levels due to anticipatory stress as discussed above. Nonetheless, these associations may represent a dysregulated hormonal response under stress in persons with a trauma history.

Relationships between hormone levels and emotion were also found. Pre-stressor OT was associated with lower pre-stress positive emotion and a trend toward higher pre-stress depression while post-stressor OT was associated with higher levels of general depression and lower levels of positive emotion. This is consistent with previous findings: Taylor et al (2006) also found that OT was related to lower pre- and post-TSST positive emotion in older women. Positive mood induction has also been shown to decrease OT levels (Turner et al., 2002). Although one study found no association between peripheral OT levels and depression (Altemus et al., 2001), other studies have also found a positive association between depression and oxytocin: Parker et al. (2010) found evidence for elevated plasma OT in depressed patients while Cyranowski et al. (2008) showed that depressed women had higher OT levels while recalling situations where they felt love or infatuation. Additionally, OT administration has been shown to decrease depressive symptoms in rats (Arletti & Bertolini, 1987). Therefore, higher OT levels in depression may represent an endogenous compensatory mechanism whereby OT is released in an attempt to counter feelings of dysphoria. Additionally the negative association between OT decrease during early stress recovery and decrease in depression during stress recovery further suggests that sustained elevated OT levels after stress are necessary to attenuate post-stress depression. Post-stress OT was also associated with lower subjective stress levels post-stressor as well as less increase in stress during the TSST. These results are consistent with findings for the anxiolytic
effects of OT administration (Heinrichs et al., 2003). Taken together, these results suggest that under stress, OT may play a role in attenuating negative emotion. We further elaborate on this hypothesis in the final discussion section.

Conclusions

In this study, we show a distinctive relationship between cortisol and OT for the control group: elevated cortisol after stress is associated with decreased OT during OT recovery. This association was not found in DPD patients. Instead, post-stress dissociation was associated with a lesser decrease in OT during stress recovery in the combined group as well as lower levels of subjective stress reactivity in depersonalized individuals. DPD patients presented with elevated cortisol and a tendency toward elevated OT levels. DPD patients also showed higher peak OT levels which occurred earlier than the control group. The reported lower subjective stress but measured higher levels of stress hormones demonstrate the physiological components of emotional dyregulation in DPD. While Experiment 3 utilized a stranger-evoked performance-based stressor, in experiment 4 we investigated the relationship between stress and hormones using a reflective stress task which asked participants to recall a personally relevant stressful incident.
CHAPTER FOUR

Aim IV: To Investigate Relationship between Cortisol, Oxytocin and Depersonalization during a Personally Relevant Psychosocial Stressor

Experiment 3 demonstrated elevated cortisol and OT levels but no significant changes in subjective stress in DPD patients. Depersonalization was also positively related to the increase in cortisol in response to psychosocial stress in the combined group. However, there were several limitations to Experiment 3. Anecdotally, some DPD patients reported that public speaking is not stress-inducing. Some also indicated that engaging with others actually distracted them from their depersonalization symptoms and made them feel more connected and in their bodies. Thus, a stressor that is personally relevant may induce higher levels of subjective stress in depersonalized individuals. As well, experiment 3 comprised of a small sample size: 10 depersonalized individuals and 15 normal controls. Experiment 4 addressed these limitations by employing a larger sample of non-clinical undergraduate students with a wide range of levels of dissociation who underwent a personally relevant social stressor.

For experiment 4, 55 undergraduate students from psychology 100 courses at Hunter College underwent the “Stressful Event Speech,” a stressor which allows the subject to recall and relive a personally relevant stressful event. Participants described a stressful interpersonal event to an experimenter and then watched a video-recording of themselves recalling the event. Saliva samples and subjective ratings were collected directly before, immediately following, and at 20 minutes and 40 minutes post stress task completion, and stress, cortisol, and oxytocin levels were assessed.
**Hypothesis:** We expected that subjective ratings of stress and cortisol and oxytocin levels would increase in response to the stressor. We also expected that depersonalization would be positively related to levels of subjective stress, cortisol, and oxytocin levels.

**Main findings:** There was a significant increase in subjective reports of stress and depression as well as salivary cortisol levels directly following the stress task. The cortisol surge inversely related to dissociation, and depersonalization was associated with more decrease in OT under stress but less OT decrease during stress recovery. However, depersonalization was associated with increased subjective stress for women in the luteal phase only.

**Methods**

**Participants**

Participants were 55 undergraduate Psychology 100 students (21 females, 32 males, mean age= 18, SD =4.15) who received research credit for participation. Six women were in the follicular phase of the menstrual cycle, 12 were in the luteal phase, and 3 women did not report. Average household income was $62,700. Thirty-one percent were Caucasian, 26% were Latino, 16% were Asian, 4% were African American, and 18% self-identified as “other.” Four women were on birth control. Participants had been instructed to refrain from eating, drinking and smoking for at least 1 hour prior to study participation. Demographic and clinical characteristics are presented in Table 8. The study was approved by the Institutional Review Board of Hunter College.
Stressful Event Speech

The Stressful Event Speech (SES) involves describing a stressful interpersonal incident while the speech is recorded and then watching the performance of the speech. Participants were instructed as follows:

For this task, you will describe an interpersonal experience that you had that caused you stress or anger (for instance, a conflict or argument with 1 or more people). You should describe the setting leading up to the incident, describe the incident, explain how the incident and the other person(s)'s responses made you feel, and describe your own physical and behavioral response. After a 2 minute preparation period you will begin describing the incident. Try to feel exactly how you felt during the incident and relive the event.

After the 2 minute preparation period, participants were asked spend 3 minutes recounting the stressful event while their speech was video-recorded. During the speech, the experimenter maintained constant eye contact and nodded empathetically. Following the speech, participants watched themselves giving the speech and were instructed to try to feel the same way they felt when the incident first happened.

Procedure

Figure 10 presents the procedure for Experiment 4. All experiments occurred between 1 and 5pm except for 6 that occurred at 10 am. Upon arrival, participants signed an informed consent and completed the following baseline questionnaires: a demographic questionnaire, the
Dissociative Experiences Scale, The Cambridge Depersonalization Scale, The Childhood Trauma Questionnaire, Beck’s Depression Inventory, Beck’s Anxiety Inventory, the Toronto Alexithymia Scale, the Emotion Regulation Questionnaire, and the Relationships Scale Questionnaire. Participants then rinsed their mouth and rested in an empty room alone for 10 minutes. Before the stress task (pre-SES) participants completed the peritraumatic Experiences Dissociative Experiences Questionnaire (PEDQ), the Positive and Negative Affect Scale (PANAS), and the Profile of Mood States-short form (POMS-SF) and saliva samples were taken. Participants then underwent the SES. Participants completed the subjective stress scale, the PDEQ, PANAS, and POMS-SF and a saliva sample was taken both immediately following (post-SES) and 20 minutes after the SES ended (SES+20 min). Participants were then debriefed.

