35% CARBON DIOXIDE REACTIVITY IN A BULIMIA NERVOSA SAMPLE

by

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Abstract

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This study extended research on the specificity of the effects of the carbon dioxide (CO_2) challenge by examining panic reactivity in participants with bulimia nervosa (BN) ($n = 15$) compared to those without bulimia nervosa ($n = 31$). All participants completed self-report measures assessing state and trait anxiety, depression, anxiety sensitivity (AS), distress tolerance (DT), discomfort intolerance (DI), and eating disorder features. They subsequently breathed two vital capacity inhalations: room air and 35% CO_2-enriched air. Reactivity to room air was not different between groups. However, participants with BN displayed greater reactivity to CO_2 compared to the participants without BN. AS, DI, and DT could not be tested as potential mediators in the association between diagnostic group and reactivity because these constructs were not associated with reactivity. Eating disorder features and frequency of binges and purges were also not associated with reactivity. Detailed implications and suggestions for further research are discussed.

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35% Carbon Dioxide Reactivity in a Bulimia Nervosa Sample

The 35% carbon-dioxide (CO_2) challenge procedure is known to produce symptoms of natural panic attacks in persons with panic disorder (PD). It was previously thought that this reaction was specific to those with PD; other persons, including those with other clinical disorders, did not react to CO_2 in such a way. Thus, the 35% CO_2 challenge was identified as a marker for PD pathophysiology. However, further research revealed that persons with certain clinical disorders aside from PD do, in fact, react to CO_2. These include social anxiety disorder, situational-specific phobia, premenstrual dysphoric disorder, and sporadic unexpected panic attacks without a diagnosis of PD. Additionally, first and second- degree relatives of persons with PD also react to CO_2. There might therefore be a panic-phobic spectrum of disorders all characterized by a vulnerability to CO_2. The present study investigated CO_2 reactivity in persons with bulimia nervosa (BN), a disorder that would fall outside of this panic-phobic spectrum, compared to persons without BN. The goal was to further examine the specificity of the effects of 35% CO_2. A literature review examining the research to-date is below, followed by the specific hypotheses, methods and results of the present study.

Panic attacks are characterized by fear accompanied with physiological symptoms, such as breathlessness, dizziness and a racing heart (McNally, 1994). The CO_2 challenge is a procedure wherein symptoms of natural panic attacks are reproduced in a controlled lab context (Verburg, Pols, de Leeuw, & Griez, 1998). This procedure was developed in order to gain more insight into the pathophysiology of PD, which is characterized by spontaneous and unexpected panic attacks. Typically, the information obtained from individuals with PD about their attacks is subjective and retrospective, and thus difficult to study. Producing panic in the laboratory allows for more objective and direct measures of panic phenomena. The CO_2 challenge has been established as a valid and reliable experimental procedure to test biological models of panic (e.g.,

Coplan, Gorman, & Klein, 1992; Klein, 1993). Such models propose that panic attacks occur due in part to aberrant respiratory stimulation in the brain. A number of other agents have been tested for their ability to simulate panic-like symptoms, including the following: cholecystokinin-tetrapeptide (CCK-4; Bradwejn, Koszycki, & Shriqui, 1991), flumazenil (Nutt, Glue, Lawson, & Wilson, 1990), and sodium lactate (Pitts & McClure, 1967). Notably, these panicogenic agents are still in use, but receive less empirical attention compared to CO_2. The CO_2 challenge is often used in laboratory studies because of its non-invasive nature.

Carbon Dioxide as a Panic Provocation

CO_2 is a component of normal respiration. In normal respiration, oxygen (O_2) is removed from inhaled air and transferred through the bloodstream to bodily tissues, in order to meet metabolic needs. CO_2, a metabolic by-product, is removed from the body upon exhalation. Hyperventilation occurs when more CO_2 is exhaled than is produced by cellular metabolism. It is characterized by either an increased respiration rate (number of inspirations per minute) or increased tidal volume (amount of air inhaled per breath), or both. Hyperventilation results in hypocapnia, which is a loss of CO_2 from the blood (McNally, 1994). Laboratory studies have shown that hyperventilation of normal air causes physical symptoms similar to those of panic (e.g., Lum, 1975). To better understand this interaction, Gorman and colleagues (1984) submitted a group of individuals with PD to voluntary hyperventilation, and a group without PD to breathe a mixture containing 5% CO_2 for 20 minutes. This composition of CO_2 is 875 times greater than that in normal air (0.04%), thereby producing higher levels of CO_2 in the blood (i.e., hypercapnia) and resulting in the opposite effect of hyperventilation (i.e., hypocapnia).

Contrary to what was expected, it was the CO_2 condition that proved to be panicogenic, not the forced hyperventilation (Gorman et al., 1984). Subsequent experiments (e.g. Griez , Zandbergen, Lousberg, & van den Hout, 1988) confirmed that acute hypocapnia, induced by

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voluntary hyperventilation, is neither sufficient nor necessary to induce panic in people with PD and without PD. With an interest in establishing CO_2 as a panicogenic agent, researchers continued to investigate the potency of CO_2 in eliciting panic. In a seminal study, Griez, Lousberg, van den Hout, and van der Molen (1987) observed that a single inhalation of 35% CO_2 instantaneously elicited panic-like physical symptoms and high levels of subjective anxiety in 12 people with PD. These symptoms were comparable to those produced upon breathing 5% CO_2 for 20 minutes. Thus began the use of CO_2 as a panicogenic agent in studies of the pathophysiology of panic.