**Saliva Collection and Hormone Assays**

Saliva collection was performed using passive drool method. Saliva was frozen within 30 minutes of collection. On the day of extraction, samples were allowed to thaw at room temperature for 1.5 hours. Saliva was spun at 25,000 rpm and .8 mL was aliquoted for extraction. Extraction and OT assay was performed consistent with procedures in study 3. Samples were refrozen for cortisol assay on a separate day which was also performed consistent with procedures in study 3.

**Statistical Analyses**

Five extreme scores were converted to within 3 standard deviations above the mean and one missing data point was replaced with the mean score. Two participants who had more than 1 extreme score or missing data point were excluded. State emotion levels were assessed using PANAS positive and negative affect subscales, POMS-SF depression subscale, and a “stress”
score which was calculated by averaging POMS-SF tension-anxiety and anger-hostility subscales at each time point. Stress reactivity scores were calculated for stress score, negative affect, transient dissociation, oxytocin, and cortisol levels (Post-SES – Pre-SES) and well as for positive affect (pre-SES – post-SES). Stress recovery scores were calculated for all measures as post-SES – SES+20 min. Total OT decrease was calculated as pre-SES OT levels – SES+20 OT levels.

We conducted RM-ANOVA’s for all state emotion questionnaires and hormone levels assessed at the 3 time points (pre-SES, post-SES, SES+20 min). Pearson product moment correlations were performed between hormone levels and emotion measures. We also performed partial correlations controlling for anxiety (BAI score) and depression (BDI score) between depersonalization measures and hormone levels.

Results

Changes in Subjective Emotionality

Figures 11 A-D present changes in subjective emotion for the group. Although negative affect increased in response to the stressor and returned to baseline by + 20 min (main effect for Time: $F_{1.58, 80.49} = 13.11, p <.001$), positive affect decreased in response to the SES and never recovered (main effect for time: $F_{2,104} =12.99, p <.001$. The SES induced subjective stress which returned to baseline by +20 min (stress main effect for time: $F_{1,74, 90.34}=11.62, p < .001$). Depression levels also increased in response to the SES and returned to baseline by SES + 20 (main effect for time: $F_{2,102}= 8.65, p <.001$; data not shown). The SES also induced dissociation in the group with levels of dissociation returning to baseline by +20 min (main effect for time: $F_{2,104} = 6.35, p < .05$).

Changes in Salivary Cortisol and Oxytocin Levels
Figures 12 presents oxytocin and cortisol levels during the Stressful Event Speech. Cortisol levels significantly changed in response to the SES (main effect for time: F_{2,104} = 6.11, P<.05). Cortisol levels increased under stress (paired t_{52}=-2.05, p < .05) and decreased during stress recovery (paired t_{52}=3.72, p < .001). Oxytocin levels significantly decreased in response to the SES (main effect for time: F_{1.63,44.12}=6.92, p < .05) with a significant decrease in OT occurring during stress recovery (paired t_{27}=2.19, p<.05) and from the beginning to the end (paired t_{27}=4.60, p<.001).

We found no significant differences between men and women for cortisol and oxytocin levels across the study. However, exploratory Mann Whitney U tests indicated that compared to women in the luteal phase of the menstrual cycle, men tended toward higher Pre-SES OT levels (Z=-1.89, p = .06; see Figure 14B) as well as higher Post-SES cortisol levels (Z = -1.86, p = .06; see Figure 13B) and higher final cortisol levels (Z = 1.79, p = .07; see Figure 13B). Compared to women in the luteal phase of the menstrual cycle, women in the follicular phase tended toward higher OT levels at the Pre-SES time point (Z = -1.84, p = .07) and Post-SES time point (Z = -1.84, p = .07; see figure 14B). There were no significant differences in hormone levels between women in the follicular phase and men.

Correlations between Oxytocin and Cortisol Levels

Post-stress cortisol levels were positively correlated with the stress recovery decrease in OT (r=.445, p<.05) and the total OT decrease (r=.387, p < .05; data not shown). Total OT decrease was also positively correlated with final cortisol levels (SES+20 min; r = .420, p < .05) as well as cortisol stress reactivity at the level of a trend (r = .364, p = .06). Thus, higher cortisol levels were associated with more decrease in OT with both hormones declining after stress.
Sex differences for the relationship between cortisol and oxytocin were also found. In men, Pre-SES cortisol levels were associated with less OT decrease during the stressor ($r=-.766$, $p < .01$) and more OT decrease during stress recovery ($r=.662$, $p < .05$). For women, Post-SES cortisol levels were associated with more OT decrease during stress recovery ($r=.547$, $p < .05$).

**Correlations between Hormone levels and Emotionality**

As shown in Table 9, several emotional states were related to levels of oxytocin. Pre-SES OT levels were associated with lower negative affect and stress, as well as with a lesser decrease in positive affect during stress recovery. Post-stressor OT levels were also related to less decrease in positive affect during stress recovery period.

Decrease in OT during the stress recovery period was associated with greater decrease in positive affect during the stress task and less decrease in positive affect during recovery. Decrease in OT during stress recovery was also associated with less general use of emotion regulation reappraisal strategies. Higher levels of pre-SES and SES+20 depression as well as post-SES levels of stress were associated with less total decrease in OT.

For cortisol, only a negative relationship between post-stressor cortisol and reduced positive affect during the task was significant suggesting that cortisol may not play as great a role as OT in changes in emotion as related to reflection on past stressful interpersonal incidents. Additionally, emotional suppression was positively correlated with cortisol stress reactivity, an indication that emotional suppression facilitates an increased sympathetic nervous system response.
Correlations between Hormone levels, Dissociative Symptoms and History of Childhood Trauma

As shown in Table 10, dissociation, as measured by the DES total score, and depersonalization, as measured by the DES-DPS score, follow a differential pattern of OT stress responsivity. Depersonalization was negatively correlated with OT increase during the stressor (OT stress reactivity), with post-SES OT levels, and with OT decrease during stress recovery. Final transient dissociation levels (SES+20 min) were negatively correlated with pre-stressor OT, post-stressor OT, decrease in OT during stress recovery, total OT decrease, as well as cortisol levels at all time points.

The negative association between depersonalization and OT increase during the stressor and negative relationship between depersonalization and OT decrease during recovery was intriguing. We, therefore identified 9 highly depersonalized individuals who scored above a cutoff score of 12 on the DES depersonalization subscale which was consistent with our cut off score for control groups of previous experiments (mean depersonalization score= 23.70, SD = 7.58). We then conducted an RM ANOVA with the within variable of time (the 3 OT time points) and between variable of depersonalization (4 “high depersonalized” individuals vs. 24 “low depersonalized”). There was an interaction between depersonalization and time: F 2, 53 = 4.40, p < .05. While low depersonalized individuals showed a consistent and significant gradual decrease in OT, high depersonalized individuals demonstrated a significant sharp decrease in OT during stressor followed by an increase during stress recovery which was non-significant (see Figure 15).

The only significant correlations found for childhood trauma were negative associations between sexual abuse and pre-SES and SES+20 cortisol levels.
When we explored sex differences in the relationship between depersonalization and hormones, we found an association between increase in subjective stress during the SES and depersonalization for women in the luteal phase ($r = .599, p = .04$) but not women in the follicular phase ($r = .146, p = .78$) or men ($r = .165, p = .37$; data not shown). As well, men demonstrated a negative correlation between depersonalization and total OT decrease ($r=.689, p=.03$) while women showed no relationship between hormones and depersonalization (data not shown).

**Discussion**

In this experiment, we further explored the interaction between oxytocin and cortisol as they relate to subjective emotionality and depersonalization. For the SES, cortisol responded immediately to the stressor: Cortisol increased during the stressor and returned to baseline levels during the 20 minute recovery period. In contrast, oxytocin showed a more latent response, demonstrated by a significant decrease in levels during stress recovery and between pre-SES and final (SES+20 min) levels. Additionally, cortisol and changes in oxytocin levels were directly related: Consistent with results of control group in experiment 3, post-SES cortisol levels and cortisol stress reactivity were associated with decreases in OT. Germane to these results, Pierrehumbert et al (2010) also found a decrease in OT in response to social stress as well as a negative relationship between oxytocin and cortisol under stress. These findings demonstrate, not only the responsiveness of OT system to stress, but that under stress, heightened cortisol may trigger changes in the OT system function that lead to decreased peripheral OT levels. Possible mechanisms for these changes are put forth in our final discussion.
Oxytocin was also related to state levels of emotion. Interestingly, higher pre-stressor OT levels were associated with less pre-stressor negative affect and stress. High pre-stressor OT as well as post-stressor OT levels were also associated with less decrease in positive emotion during the stress recovery period and may suggest that OT works to prevent diminished positive emotion in emotionally challenging contexts. These results highlight the inverse relationship between OT and negative emotion, further supporting previous evidence for OT as a “feel good” hormone. Additionally, higher OT levels may predict resilience to emotional stress.

A greater decrease in OT across the study (Total OT decrease) was associated with less post-stressor negative affect, stress, depression, and less increase in depression under stress. These findings suggest that decreases in OT in response to stress may be adaptive, associated with better relationship skills and somehow bestowing protective effects from negative affect under stress. Moreover, less OT decrease in response to stress confers emotional dysregulation and poor relationship coping skills.

OT levels may demonstrate a distinctive pattern for depression: increased depression during the stressor (depression stress reactivity) was positively related to final OT levels (SES+20 min) but negatively related to the total decrease in OT across the study. These results suggest that for depressed persons who may not recover from stress-induced depression, prolonged depression may be associated with higher OT levels. This is consistent with results of experiment 3 in which depression was associated with higher OT levels and less decrease in OT post-stress. Previous studies have demonstrated elevated levels of OT in depression in response to emotional induction or stress (Parker et al., 2010; Cyranowski et al., 2008). This change may indicate that depression facilitates an OT release in response to stress which persists during the recovery period. Alternately, individuals who are susceptible to depression may have
dysregulated OT metabolism. These hypotheses are further explained in the final discussion section.

Interestingly, decrease in positive emotion during the stressor was associated with more OT release during stress recovery and less post-stressor cortisol while decrease in positive emotion during stress recovery was associated with less OT release during stress recovery. Changes in positive mood during stress may be beneficial and lead to reduced physiological stress. However, rumination after stress may be indicated by dysregulated OT activity.

Dissociation and depersonalization were related to oxytocin and cortisol. When controlling for anxiety and depression, transient dissociation was associated with lower cortisol levels at all 3 time points. These results are similar to those of Simeon et al (2007) who found an inverse relationship between cortisol reactivity and dissociation, suggesting a dysregulated HPA axis in depersonalization. Transient dissociation was also associated with lower pre- and post-OT levels. When we controlled for anxiety and depression, both dissociation and depersonalization were negatively associated with OT stress reactivity (OT increase under stress). However, depersonalization, but not total dissociation, was negatively related to OT recovery (decrease in OT post-stressor). Thus unlike our depression findings, a dysregulated OT stress system for depersonalization may be associated with increased early OT metabolism and/or decreased OT production in response to stress.

For this study, there were few associations between cortisol and emotion: post-stress cortisol was negatively related to positive affect decrease under stress and cortisol reactivity was positively related to emotional suppression. The relationship between cortisol and emotion may therefore be more associated with energy levels. For instance, Gross’ (1998) found association
between emotional suppression and increased heart rate, skin conductance, and temperature. Lam et al (2009) also found that suppression predicted the cortisol surge in response to the Trier Social Stress Test.

Consistent with previous studies (Salonia et al., 2005; Skukovski et al., 1989), women in the follicular phase of the menstrual cycle tended toward higher OT levels (Pre-SES and Post-SES OT) than women in the luteal phase. Additionally, men tended toward higher Pre-SES OT levels and higher Post-SES cortisol and final cortisol levels than women in the luteal phase. We also found an association between depersonalization and total OT decrease in men but not women. However, the positive relationship between depersonalization and increase in subjective stress during the SES was found in women in the luteal phase but not women in the follicular phase or men suggesting that lower estrogen levels in the luteal phase may impart and emotional vulnerability for women. These results further emphasize the importance of considering gender differences and menstrual phase in clinical research.

Conclusions

Cortisol and OT show a clear association under stress with increased cortisol under stress being related to decreased OT after stress. The OT system may be related to emotional changes to stress: high OT prior to stress and OT decrease after stress may be protective against emotional discord, but low OT release in response to stress may indicate emotional dysregulation. Unlike experiment 3, dissociation was associated with lower levels of cortisol and OT as well as OT decrease under stress, but less decrease in OT during stress recovery. Lesser decrease in OT during stress recovery was also associated with self-reported emotional dysregulation suggesting the failure to decrease OT after stress may be a key symptom of
emotional dysregulation in DPD. For this task, depersonalization may be associated with lower levels of post-stress OT and more OT decrease under stress but less OT decrease (perhaps even OT increase) during stress recovery suggesting dysregulated stress response in the OT system for depersonalization. These results expand previous observations of a dysregulated HPA axis in depersonalization (Simeon et al., 2007) by providing preliminary evidence for a relationship between cortisol, oxytocin, and depersonalization.
CHAPTER FIVE

Final Discussion

In this series of studies, we investigated how depersonalization affects emotion regulation in both a physiological and subjective context. Experiments 1 and 2 examined the ability of DPD patients to modulate emotion to affective stimuli both subjectively (experiments 1 and 2) and physiologically as demonstrated by heart rate and skin conductance response (experiment 2).