Several recognized methods of CO_2 delivery exist: the steady-state method (5 – 7% CO_2), the Read re-breathing technique (5 – 7% CO_2), and the single- or double-breath inhalation (35% CO_2; for a review, see Rassovsky & Kushner, 2003). However, the physiological process that produces panic differs depending on the delivery method. Specifically, panic from the single- or double-breath inhalation is produced immediately by hypercapnia (respiratory acidosis) followed by a hypocapnic overshoot (respiratory alkalosis), while panic during the steady-state method and the Read re-breathing technique is produced gradually through respiratory acidosis alone. For this reason, it is difficult to compare the results of panic provocation studies with different delivery methods. More generally, it has been questioned whether a delivery method utilizing 5 – 7% CO_2 over an extended time is a valid panic provocation (e.g., Bailey, Kendrick, Diaper, Potokar, & Nutt, 2007; Sanderson & Wetzler, 1990).

The single- or double-breath inhalation of 35% CO_2 balanced with 65% oxygen is known to produce the highest level of CO_2 exposure, albeit for the shortest time. The CO_2/O_2 mixture is administered through a mask or mouthpiece, panic attack symptoms are produced immediately, within a matter of seconds, and wane after 30-60 seconds. Participants of such studies are told that they will inhale two different gases with various CO_2 concentrations, which may induce

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short-lived effects ranging from hardly noticeable changes to strong, autonomic or anxiety-like symptoms (Schruers, 2001). The procedure is consistent, easily administered, and well tolerated (Griez & van den Hout, 1984). These practical advantages have prompted many researchers to utilize the *35% CO_2 challenge* (as described by Griez et al., 1987), and, more recently, this method has become standardized (Battaglia et al., 2007; Griez & Verburg, 1998). For this reason, all studies mentioned in this thesis utilized the 35% CO_2 challenge procedure (unless otherwise specified) and thus results can be compared.

The Carbon Dioxide Challenge and Its Relationship to Panic Disorder

Over two decades of research has now established that the 35% CO_2 challenge incites panic symptoms in many individuals with PD (e.g., Gorman et al., 1990; Perna et al., 1994). Moreover, to gain validity as a panic-provocation procedure, numerous studies have demonstrated the specificity of the effects of CO_2 to PD. In other words, among individuals with various anxiety disorders, all of whom displayed high levels of anxiety, only those with PD displayed panic reactivity to CO_2. Such studies included a comparison 'non-clinical control' group that consisted of individuals without any Axis-I psychopathology. For example, CO_2-panic was found to be significantly higher in people with PD than in people with obsessive-compulsive disorder (OCD) and non-clinical controls (Griez, de Loof, Pols, Zandbergen, & Lousberg, 1990). A study comparing people with PD to those with generalized anxiety disorder (GAD) (Verburg, Griez, Meijer, & Pols, 1995) found similar results, such that those with PD experienced a marked increase in anxiety after CO_2 inhalation while there was no significant reaction in those with GAD. In other research, individuals with animal phobias had the same response as non-clinical controls (Verburg, Griez, & Meijer, 1994). Moreover, one study to date found that individuals with eating disorders reacted similarly to non-clinical controls (Perna, Casolari, et al., 2004).

The specificity of CO_2-induced panic to PD led researchers to posit biological explanations for the reaction. Several hypotheses have been put forth. Klein's suffocation false alarm hypothesis has received considerable attention in the literature. According to Klein (1993), CO_2-induced panic in people with PD suggests a hypersensitivity to suffocation cues, or in other words, a low threshold for firing a hypothetical suffocation alarm. This alarm can be activated by rising levels of CO_2 that signal an impending loss of oxygen. Another biological theory focuses on a dysregulation in the serotonergic system of people with PD (Coplan et al., 1992; Maron & Shlik, 2006). This approach overlaps with Klein's theory, as a decrease in serotonin influences anxiety-related mechanisms including respiratory control, which can result in panic symptoms.

Some evidence is consistent with a biological explanation for CO_2-induced panic. For example, a familial vulnerability to PD increases reactivity to the challenge in relatives without PD (Perna, Cocchi, Allevi, Bussi, & Bellodi, 1999; van Beek & Griez, 2000). Additionally, manipulating serotonin (5-HT) in the body alters reactivity to CO_2. Decreased serotonergic functioning increases the likelihood of CO_2-induced panic, as shown by tryptophan depletion challenge studies (Klassen, Klumperbeek, Deutz, van Praag, & Griez, 1998; Schruers et al., 2000). Tryptophan is an essential amino acid found in the human diet, and its depletion reduces serotonin in the body (Klaassen et al., 1998). Compared to a placebo mixture, participants in a tryptophan depletion group (19 males without any Axis I psychopathology) demonstrated increased panic symptoms after the 35% CO_2 challenge (Klaassen et al., 1998). Similar results were found in 24 people with PD (Schruers et al., 2000). Moreover, another study demonstrated that panic reactivity was significantly enhanced in healthy individuals who were given a 5-HT antagonist (metergoline), compared to other healthy individuals who were given a placebo prior to the inhalation (Ben-Zion, Meiri, Greenberg, Murphy, & Benjamin, 1999). Conversely, people

who take medication that blocks the reuptake of serotonin (i.e., SSRIs) do not experience panic in response to CO_2 (e.g., Perna, Bertani, et al., 2004).