The superior ability of DPD patients to subjectively suppress negative emotion that was found in study 1 was also confirmed with physiological results of study 2: Heart rate demonstrated a greater ability to suppress emotion but a lesser ability to enhance emotion in DPD patients compared to a normal control group. This superior ability to suppress emotion corresponds with the hypoemotionality reported by depersonalized individuals: Unlike skin conductance response which appears to be governed only by the sympathetic nervous system and represents changes in arousal, heart rate response has been indicated in both sympathetic and parasympathetic nervous system functioning and may be associated with arousal as well as emotional salience (see Lang et al., 1993 for review). Given that skin conductance response yielded no differences between the groups, the sympathetic nervous system may not be dysfunctional in depersonalized individuals. Thus, emotional suppression (and the inability to enhance emotion) in DPD may be governed by a dysregulated parasympathetic nervous system. Germane to this point, Phillips et al. (2001) found that compared to healthy control group, DPD patients showed more limbic activity while viewing neutral pictures but more prefrontal cortex activity and less limbic activity when viewing emotional pictures. Hence, during emotional suppression, DPD patients may demonstrate increased activity in the prefrontal cortex. However, during attempts to enhance emotion, the prefrontal cortex may not disengage, and the
parasympathetic system may impede DPD patients’ ability to fully experience and then magnify the emotion. Future studies should consider neurological assessments for DPD patients like fMRI to determine if the prefrontal cortex is overactive while limbic areas are less active during emotion regulation.

Inconsistent with the 1st study, we did not find a superior ability to subjectively suppress unpleasant emotion (emotional salience) in the second. Instead, for study 2, controls showed a better ability to modulate emotion to unpleasant pictures compared to pleasant pictures while DPD patients showed no difference in subjective ability to regulate emotion. Discrepancies between the results of the studies may be due to methodological differences. In experiment 1, arousal levels for pleasant pictures were lower. More importantly, task design was different for the two studies. In study 2, since picture ratings were done online directly following emotion regulation, it may have been difficult for patients to switch from actively regulating the emotion to the cognitive task of emotional assessment. Pictures in study 2 were presented for 12 seconds whereas in study 1, pictures were only presented for 2 seconds. This longer exposure to emotional pictures may have facilitated more withdrawal from the pictures and lead to less variance in emotional ratings between conditions for the DPD group. On the other hand, as picture ratings in study 3 were conducted at the end of the protocol, they may not fully reflect the experience of the moment. Furthermore, an antecedent-focused emotion regulation strategy was utilized in study 1 (instruction given before stimulus) while a response-focused emotion regulation strategy was employed for in study 2. In accordance with our earlier speculation of the top-down prefrontal inhibition of emotional responses in DPD, it might be that the mechanism of suppression of subjective emotionality can be better implemented in anticipation of an emotion but is less effective when the emotional experience is in process.
Experiments 3 and 4 explored how stress affects subjective emotion as well as oxytocin and cortisol levels in depersonalization. Oxytocin levels in both studies were similar and consistent with salivary measurements in previous studies (Carter, Pournajafi-Nazarloo, Kramer, Ziegler, White-Traut, Bello, et al., 2007). Another consistent finding across both studies was the clear association between post-stressor cortisol and decrease in OT during stress recovery. Similarly, Pierrehumbert et al. (2010) found an inverse relationship between cortisol and oxytocin during stress, however, this study did not investigate the timing of this association. The temporal relationship between increased cortisol and decreased oxytocin demonstrates not only the responsiveness of OT system to stress, but that under stress, heightened cortisol may trigger changes in the OT system function that lead to decreases in endogenous OT concentrations.

We propose two theories for this relationship: 1) Higher cortisol may facilitate OT metabolism. This can be studied by using a fluorescent marker for OT receptors under Positron emissions tomography scan while participants perform the stress task to determine changes in receptor expression. Increased OT receptor proliferation could indicate OT is being metabolized more quickly in response to stress. Conversely, a decrease in OT receptors could signal dysfunction in the OT system in special populations. 2) Alternately, emotional stress could hinder OT production. Assessment of higher post- vs. pre-stressor OT in cerebral spinal fluid and periphery could demonstrate such changes. It is important to note, however, that oxytocin is produced by several organs in the body in addition to the brain (Kiss and Mikkelsen, 2005). It would, therefore, be difficult to determine if a decrease in peripheral OT were due solely to decreases in CSF concentrations or brain structures.
As demonstrated by study 3 but not study 4, oxytocin may increase in response to psychosocial stress. In rats, increased OT in response to psychosocial stress has been shown to correspond with OT release in the brain (Bosch et al., 2004; Engelmann et al., 2004). However, OT increases under stress may be dependent on the type of stress experienced and the duration of exposure to the stressor. Under social stress, OT may be working through two separate but related systems. In one, biological stress may foster OT release. In another, emotional stress may facilitate OT metabolism or hinder OT production (as described above). Performance-related stress like the Trier Social Stress Test may encompass physiological demands of the “fight or flight” system due to its social encounter. These physical demands may, therefore induce OT release in an attempt to attenuate the stress. Indeed, the TSST is a demonstrated physical stressor, shown to increase heart rate (Kirschbaum et al., 1993) and skin conductance (Jezova et al., 2004). Additionally, during the TSST, participants change location several times as preparation, speech and rest all take place in different rooms, and the stress task is performed standing up with participants often moving or walking around. In contrast, the reflective stress experienced by the SES may not be a physically demanding given that the encounter is only remembered and not actually experienced. As well, unlike the TSST, participants in the SES remain seated in the same room. It should be noted, however, that cortisol increased in response to both stressors which suggests that assessment of changes in cortisol and oxytocin under stress as well as the decrease in oxytocin post-stressor may convey more about the stress response than cortisol or oxytocin alone. As well, the TSST is a 15 minute stressor while the SES lasts only 8 minutes. It is also possible that lengthening the time frame for the SES may yield similar increases in OT during the stressor as demonstrated by the TSST.
In experiment 3, OT increased under stress and decreased post-stressor in the control group but not the DPD group. Other studies have failed to show any changes in OT in response to the TSST (Altemus et al, Taylor et al., 2006; Parker et al., 2010; Grewen and Light, 2010). However, Pierrehumbert et al. (2009) demonstrated a tendential increase in OT under stress followed by a significant decrease after stress in a combined sample of women with childhood sexual abuse, cancer survivors, and normal control participants. Discrepancies in results may be due to methodological differences in the timing of assessment of basal OT and post-TSST OT levels as well as the population sampled. For instance, our results suggest populations with high levels of depression, dissociation, or emotional dysregulation may demonstrate less OT decrease after stress. Additionally, associations between post-stress cortisol and OT stress recovery were only found for the recovery period occurring 20 minutes after the stressor ended and not later. Longer recovery from the TSST did not reveal this association suggesting that OT’s reaction to physiological stress may be immediate and cease quickly.

For both studies, subjective stress was associated with lower levels of OT: these associations occur before the stressor for the SES and after the stressor for the TSST. Discrepancies in the timing of these associations may also be due to differences in methodology. For the TSST, pre-stressor levels may not represent a true baseline since participants were informed of the nature of the stress task they would perform and therefore some participants may have demonstrated elevated OT levels in anticipation of the task. The participants in our TSST experiment represent a peculiarly heterogeneous sample-comprising of both DPD patients and normal control participants. As well, both experiments involve a very small sample size: 25 participants for the first study and 30 participants for the 2nd. Nonetheless, this inverse
relationship between OT and subjective stress is consistent with the finding for anxiolytic effects of OT.