Other Psychological Conditions Associated With Panic Reactivity to CO_2

Other findings suggest that biological factors are insufficient to drive panic in CO_2-challenge studies. For example, individuals with mood disorders (major depressive disorder and bipolar disorder) respond to CO_2 like non-clinical controls (Perna, Barbini, Cocchi, Bertani, & Gasperini, 1995). Considering that serotonergic abnormalities are also present in individuals with mood disorders (as well as GAD), the finding that populations with mood disorders or GAD (Verburg et al., 1995) do not panic to CO_2 is evidence that serotonin abnormalities cannot fully explain CO_2-induced panic.

Further complicating matters, research on the specificity of CO_2-panic has consistently revealed that individuals without a diagnosis of PD but with other psychopathology do indeed experience panic in the CO_2 challenge. This includes individuals who experience sporadic unexpected panic attacks without an Axis-I diagnosis (e.g., Perna, Gabriele, Caldirola, & Bellodi, 1995), and individuals who fall within diagnostic groups other than PD and do not experience sporadic unexpected panic attacks. These diagnostic groups include: situational and natural environment phobias (e.g., Verburg, 1994), social anxiety disorder (e.g., Caldirola, Perna, Arancio, Bertani, & Bellodi, 1997; Schmidt & Richey, 2008), and premenstrual dysphoric disorder (e.g., Harrison et al. 1989). In addition, while some studies have found that trait anxiety and state anxiety prior to the CO_2 challenge is not sufficient for a panic response, other studies have found the opposite; trait and state anxiety do, in fact, predict a panic response to CO_2 (see Zvolensky & Eifert, 2001 for a review). Results are thus inconclusive regarding whether state and trait anxiety influence panic reactivity. Moreover, a recent study found that people with post-traumatic stress disorder (PTSD) also panicked in response to CO_2 (Muhtz, Yassouridis, Daneshi,

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Braun, & Kellner, 2011). A previous study, however, found opposing results; CO_2 reactivity in those with PTSD was indistinguishable from that of non-clinical controls and was also significantly less than those with PD (Talesnik, Berzak, Ben-Zion, Kaplan, & Benjamin, 2007). Conclusive findings regarding whether PTSD enhances reactivity to CO_2 cannot be revealed without replication.

Psychological Constructs Associated With Panic Reactivity to CO_2

Another important finding in the CO_2 literature is that some individuals without any psychopathology experience panic in the CO_2 challenge (e.g., Schmidt, Richey, Cromer, & Buckner, 2007). Studying the reactions of healthy, non-clinical controls holds particular promise to address what factors are necessary and sufficient to cause CO_2-induced panic, as these individuals arguably should not have the biological dysregulations characterizing those with psychopathology (McNally, 1994). Three particular psychological constructs are shown to be involved in the experience of panic attacks: anxiety sensitivity, discomfort intolerance, and distress tolerance.

Anxiety sensitivity (AS; Reiss & McNally, 1985) is characterized by a belief that the experience of anxiety has negative implications, such as illness, embarrassment or additional anxiety. Discomfort intolerance (DI; Schmidt, Richey, & Fitzpatrick, 2006) is defined as an inability to withstand uncomfortable physical sensations. Distress tolerance (DT; Simons & Gaher, 2005) is a measure of the degree to which an individual is able to withstand negative emotions. Correlations demonstrate that DI is related to both DT ($r = -.25$, $p < .001$; Howell, Leyro, Hogan, Buckner, & Zvolensky, 2010) and AS ($r = .28$, $p < .001$; Howell et al., 2010). AS and DT are also related ($r = -.47$, $p < .001$; Keough, Riccardi, Timpano, Mitchell, & Schmidt, 2010). Although these constructs overlap, the low-to-moderate correlations amongst them imply that they are likely distinct.

AS is a cognitive risk factor for panic and anxiety psychopathology. As measured by the Anxiety Sensitivity Index (ASI; Reiss, Peterson, Gurskey, & McNally, 1986), AS predicted the development of spontaneous panic attacks after controlling for a history of panic attacks and trait anxiety (Schmidt, Lerew, & Jackson, 1997). High AS has also been implicated as a significant predictor of CO_2-panic in individuals with PD (Perna, Romano, Caldirola, Cucchi, & Bellodi, 2003; Schmidt, Lerew, & Jackson, 1997) and in non-clinical samples (e.g., Eifert, Zvolensky, Sorrell, Hopko, & Lejuez, 1999). Additional research on the potency of AS to predict CO_2-panic has revealed anomalies as well, considering that people with depression are characterized by relatively high AS (e.g., Otto, Pollack, Fava, Uccello, & Rosenbaum, 1995) but no panic reactivity to CO_2 (Perna, Barnini, Cocchi, Bertani, & Gasperini, 1995). DI is also seen as a risk factor for panic and anxiety psychopathology. In a non-clinical sample with no history of panic attacks or Axis-I disorders, DI, as measured by the Discomfort Intolerance Scale (DIS; Schmidt et al., 2006), predicted increased panic reactivity to CO_2 (Schmidt et al., 2007). Lastly, DT is seen as a risk factor for psychopathology and certain disorders (for a review, see Leyro, Zvolensky, & Bernstein, 2010). Low levels of DT have been linked with high levels of anxiety sensitivity (Bernstein, Zvolensky, Vujanovic, & Moos, 2009). One study to date has looked at DT along with DI and AS as they relate to CO_2-panic in participants without psychopathology (Kutz, Marshall, Bernstein, & Zvolensky, 2010); 10% CO_2 was utilized. Scores on each of these three constructs were correlated with panic reactivity after the CO_2 challenge. AS, however, was the only significant unique predictor of panic reactivity (Kutz et al., 2010).