The relationship between OT and emotion is, however, very complex. In addition to associations between OT and decreased stress, both studies also suggest that after stress, less positive emotion is related to higher OT. This relationship was significant in experiment 3 and tended toward significance in experiment 4. These results are consistent with Taylor et al. (2006) who also found a negative association between positive emotion and pre- and post- stress OT levels. Experiments 3 and 4 also demonstrated an association between depression and OT. In experiment 3, general levels of depression and less decrease in depression after stress were associated with elevated post-stressor OT levels while pre-stressor depression was associated with pre-stressor OT at the level of a trend. In experiment 4, the increase in depression under stress was associated with final OT levels and less total decrease in OT during the study while general levels of depression were associated with final OT at the level of a trend. Although one previous study found no relationship between OT levels and depression (Altemus et al., 2001), in other studies, depressed participants presented with higher OT levels (Parker et al., 2010; Cyranowski et al., 2008). Additionally, rat studies have indicated that OT attenuates depressive symptoms (Arletti & Bertolini, 1987). Thus, elevated OT levels in depression may indicate an endogenous reflexive mechanism of the hormonal stress response. Oxytocin may be released in order to alleviate feelings of depression. Indeed, prairie voles exposed to chronic social isolation demonstrated increased anhedonia as well as greater OT release after stress and were characterized by a greater number of OT cells in the PVN (Grippo, et al., 2007). However, endogenous OT release may not be sufficient in alleviating symptoms and depressed patients may benefit from OT replacement. This relationship may also explain why high levels of OT can
indicate elevated stress but that OT administration can also relieve stress. Very anxious and depressed individuals may require more OT than their system normally produces.

The association between hormones and depersonalization differed in the 2 studies. In experiment 3, DPD patients showed elevated OT and cortisol levels throughout, while in experiment 4 depersonalization scores in the non-clinical sample of undergraduate students were associated with less post-stress OT and greater decrease in OT during the stressor. However, in both studies, depersonalization was associated with less decrease in OT during the 1st 20 minutes of stress recovery. Previous studies have also been unclear with respect to hormone levels and DPD. Two studies have demonstrated elevated basal cortisol levels in DPD (Simeon et al., 2001; Simeon et al., 2007) while one found lower basal cortisol levels for DPD patients (Stanton et al., 2001). Correspondingly, in another study depersonalization in a non-clinical sample of undergraduates was associated with greater cortisol stress reactivity (Giesbrecht et al., 2007). However, Simeon et al (2007) found no difference in cortisol stress reactivity between DPD patients and healthy controls. It is important to note that depersonalization found in the general population is often an indication of other conditions like anxiety or symptoms of psychosis and may not represent depersonalization disorder as diagnosed via SCID-D. Thus, some differences between studies 3 and 4 may be due to discrepancies in the characteristics of depersonalization between the groups.

Differing results between previous studies in the literature may also be due to a failure to account for sex differences. In our small sample of experiment 3, we found that male participants had higher cortisol levels and tended toward higher OT levels than female participants in the follicular phase. Additionally, male participants were more responsive to stress than follicular-phased female participants. As well, male DPD patients showed higher
cortisol levels than normal male control participants overall, however female DPD patients female control participants did not differ in OT or cortisol levels. Additionally, our finding of higher OT levels for women in the follicular phase than women in the luteal phase is consistent with previous studies (Salonia et al.; Skukowski et al., 1089). As well, an association between depersonalization and OT decrease was found in men while a positive relationship between subjective stress reactivity and depersonalization was found in women in the luteal phase. These findings suggest gonadal hormones may play a protective role in emotional responsivity. Thus, future studies should consider sex differences and menstrual cycle phase of female participants.

Discrepancies between hormone results of experiment 3 and 4 may also be due to methodological differences. Elevated cortisol levels in DPD in study 3 may be an indication of anticipatory stress: Subjects were aware they would be performing a stress task. Higher anticipatory stress in DPD compared to normal controls would be consistent with the elevated anxiety and depression often reported with DPD. In contrast, for study 4 which comprised of a non-clinical sample, there was no association between depersonalization and elevated cortisol levels. Additionally, unlike the TSST, the SES may induce a weaker cortisol stress response in depersonalized undergraduates due to differences in physiological demands and the shorter duration of the SES.

The positive relationship between depersonalization and less OT decrease during early recovery for both studies is intriguing. Exploratory analyses in study 4 indicated that in depersonalized participants there was a dramatic and significant decrease in OT during the stress but a pattern of increase in OT during early stress recovery. This result suggests that for depersonalized individuals, a rapid metabolism or decreased production of OT is initiated during emotional distress. However, this decrease in OT is not sustained leading to less decrease in OT
for depersonalized individuals during stress recovery. This change may indicate dysfunction in the OT system such as dysregulated OT production, metabolism, OT receptor proliferation or mutations of the OT receptor. Thus, these physiological processes represent possible areas of future investigation using brain imaging techniques for visualizing and quantifying the OT system.

It is plausible that for experiment 4, the decrease in OT during stress demonstrated by depersonalized participants may represent a pattern of emotional suppression or withdrawal during distress. Correspondingly, DPD patients in study 3 did not report an increase in subjective stress despite a clear cortisol stress reactivity. The dichotomy between subjective stress and the physiological responsivity may be due to high levels of alexithymia in DPD. Alexithymia was positively related to post-stress OT in study 3, further suggesting that emotional confusion in DPD patients may in part be related to dyregulated OT. Furthermore, Study 4 demonstrated an association between less decrease in OT during stress recovery and emotional dysregulation suggesting less decrease in OT during stress recovery may be a biomarker for emotional and relational distress. Hence, this lack of post-stressor OT decrease demonstrated by depersonalized individuals in both experiments may be indicative of their emotional dysregulation. Thus, DPD patients may benefit from better regulation of their OT system.

Our studies had several limitations. All studies involved very small sample sizes. Studies 1 through 3 included medicated patient populations. For study 3, all participants were aware of the stress procedure. Study 4 utilized an undergraduate sample whose symptomology may not be consistent with a patient population or healthy controls. Future studies should control for these limitations and include appropriate depressed control subjects.
In summary, we found that emotional induction (both by visual stimuli or a stress task) engenders subjective and physiological emotional dysregulation in depersonalized individuals. Our findings have several therapeutic implications. DPD patients may benefit from interventions such as heart rate variability biofeedback to identify patterns of physiological suppression in response to emotion. In conjunction with heart rate variability biofeedback, psychotherapeutic interventions like Dialectic Behavioral Therapy could help DPD patients identify and communicate their emotions and ultimately suppress less in order to feel safe enough to fully engage in the emotional experience. DPD patients may also benefit from hormonal interventions to better stabilize OT levels allowing for a deeper emotional experience.
TABLES
Table 1

Demographic and clinical characteristics for DPD Patients and Normal Controls who performed Emotion Regulation Task 1 (without physiological measures)