It is important to recognize that the aforementioned psychological constructs influence CO_2-panic not only in non-clinical control groups, but also in clinical groups. To be more specific, CO_2-induced panic in clinical groups likely results from a combination of psychological factors and biological vulnerabilities. Consequently, certain psychological constructs that are

associated with certain clinical disorders may also be implicated in panic reactivity to CO_2. That having been said, it is important to note that even in clinical groups – persons who have both psychological and biological vulnerabilities to CO_2 panic – there are some people who do not react.

The Carbon Dioxide Challenge and Eating Disorders

The DSM-IV-TR identifies anorexia nervosa (AN) and bulimia nervosa (BN) as two distinct eating disorder (ED) categories (APA, 2000). AN is characterized by an inability to maintain a normal body weight. There are two subtypes of AN: (1) restricting type (AN-R), which involves dietary restraint; and (2) binge-purge type (AN-BP), which involves both dietary restraint and episodes of binge-eating and purging. BN is characterized by recurrent binge-eating and extreme weight-control behaviour. There are also two subtypes of BN: (1) purging type (BN-P), which involves recurrent self-induced vomiting or laxative misuse to control weight; and (2) non-purging type (BN-NP), which involves behaviours aside from purging to control weight, such as extreme exercising (APA, 2000).

As previously mentioned, one study to date has employed a sample of individuals with EDs as a further test of the specificity of CO_2-induced panic (Perna, Casolari, et al., 2004). Perna, Casolari, et al. (2004) used a sample of 14 females with EDs (AN-R = 5, AN-BP = 3, BN-P = 6), 14 females with PD and 14 females as non-clinical control participants. Those in the ED and control groups did not have a family history of PD or a personal history of spontaneous panic attacks, and they were free from concurrent Axis I disorders. Findings revealed that an ED diagnosis did not predict panic reactivity to CO_2. Yet, despite this non-significant finding (Perna, Casolari, et al., 2004), there is adequate reason to suspect a possible relationship between CO_2-panic and EDs.

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Perna, Casolari, et al. (2004) outlined the following reasons for why studying people with eating disorders provides an important examination of the specificity of CO_2-panic: 1) frequent co-morbidity between ED and anxiety disorders, particularly PD; 2) a common genetic loading between BN and PD; 3) the effects of lactate infusion in people with BN; specifically, those with BN were found to react more than those without BN to a sodium lactate infusion, which, as previously mentioned, is another method of provoking panic in the laboratory (e.g., Lindy et al., 1998; Pitts & McClure, 1967). These reasons are elaborated on below.

1) Numerous studies have demonstrated high rates of co-morbidity in people with an AN or BN diagnosis. For example, the presence of at least one anxiety disorder was found in 63.5% of one ED sample (Kaye, Bulik, Thornton, Barbarich, & Masters, 2004) and in 71% of another ED sample (Godart et al., 2003). The co-morbidity of PD in particular varies amongst the ED diagnostic categories. For instance, Godart et al. (2003) demonstrated the prevalence of PD in an AN sample (AN-R 5.4%; AN-BP 14.5%) and in a BN sample (BN-P 20.9%; BN-NP 21.1%). These data suggest that the rate of co-morbidity is greater between PD and EDs characterized by cycles of bingeing and compensating compared to PD and restricting anorexia. Other studies have demonstrated similar findings (e.g., see Godart, Flament, Perdereau, & Jeammet, 2002 and Swinbourne & Touyz, 2007 for reviews), although some not as varied. For example, Kaye et al. (2004) found a PD prevalence rate of 9.3% in AN-R, 10.9% in AN-BP, and 11% in BN (purging and non-purging types were not specified). Additional speculation regarding an association between PD and bingeing/compensating is derived from case reports (Chesler, 1997) in which binge episodes triggered panic attacks in four women, aged 17-40, two of whom did not have PD. Of course, this suggestion must be bolstered by empirical research. Overall, an association is suggested between PD and ED, particularly EDs characterized by bingeing and compensatory behaviour.

2) Kendler et al. (1995) found a common genetic loading between PD and BN. This study investigated possible genetic influences of six psychological disorders prevalent in women: PD, MDD, GAD, BN, specific phobia, and alcoholism. A genetic factor was found to load most heavily on specific phobia, PD, and BN. This research is compelling evidence for a biological association between PD and BN.

3) Several studies have examined the panic effects of lactate infusion in people with BN compared to non-clinical control participants. Sodium lactate (Pitts & McClure, 1967) was identified as a panicogenic agent, and studies have tested whether sodium lactate causes reactivity only in those with PD, or also in persons with other disorders such as BN. In other words, researchers have questioned whether reactivity to sodium lactate is specific to PD or whether it characterizes, instead, a range of psychological conditions. In several studies, people with BN were tested with sodium lactate because of research associating PD and BN (e.g., Lindy et al., 1988). Results in one study showed a trend toward greater increases in anxiety ratings after lactate administration in participants with BN compared to control participants (George, Brewerton, & Jimerson, 1986). Two additional studies found that participants with BN reacted to lactate infusions with significantly greater anxiety than control participants (Lindy et al., 1988; Pohl, Yeragani, Balon, & Lycaki, 1989). A PD group was not included in these studies (i.e., no comparison was made between reactivity in people with BN to reactivity in people with PD).