<table>
<thead>
<tr>
<th>Measure</th>
<th>DPD Patients Mean (SD)</th>
<th>Controls Mean (SD)</th>
<th>t (df)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>30.31 (10.77)</td>
<td>30.87 (9.46)</td>
<td>-0.15 (29)</td>
<td>ns</td>
</tr>
<tr>
<td>Gender (F/M)</td>
<td>4/12</td>
<td>3/12</td>
<td>X^2(1)=0.11</td>
<td>ns</td>
</tr>
<tr>
<td>Handedness (R/L/A)</td>
<td>13/2/1</td>
<td>13/1/1</td>
<td>X^2(2)=0.30</td>
<td>ns</td>
</tr>
<tr>
<td>Education</td>
<td>Median: BA</td>
<td>Median: HS</td>
<td>X^2(1)=1.64</td>
<td>ns</td>
</tr>
<tr>
<td>Marital Status</td>
<td>Mode: single</td>
<td>Mode: single</td>
<td>X^2(3)=2.55</td>
<td>ns</td>
</tr>
<tr>
<td>Income</td>
<td>61,154</td>
<td>45,583</td>
<td>1.04(23)</td>
<td>ns</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Mode: Caucasian</td>
<td>Mode: African American</td>
<td>X^2(4)=20.99</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>DES-Total</td>
<td>26.85 (12.50)</td>
<td>7.02 (9.00)</td>
<td>-5.04(29)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DES-AMN</td>
<td>7.40 (8.25)</td>
<td>1.89 (3.88)</td>
<td>-2.40(21.61)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>DES-ABS</td>
<td>28.83 (17.40)</td>
<td>9.58 (12.15)</td>
<td>-3.55(29)</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>DES-DPS</td>
<td>40.73 (14.93)</td>
<td>1.22 (2.13)</td>
<td>-10.47(15.65)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DES-Taxon</td>
<td>26.09 (10.75)</td>
<td>3.17 (4.65)</td>
<td>-7.79(20.70)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CDS</td>
<td>128.31 (51.13)</td>
<td>13.67(20.78)</td>
<td>-8.27(20.08)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CTQ-emotional abuse</td>
<td>10.56 (6.16)</td>
<td>8.27 (4.56)</td>
<td>-1.17(29)</td>
<td>ns</td>
</tr>
<tr>
<td>CTQ-emotional neglect</td>
<td>11.94 (5.45)</td>
<td>8.07 (3.79)</td>
<td>-2.28(29)</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>CTQ-physical abuse</td>
<td>5.25 (0.77)</td>
<td>6.93 (2.74)</td>
<td>2.36(16.10)</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>CTQ-physical neglect</td>
<td>5.69 (8.00)</td>
<td>6.13 (1.64)</td>
<td>0.21(29)</td>
<td>ns</td>
</tr>
<tr>
<td>CTQ-sexual abuse</td>
<td>6.25 (2.59)</td>
<td>5.80 (1.78)</td>
<td>-0.56(29)</td>
<td>ns</td>
</tr>
<tr>
<td>STAI-Y2</td>
<td>49.19 (9.83)</td>
<td>32.33(10.10)</td>
<td>-4.71(29)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BDI</td>
<td>15.38 (9.80)</td>
<td>3.53 (3.85)</td>
<td>-4.48(19.78)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PANAS-Past Week Positive</td>
<td>26.50 (10.29)</td>
<td>37.40 (6.95)</td>
<td>3.43(29)</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>PANAS-Past Week Negative</td>
<td>24.31 (8.40)</td>
<td>13.20 (4.33)</td>
<td>-4.67(22.75)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ERQ-Suppression</td>
<td>14.19 (5.91)</td>
<td>11.20 (2.96)</td>
<td>-1.80(22.36)</td>
<td>&lt;.10</td>
</tr>
<tr>
<td>ERQ-Reappraisal</td>
<td>26.81 (8.69)</td>
<td>32.40 (8.02)</td>
<td>1.86(29)</td>
<td>&lt;.10</td>
</tr>
<tr>
<td>TAS-Total</td>
<td>51.00 (15.87)</td>
<td>38.07 (12.49)</td>
<td>-2.51(29)</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

DES: Dissociative Experiences Scale; DES-AMN: DES Amnesia subscale; DES-ABS: DES Absorption subscale; DPS: DES Depersonalization subscale; CDS: Cambridge Depersonalization Scale; CTQ: Childhood Trauma Questionnaire; STAI-Y2: State-Trait Anxiety Inventory-general; BDI: Beck’s Depression Inventory; PANAS: Positive and Negative Affect Scale; ERQ: Emotion Regulation Questionnaire; TAS: Toronto Alexithymia Scale.
### Table 2

#### Demographic and clinical characteristics of DPD Patients and Normal Controls who Underwent the Trier Social Stress Test

<table>
<thead>
<tr>
<th>Measure</th>
<th>DPD Patients Mean (SD)</th>
<th>Controls Mean (SD)</th>
<th>Z(df)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>29.00 (9.21)</td>
<td>30.47 (8.37)</td>
<td>-0.67</td>
<td>ns</td>
</tr>
<tr>
<td>Gender (F/M)</td>
<td>6/4</td>
<td>10/5</td>
<td>0.12</td>
<td>ns</td>
</tr>
<tr>
<td>Education</td>
<td>Median</td>
<td>Median</td>
<td>2.81</td>
<td>0.09</td>
</tr>
<tr>
<td>Marital Status</td>
<td>Mode: single</td>
<td>Mode: single</td>
<td>1.89</td>
<td>0.06</td>
</tr>
<tr>
<td>Income</td>
<td>80,625</td>
<td>48,231</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Mode: Mode</td>
<td>X²(3)=9.40</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>DES-Total</td>
<td>17.46 (6.56)</td>
<td>4.12 (4.58)</td>
<td>-3.64</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DES-AMN</td>
<td>0.83 (2.12)</td>
<td>1.44 (2.17)</td>
<td>-0.97</td>
<td>ns</td>
</tr>
<tr>
<td>DES-ABS</td>
<td>11.13 (6.41)</td>
<td>5.92 (6.06)</td>
<td>-2.19</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>DES-DPS</td>
<td>38.17 (14.06)</td>
<td>0.89 (1.88)</td>
<td>-4.35</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DES-DAX</td>
<td>19.50 (8.52)</td>
<td>1.58 (3.15)</td>
<td>-4.15</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CDS</td>
<td>105.84 (49.12)</td>
<td>14.07 (15.55)</td>
<td>-4.05</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CTQ-total</td>
<td>43.00 (7.69)</td>
<td>36.67 (14.77)</td>
<td>-3.84</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>CTQ-emotional abuse</td>
<td>11.40 (3.44)</td>
<td>7.00 (2.13)</td>
<td>-3.57</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CTQ-emotional neglect</td>
<td>12.40 (4.25)</td>
<td>9.07 (2.89)</td>
<td>-2.04</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>CTQ-physical abuse</td>
<td>5.70 (1.64)</td>
<td>7.20 (3.17)</td>
<td>-1.57</td>
<td>ns</td>
</tr>
<tr>
<td>CTQ-physical neglect</td>
<td>7.00 (1.25)</td>
<td>7.40 (4.61)</td>
<td>-1.11</td>
<td>ns</td>
</tr>
<tr>
<td>CTQ-semen abuse</td>
<td>6.50 (1.96)</td>
<td>6.00 (3.87)</td>
<td>-1.83</td>
<td>0.07</td>
</tr>
<tr>
<td>BAI</td>
<td>12.40 (8.87)</td>
<td>1.60 (1.59)</td>
<td>-4.12</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BDI</td>
<td>17.10 (10.48)</td>
<td>2.60 (4.00)</td>
<td>-3.24</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>RES-secure</td>
<td>13.50 (5.23)</td>
<td>17.53 (3.52)</td>
<td>-1.98</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>RES-Fearful</td>
<td>11.30 (5.73)</td>
<td>8.40 (4.85)</td>
<td>-0.98</td>
<td>ns</td>
</tr>
<tr>
<td>RSQ-Preoccupied</td>
<td>14.80 (3.19)</td>
<td>12.00 (2.27)</td>
<td>-2.16</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>RSQ-Dismissing</td>
<td>18.50 (5.38)</td>
<td>18.47 (4.78)</td>
<td>-0.45</td>
<td>ns</td>
</tr>
<tr>
<td>ERQ-Suppression</td>
<td>14.10 (5.76)</td>
<td>14.13 (4.45)</td>
<td>-0.91</td>
<td>ns</td>
</tr>
<tr>
<td>ERQ-Reappraisal</td>
<td>27.40 (10.96)</td>
<td>31.00 (6.64)</td>
<td>-2.22</td>
<td>ns</td>
</tr>
<tr>
<td>DERS-non acceptance</td>
<td>11.30 (3.65)</td>
<td>9.80 (3.55)</td>
<td>-0.95</td>
<td>ns</td>
</tr>
<tr>
<td>DERS-goals</td>
<td>15.70 (4.81)</td>
<td>12.13 (3.85)</td>
<td>-1.95</td>
<td>0.05</td>
</tr>
<tr>
<td>DERS-impulse</td>
<td>7.40 (3.13)</td>
<td>6.47 (1.77)</td>
<td>-0.67</td>
<td>ns</td>
</tr>
<tr>
<td>DERS-strategies</td>
<td>16.80 (6.39)</td>
<td>10.27 (2.12)</td>
<td>-2.23</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>DERS-awareness</td>
<td>15.10 (4.91)</td>
<td>13.67 (3.79)</td>
<td>-0.42</td>
<td>ns</td>
</tr>
<tr>
<td>DERS-clarity</td>
<td>13.60 (6.22)</td>
<td>7.87 (2.53)</td>
<td>-2.55</td>
<td>&lt;0.05</td>
</tr>
<tr>
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<td>40.53 (10.64)</td>
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<td>&lt;0.05</td>
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DES: Dissociative Experiences Scale; DES-AMN: DES Amnesia subcale; DES-ABS: DES Absorption subcale; DPS: DES Depersonalization subscale; CDS: Cambridge Depersonalization Scale; CTQ: Childhood Trauma Questionnaire; BAI: Beck’s Anxiety Inventory; BDI: Beck’s Depression Inventory; RES: Relationship Scale Questionnaire; ERQ: Emotion Regulation Questionnaire; DERS: Difficulties in Emotion Regulation; TAS: Toronto Alexithymia Scale.
### Table 3

**Correlations between Cortisol and Oxytocin for the Combined Group during the Trier Social Stress Test (TSST)**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Pre-TSST OT</th>
<th>Post-TSST OT</th>
<th>OT Stress Reactivity</th>
<th>Early OT Stress Recovery</th>
<th>OT Total Stress Recovery</th>
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<tbody>
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<td>Pre-TSST Cortisol</td>
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<td>.042</td>
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<td>-.146</td>
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<td>.181</td>
<td>.066</td>
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<td>Early Cortisol Stress Recovery</td>
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<td>.244</td>
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<td><strong>.573</strong></td>
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<tr>
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<td>.134</td>
<td>.281</td>
<td>.302</td>
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**Note:** †P<.10, **P< .01, * P< .05. Stress Reactivity: Post-Stress – Pre-Stress measurement. Stress Recovery: Post-Stress- TSST+ 20 measurement. Total Stress Recovery: Post-Stress – TSST + 40 measurement.
Table 4
Correlations between Cortisol and Oxytocin for the Control Group during the Trier Social Stress Test (TSST)

<table>
<thead>
<tr>
<th>Measure</th>
<th>Pre-TSST OT</th>
<th>Post-TSST OT</th>
<th>OT Stress Reactivity</th>
<th>Early OT Stress Recovery</th>
<th>OT Total Stress Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-TSST Cortisol</td>
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<td>Post-TSST Cortisol</td>
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<td>Cortisol Stress Reactivity</td>
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<td>.064</td>
<td>.471†</td>
<td>.241</td>
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<td>Early Cortisol Stress Recovery</td>
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<td>-.121</td>
<td>.607†</td>
<td>.617*</td>
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<td>Cortisol Total Stress Recovery</td>
<td>-.182</td>
<td>.030</td>
<td>.020</td>
<td>.594*</td>
<td>.382</td>
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Note: †P<.10, ** P< .01, * P< .05. Stress Reactivity: Post-Stress – Pre-Stress measurement. Stress Recovery: Post-Stress- TSST+ 20 measurement. Total Stress Recovery: Post-Stress – TSST + 40 measurement.
Table 5
Correlations between Cortisol and Oxytocin for DPD Group during the Trier Social Stress Test (TSST)

<table>
<thead>
<tr>
<th>Measure</th>
<th>Pre-TSSST OT OT</th>
<th>Post-TSSST OT OT</th>
<th>OT Stress Reactivity</th>
<th>Early OT Stress Recovery</th>
<th>OT Total Stress Recovery</th>
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<td>Post-TSSST Cortisol</td>
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<td>Cortisol Total Stress Recovery</td>
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<td>.258</td>
<td>.270</td>
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<td>.133</td>
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Note: †P<.10, **P<.01, *P<.05. Stress Reactivity: Post-Stress – Pre-Stress measurement. Stress Recovery: Post-Stress- TSST+ 20 measurement. Total Stress Recovery: Post-Stress – TSST + 40 measurement.
Table 6

<table>
<thead>
<tr>
<th>Measure</th>
<th>Pre-TSST OT</th>
<th>Post-TSST OT</th>
<th>OT Stress Reactivity</th>
<th>Early OT Stress Recovery</th>
<th>Total OT Stress Recovery</th>
<th>Pre-TSST Control</th>
<th>Post-TSST Control</th>
<th>Cortisol Stress Reactivity</th>
<th>Early Cortisol Stress Recovery</th>
<th>Total Cortisol Stress Recovery</th>
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Note: *p<.05, **p<.01, ***p<.001.
Table 7