Perna, Casolari, et al. (2004) did not consider two additional, and particularly important, reasons why individuals with EDs could be expected to display CO_2-panic. The first reason is regarding serotonin. Individuals with AN and BN often present with serotonin abnormalities. Serotonin is responsible for regulating mood and appetite. A proposed model of BN suggests that a serotonergic deficiency drives the binge-purge cycle (Kaye, Gendall, & Strober, 1998). Individuals with BN have lower levels of tryptophan (a chemical found in food), which controls

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the production of serotonin in the brain. Binge eating increases tryptophan levels, and purging subsequently reduces them. Studies demonstrate that a serotonergic deficiency remains even in those recovered from BN (e.g., Brewerton, 1995; Kaye et al., 1998). A proposed model of AN, on the other hand, demonstrates that acutely ill individuals have reduced serotonergic activity, while long-term recovered individuals have heightened serotonergic activity (e.g., Kaye et al., 1998). This suggests that a resumption of normal eating in AN may reveal inherent abnormalities in serotonergic systems (e.g., heightened serotonergic functioning) that produce a vulnerability to restricting food intake. A greater vulnerability to experience panic in the CO_2 challenge could thus be expected in a BN sample, based on research implicating panic reactivity in study groups with low serotonin (e.g., PD; Perna et al., 1994). Perhaps the reason why Perna, Casolari, et al. (2004) did not consider serotonin was because their sample did not discern AN from BN.

The second reason for possible CO_2-panic in an ED sample that Perna, Casolari, et al. (2004) did not consider is that certain psychological factors implicated in CO_2-panic (as previously discussed) are also related to EDs: anxiety sensitivity and discomfort intolerance. Anxiety sensitivity has received empirical attention in the eating disorders. Anestis, Holm-Denoma, Gordon, Schmidt, & Joiner (2008) investigated the relationship between AS and three subscales of the Eating Disorder Inventory (EDI; Garner, Olmstead, & Polivy, 1983): Bulimia, Body Dissatisfaction and Drive for Thinness, in both an undergraduate sample and an outpatient clinical sample (individuals with a variety of Axis-I disorders). This study controlled for the effects of impulsivity, mood symptoms and anxiety symptoms to isolate the link between AS and disordered eating symptoms. In both the non-clinical and clinical samples, results indicated that ASI scores significantly predicted EDI-Bulimia scores, but did not significantly predict EDI-Body Dissatisfaction scores. ASI scores in the clinical sample but not in the non-clinical sample predicted the EDI-Drive for Thinness scores. This subscale relates to features of both AN and

BN. Of utmost importance to the current study is the relationship between ASI scores and EDI-Bulimia scores. This finding links AS to bingeing and purging. It is important to note that questions on the EDI-Bulimia subscale refer to bingeing and vomiting as a purging behaviour, in the absence of other compensatory behaviours. Some explanations may account for the significant relationship between ASI scores and EDI-Bulimia scores. This result may point to a subset of individuals with an elevated fear of somatic sensations of anxiety who might eat in an effort to reduce tension and then subsequently purge (Anestis et al., 2008). Chesler (1997) raised similar speculation in her aforementioned case study series. However, another reason for bingeing and purging – one that has received empirical support – was previously discussed. Specifically, bingeing and purging is recognized as an attempt to regulate serotonin abnormalities (Kaye et al., 1998). As such, more rigorous research is needed to bolster this case study and implicate AS as a factor in bingeing and purging.

Distress tolerance has also received empirical attention in the ED literature, particularly in BN. In one study, DT significantly predicted subclinical bulimic symptoms in an undergraduate non-clinical sample, such that lower levels of DT were related to higher levels of bulimic symptoms (Anestis, Delby, Fink, & Joiner, 2007). Further, in the same study, DT scores mediated the relationship between AS and bulimic symptoms (Anestis et al., 2007).

Taken together, two psychological factors that are related to CO_2-panic in non-clinical participants (AS and DT) are also related to people with BN. Therefore, people with BN should be more likely to panic to CO_2 compared to people without BN. It should be noted that discomfort intolerance has not yet been investigated among individuals with eating disorders. It is possible that high DI scores within this population may simply be an index of the physical symptoms associated with the disorder, such as gastric distress from frequent self-induced vomiting.

Methodological limitations of the one previous CO_2 and ED study (Perna, Casolari, et al., 2004) tempers confidence that can be placed in the findings. Most notably, this sample contained both patients with BN and patients with AN, regardless of sub-type. The mixed group of participants with EDs and small subgroups of specific ED diagnoses may have compromised significant findings. That is, an eating disorder group (as was used in Perna, Casolari, et al., 2004) contains two types of symptom profiles: individuals with restricting behaviours who refuse to eat, and individuals with bingeing/purges symptoms who overeat and compensate. Possibly, panic reactivity to CO_2 is related to one but not both of these behavioural profiles, such that persons with restricting anorexia and non-purging bulimia might respond differently than those who binge and purge (people with binge-purge AN and purging BN). The biological vulnerability in binge-purge eating disorders (i.e., low serotonin) that predicts CO_2-panic in other clinical groups supports this possibility. Numerous pathways can result in reduced serotonergic functioning (Stahl, 1998). It is possible that the pathway resulting in low serotonergic functioning in BN is different than that in other psychological disorders. Findings of high AS and low DT in people with BN also support the possibility that CO_2-panic may be related to one type of eating pathology. Alternatively, it is possible that individuals with binge/purge eating disorders and individuals with depression share a non-reactivity to CO_2, despite their well-documented serotonin abnormalities and high levels of AS. Further investigation is clearly warranted.

The Present Study

It is therefore appropriate to conduct another CO_2 challenge study investigating panic reactivity in an ED sample consisting of only binge/purge disorders (AN-BP and BN-P). Another reason to utilize both an AN-BP group and a BN-P group is because of the link found between high AS and features of both AN and BN (i.e., EDI – Drive for Thinness subscale relates to all ED diagnoses, and EDI – Bulimia subscale relates to both AN-BP and BN-P; Anestis et al.,

2008). Such research would illuminate whether AS is differentially associated with panic reactivity in people with AN and in people with BN. However, due to significant health risks in AN possibly warranting the presence of a medical doctor, the present study investigated panic reactivity in a BN sample only. If individuals with BN experienced panic in the challenge, this study would be the first evidence extending CO_2-induced panic to this diagnostic category. Moreover, if certain psychological constructs were found to be associated with panic reactivity regardless of diagnostic group, this study would also add to the growing body of research suggesting that psychological factors mediate responses to biological challenges.

Objectives

The <u>first</u> objective of this study was to further assess the specificity of the effects of the CO_2 challenge. The 35% CO_2 single-breath inhalation challenge was utilized with a sample of individuals with BN (purging type only), individuals with PD, and individuals without these disorders (control group). The following comparisons in terms of panic reactivity were investigated: (1) the BN group compared the control group, (2) the PD group compared to the control group, and (3) the BN group compared to the PD group. Panic reactivity was measured by subjective anxiety (Subjective Units of Distress Scale; Wolpe, 1973) and panic symptomatology (Acute Panic Inventory; Liebowitz, Gorman, Fryer, Dillon, & Klein, 1984). The <u>second</u> objective of this study was to determine whether certain psychological factors mediate the relationship between diagnostic status and panic reactivity. The factors examined were those that have previously been implicated in CO_2 research: anxiety sensitivity (measured by the Anxiety Sensitivity Index; ASI; Reiss et al., 1986), distress tolerance (measured by the Distress Tolerance Scale; DTS; Simons & Gaher, 2005) and discomfort intolerance (measured by the Discomfort Intolerance Scale; DIS; Schmidt et al., 2006). The <u>third</u> objective of this study was to identify whether specific facets of BN are related to CO_2-panic. Two particular variables were studied in

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relation to CO_2-panic: 1) Features of BN-P as measured by the 8 subscales of the Eating Disorder Inventory (EDI; Garner, Olmstead, & Polivy, 1983); and 2) Frequency of binges and purges over the past three months as measured by the Eating Disorders Diagnostic Scale (EDDS; Stice, Telch, & Rizvi, 2000).

Hypotheses

The following hypotheses were advanced:

1.1. Reactivity (operationalized by categorical and continuous measures) to the room air inhalation would not differ between participants with BN, participants with PD and participants without these diagnoses (control group).

1.2. According to all panic measures, participants in the BN group would display greater panic reactivity to the CO_2 inhalation compared to the control group. Participants in the PD group would also display greater panic reactivity to the CO_2 inhalation compared to the control group. Moreover, the proportion of people reacting and the degree of reactivity in the PD group would be similar to those in the BN group.

1.3. No a priori predictions were advanced regarding the associations of state anxiety and trait anxiety to panic reactivity given the mixed findings in the literature (Zvolensky & Eifert, 2001) and the lack of research in BN; these associations were examined in an exploratory fashion.

1.4. No a priori predictions were advanced regarding the associations of depressive symptoms to panic reactivity, given the lack of research in this area. However, a prediction was made regarding depressive symptoms and panic reactivity in participants with PD and participants without PD or BN diagnoses; depressive symptoms would not correlate with any of the panic measures in these groups.

2.1. Participants with BN and participants with PD would produce higher scores on measures of anxiety sensitivity and discomfort intolerance, and lower scores on a measure of distress tolerance relative participants in without these diagnoses.

2.2. Higher levels of anxiety sensitivity and discomfort intolerance and lower levels of distress tolerance would each be associated with panic reactivity, and anxiety sensitivity would be the best predictor of panic reactivity.

2.3. Anxiety sensitivity, discomfort intolerance, and distress tolerance would each mediate the association between clinical status and panic reactivity.

3.1. Scores on the EDI – Bulimia subscale and the EDI – Drive for Thinness subscale would both be positively correlated with panic reactivity in participants with BN.

3.2. No a priori hypotheses were advanced regarding the associations of the other 6 EDI dimensions to panic reactivity in participants with BN; these were examined in an exploratory fashion.

3.3. No a priori hypotheses were advanced regarding the association of BN severity (defined by the frequency of bingeing and purging) to panic reactivity; these were examined in an exploratory fashion.

Method

Participants

A total of 118 individuals indicated an interest in the study, and 102 completed the screening assessment. Of the 102 individuals who completed the screen, 42 were deemed ineligible. Ineligibility was due to the following reasons: endorsement of medical exclusionary criteria ($n = 21$), endorsement of an exclusionary Axis-I diagnosis ($n = 10$), current use of psychotropics ($n = 4$), not meeting the age requirement ($n = 4$), current substance use ($n = 2$), current suicidality ($n = 1$). Sixty individuals appeared eligible and were invited into the Psychophysiology Research Laboratory at Ryerson University to complete the study. Of these, 9 individuals either cancelled or did not show up for their study appointment, leaving a sample of 51 participants. Participants were recruited from two sources (see Appendix B for all recruitment materials). The first source was Ryerson University's Introductory Psychology Research Participant Pool ($n = 3$). These participants were recruited through SONA, Ryerson's online system for managing the participant pool. Each Introductory Psychology student received partial course credit for her participation. The second source was the Toronto community. These participants were recruited by several means: (1) flyers posted around the University of Toronto, York University and Ryerson University ($n = 19$); (2) advertisements on Craigslist.com and Kijiji.ca (online classifieds; $n = 24$); and (3) an advertisement placed in the Metro newspaper (a free, Toronto-based, daily commuter newspaper; $n = 5$). These participants were compensated $20 cash for their participation.