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<tr>
<th>Measure</th>
<th>Pre-TSST OT</th>
<th>Post-TSST OT</th>
<th>OT Stress Reactivity</th>
<th>Early/OT Stress Recovery</th>
<th>Total OT Stress Recovery</th>
<th>Pre-TSST Control</th>
<th>Post-TSST Control</th>
<th>Cortisol Stress Reactivity</th>
<th>Total Cortisol Stress Recovery</th>
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Note: †P<.10, **P<.01, *P<.05.
Table 8

*Descriptive Statistics and Clinical Characteristics for Participants who underwent the SES in Experiment 4*

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<th>Measure</th>
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DES: Dissociative Experiences Scale; DES-AMN: DES Amnesia subcale; DES-ABS: DES Absorption subcale; DPS: DES Depersonalization subscale; CDS: Cambridge Depersonalization Scale; CTQ: Childhood Trauma Questionnaire; BAI: Beck’s Anxiety Inventory; BDI: Beck’s Depression Inventory; RES: Relationship Scale Questionnaire; ERQ: Emotion Regulation Questionnaire; DERS: Difficulties in Emotion Regulation; TAS: Toronto Alexithymia Scale.
Table 9

Correlations between Hormone Levels and Emotion for Participants who Underwent the SES in Experiment 4

<table>
<thead>
<tr>
<th>Measure</th>
<th>Pre-SES OT</th>
<th>Post-SES OT</th>
<th>SES+20 OT</th>
<th>OT Stress Reactivity</th>
<th>OT Stress Recovery</th>
<th>Total OT Decrease</th>
<th>Pre-SES Cortisol</th>
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<th>SES+20 Cortisol</th>
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Note: †P<.10, **P< .01, * P< .05
### Table 10

Correlations between Hormone Levels and Childhood Trauma and Dissociation during the SES in Experiment 4

<table>
<thead>
<tr>
<th>Measure</th>
<th>Pre-SES OT</th>
<th>Post-SES OT</th>
<th>SES+20 OT</th>
<th>OT Stress Reactivity</th>
<th>OT Stress Recovery</th>
<th>Total OT Decrease</th>
<th>Pre-SES Cortisol</th>
<th>Post-SES Cortisol</th>
<th>SES+20 Cortisol</th>
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Note: †P<.10, ** P<.01, * P<.05. Values for dissociation measures were covaried by BAI and BDI scores.
FIGURES
The control group showed an increase in negative affect during the task (paired $t_{14} = -2.32$, $p < .05$) as well as an increase in anxiety during the task (paired $t_{14} = -2.30$, $p < .05$) which failed to return to baseline levels (paired $t_{14} = 2.17$, $p < .05$). For the control group, there was also a difference in positive affect before compared to during the task at the level of a trend (paired $t_{14} = 1.97$, $p = .07$). There were no changes in negative or positive affect, dissociation, or anxiety levels across the task for the DPD group.
Figure 2. Emotion Regulation Abilities for DPD patients and Normal Controls for Experiment 1

A.

B.

C.
Figure 3. Ratings and Heart Rate Ability Scores for Emotion Regulation in Experiment 2.

A.

Ability scores for HR and ratings: Enhance Ability=Enhance - Maintain; Suppress Ability=Maintain – Suppress

A. HR data indicated that the DPD Group had a lesser ability to increase and a greater ability to decrease emotion.  B. There was a trend of a group * valence interaction for rating ability. (Reprinted with permission from Elsevier Inc/1600 John F Kennedy Boulevard Suite 1800 Philadelphia PA 19103-2879 USA).
Figure 4. Experimental Procedure for Experiment 3.
Procedure: Trier Social Stress Test Experiment

TSST Procedure:
5 minute preparation
5 minute job interview
5 minute mental math

Mood Assessment Questionnaires & Saliva Sample

Baseline Questionnaires

10 minute rest

Mood Assessment Questionnaires & Saliva Sample

20 minute rest

Mood Assessment Questionnaires & Saliva Sample

20 minute rest

Mood Assessment Questionnaires & Saliva Sample

20 minute rest
Figure 5. Subjective Emotion During the Trier Social Stress Test in Experiment 3
Figure 6. Cortisol Levels for the Trier Social Stress Test

A.

B.

Note: * p < .05. A. Cortisol Levels for the Trier Social Stress Test for DPD Patients and Normal Controls. B. Cortisol Levels during the Trier Social Stress Test for Men and Women Separately
Figure 7. Gender Differences in Cortisol Levels During the Trier Social Stress Test

Note: * p < .05. ** p < .001
Figure 8. Oxytocin Levels during the Trier Social Stress Test in DPD Patients and Normal Controls

A. Oxytocin Levels for men and women combined. B. Oxytocin levels for Men and Women Separately.
Figure 9. Gender Differences in Oxytocin Levels

Note: † p < .10
Figure 10. Experimental Procedure for the Stressful Event Speech in Experiment 4

Procedure: Stressful Event Speech

Baseline Questionnaires

<--------------------- 10 minute rest

Mood Assessment Questionnaires & Saliva Sample

Stressful Event Speech

SES Procedure:
2 minute preparation
3 minute event recall
3 video viewing

Mood Assessment Questionnaires & Saliva Sample

<--------------------- 20 minute rest

Mood Assessment Questionnaires & Saliva Sample
Figure 11. Subjective Emotionality in Response to the Stressful Event Speech in Experiment 4

* p < .05; ** p < .001

Figure 11. Self-reported positive and negative affect, stress, and dissociation at 3 time points: immediately before, directly following and 20 minutes post SES. The SES significantly induced stress and dissociation and increased negative affect, all of which returned to baseline by 20 minutes post stressor. The SES also significantly decreased levels of positive affect which did not return to baseline.
Figure 12. Hormonal Response to Stressful Event Speech

Note: * p < .05; ** p < .001

Figure 12. Salivary cortisol levels at 3 time points: before, directly following, and 20 minutes post SES. A. Cortisol increased under stress and returned to baseline by SES + 20. B. Oxytocin decreased significantly after the stressor and was significantly lower than oxytocin levels before the stressor.
Figure 13.

A.

SEX DIFFERENCES IN CORTISOL LEVELS FOR THE SES

B.

Sex Differences in Cortisol for the SES
Figure 14.

A.

**SEX DIFFERENCE IN OXYTOCIN FOR THE SES**

![Graph showing sex differences in oxytocin for the SES.]

B.

Sex Differences in Oxytocin for the SES

![Graph showing sex differences in oxytocin for the SES.]

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Low-depersonalized individuals showed significant decrease in OT during stress recovery (paired $t_{24} = 3.05, p < .05$) and a significant total decrease in OT between pre-stress and final OT measurement (paired $t_{24} = 5.71, p < .001$). High-depersonalized individuals showed significant decrease in OT during the stress task (paired $t_{4} = 4.73, p < .05$) and a non-significant pattern of increase during stress recovery (paired $t_{4} = -2.32, p = .10$).
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