Participants were recruited from the aforementioned sources, and their psychological diagnoses (or lack thereof) determined the study group to which they belonged. The three study groups included: Individuals with a DSM-IV-TR diagnosis of Panic Disorder (PD), individuals with a DSM-IV-TR diagnosis of Bulimia Nervosa – Purging Type (BN-P), and participants

without either diagnosis of PD or BN. This latter group did not constitute a true healthy control group (i.e., devoid of all DSM-IV-TR Axis-I disorders). Axis-I disorders that have not been implicated in panic reactivity to CO_2 were not exclusion criteria (see below for all inclusion/exclusion criteria). Therefore, biological dysregulations inherent in some disorders (e.g., depression) may be present in this sample, namely in the subset that endorsed additional Axis-I disorders ($n = 6$). In addition, one factor consistently shown to increase CO_2-panic was not exclusionary for the BN and control groups: a history of unexpected panic attacks. The primary reason for including such participants was feasibility of obtaining a large enough sample, particularly in the BN group.

Five of the 51 participants were not considered in any analyses for the following reasons. Two participants did not complete the breathing experiments, and one participant did not meet tidal volume criteria during the CO_2 inhalation. These three participants did not have a PD or BN diagnosis. One additional participant met criteria for BN – non-purging type on the Eating Disorder Diagnostic Scale (therefore became ineligible for the BN group). Lastly, one participant was in the PD group; since only one person with PD participated in the study thus far, hypothesis testing was restricted to participants with BN (N = 15) and participants without PD or BN (N = 31). Participants without PD or BN, therefore, are subsequently referred to throughout this thesis as participants without BN. Data collection for the PD group is ongoing. Therefore, the final sample size was 46 participants.

The inclusion criteria for all groups were as follows: (1) female; (2) age between 18 and 45 years; (3) no diagnosis of AN, SAD, situation-specific phobias, or PMDD; (4) physical examination within the past 12 months. Participants in the BN group had to endorse a diagnosis of BN – Purging Type, no diagnosis of PD, and no evidence of PD diagnoses in first and second-degree relatives. Participants in the non-BN group had to endorse no diagnosis of PD or BN, and

no evidence of PD diagnoses in first and second-degree relatives. All diagnostic criteria were confirmed by the Mini-International Neuropsychiatric Interview (M.I.N.I.; Sheehan et al., 2004), which is consistent with previous studies (e.g., Perna, Casolari, et al., 2004).

Medical exclusion criteria for all groups were also consistent with previous studies (e.g., Perna, Casolari, et al., 2004) and were as follows: (a) current pregnancy; (b) personal medical history of brain tumor, cerebral aneurysm, cerebral hemorrhage, stroke, transient ischemic attack, heart attack, heart disease, coronary artery disease, congestive heart failure, mitral valve prolapse, diabetes, history of fainting (for example, vasovagal syncope or otherwise unexplained fainting episodes), renal disease, heart murmur, cardiac arrhythmia, respiratory disease, lung disease, basilar artery migraine, asthma, epilepsy, hemiplegic migraine, seizures, liver disease, kidney disease, ophthalmoplegic migraine, hypertension, or cerebrovascular accident; (c) family history (first degree relatives) of cerebral aneurysm, cerebral hemorrhage, or hemiplegic migraine; (d) endorsement of any of the three headache symptom questions that screen for complicated migraine (refer to the Medical History Questionnaire, appendix D); (e) use of psychotropic medications except for benzodiazepines occasionally (less than twice a week and also not within 5 half lives of the challenge); and (f) use of a medication that can significantly affect heart rate (examples include beta-blockers, calcium channel blockers, and tricyclic antidepressants). These medical exclusion criteria were necessary for 3 reasons: (1) to make sure that no participants had a personal history of any medical conditions that might theoretically pose a risk in the CO_2-enriched air challenge [exclusion criteria (b) and (d)] and to make sure that no participants have a family history of highly heritable conditions that might pose a risk in the CO_2-enriched air challenge [exclusion criterion (c)]; (2) to make sure that no participants are taking medications known to minimize their reaction to the CO_2-enriched air inhalation [exclusion criterion (e)]; and

(3) to make sure that no participants are taking a medication whose effect on heart rate might theoretically be a risk in the breathing experiments [exclusion criterion (f)].

Measures

All participants were asked to report on their age and ethnicity. In addition, the following measures were used:

Diagnostic Interviews

Mini-International Neuropsychiatric Interview (*M.I.N.I.;* Sheehan et al., 2004). The M.I.N.I. is a brief semi-structured diagnostic interview that assesses current and lifetime DSM-IV Axis-I disorders. In the current study, questions from the M.I.N.I. were asked over the telephone to screen for the following: mood disorders (Major Depressive Disorder, Dysthymia, Premenstrual Dysphoric Disorder), anxiety disorders (Panic Disorder, Agoraphobia, Social Phobia), and eating disorders (AN Restricting Type, AN Binge-Eating/Purging Type, BN Purging Type, BN Non-Purging Type). The full M.I.N.I. was then conducted with potential participants in the lab to confirm eligibility and to diagnostically characterize the sample. This widely used diagnostic interview was chosen because of its reasonable length (approximately 20 minutes) and acceptable psychometric properties (Sheehan et al., 1998). M.I.N.I. diagnoses resulted in good to very good inter-rater and test-retest reliability; these psychometric properties are comparable to those of the SCID-I (First, Spitzer, Gibbon, & Williams, 2001). For the main diagnoses of interest, kappa was found to be .78 for BN, and .80 for Panic Disorder – lifetime (Sheehan et al., 1998).

Structured Clinical Interview for DSM-IV-TR Axis I Disorders *(SCID;* First et al., 2001). The SCID is a semi-structured diagnostic interview that assesses current and lifetime DSM-IV Axis-I disorders. In the current study, the SCID was used only to assess for Situation-

Specific Phobias. The inter-rater reliability for diagnosing Specific Phobias from the SCID was found to be .83 (Lobbestael, Leurgans, & Arntz, 2011).

Medical Screening Measure

Medical History Questionnaire (appendix D). Dr. Kristin Vickers adapted this questionnaire from those used by other psychophysiology researchers in the United States. It was approved by Harvard University's Research Ethics Board for the purpose of Dr. Vickers' dissertation and subsequently by Ryerson University's Research Ethics Board for Dr. Vickers' ongoing lab projects. Some questions are simply information gathering (e.g., do you smoke cigarettes) and are included because this type of information may be useful for subsequent analyses. Other questions are important for exclusionary purposes (as outlined under *participants*). Any response of *yes* or *not sure* on such questions would deem potential participants ineligible.

Symptom Measures

Eating Disorder Diagnostic Scale (*EDDS;* Stice et al., 2000). The EDDS is a 22-item self-report measure designed to assess the DSM-IV-TR diagnostic criteria for AN, BN, and Binge-Eating Disorder (BED). Responses are typically used to group participants into one of these three eating disorder diagnostic categories, or a non-eating disordered category. An overall symptom composite score can also be calculated, which reflects each participant's overall level of eating pathology. In the current study, this measure was used to characterize the BN participants and verify their ED diagnosis. Among a female sample, the EDDS has demonstrated acceptable test-retest reliability ($r = .87$) and criterion validity with both the Eating Disorder Examination (EDE; Fairburn & Cooper, 1993) and the SCID, which are the "gold standard" ED diagnostic measures. For AN, $\kappa = .93$; for BN, $\kappa = .81$; for BED, $\kappa = .74$. (Stice, Fisher, &

Martinez, 2004; Stice et al., 2000). The symptom composite evidenced acceptable internal

consistency across items (α = .89; Stice et al., 2000).

Eating Disorder Inventory (*EDI;* Garner et al., 1983). The EDI is a self-report

questionnaire consisting of 64 items that assess pathological eating, cognitions, and behaviours

that are common in both AN and BN. Participants are asked to rate each item on a scale from 1

(*never*) to 6 (*always*). The EDI yields 8 subscale scores: Drive for Thinness, Perfectionism,

Bulimia, Body Dissatisfaction, Ineffectiveness, Interpersonal Distrust, Interoceptive Awareness,

and Maturity Fears. Higher scores are indicative of greater psychological and behavioural traits

that are common in AN and BN. In a BN sample, the internal consistency reliability was found to

be high within each of the 8 subscales (ranging from α = .83 – .91) and for the total scale (α =

.96; Schaefer, Maclennan, Yaholnitsky-Smith, & Stover, 1998).

Beck Depression Inventory – Second Edition (*BDI-II;* Beck, Steer, & Brown, 1996).

The BDI-II is a 21-item self-report questionnaire that assesses for the presence and severity of

depressive symptoms (e.g., anhedonia, appetite changes, sleep difficulties) within the past two

weeks (Beck, Steer, Ball, & Ranieri, 1996). Each item is rated on a 4-point scale, ranging from 0

to 3. On two items (16 and 18) there are 7 options to indicate either an increase or decrease of

appetite and sleep. Higher scores are indicative of greater depressive symptoms. The BDI-II was

used in the current study to measure participants' depressive symptoms, and to ensure that

current suicide risk was not present (question 9, *suicidal thoughts or wishes*). Internal consistency

reliability for the BDI-II was found to be excellent among psychiatric outpatients (α = 0.91;

Steer, Ball, Ranieri, & Beck, 1997), and college students (α = .90; Storch, Roberti, & Roth,

2004). Additionally, criterion validity has been established in a college student population, as

BDI-II scores were significantly correlated with the number of depressed mood symptoms

endorsed on the SCID-I (r = .83; Sprinkle et al., 2002).

State-Trait Inventory for Cognitive and Somatic Anxiety – State Version and Trait Version (*STICSA*; Ree, MacLeod, French, & Locke, 2000). The STICSA was designed to assess state and trait anxiety, and to improve upon several limitations of the State-Trait Anxiety Inventory (STAI; e.g., an inability to adequately discriminate between symptoms of anxiety and depression). The STICSA replicates the STAI's format of independent state and trait scales. Both the state and trait scales were used in the current study. They each contain the same 21 self-reported items (e.g., my breathing is fast and shallow), which reflect both the cognitive and somatic symptoms of anxiety. The state scale assesses how respondents "feel right now, at this very moment, even if it is not how you usually feel." The trait scale assesses "how often, in general, the statement is true of you" (Ree et al., 2000). Responses are rated on a 4-point Likert scale, ranging from 1 (*not at all*) to 4 (*very much so*). Higher scores reflect greater anxiety. Internal consistency was found to be $\alpha = .92$ for the state scale, and $\alpha = .91$ for the trait scale. Similar alphas were found in a college sample (Gros, Antony, Simms, & McCabe, 2007). Adequate convergent validity was demonstrated between the anxiety subscale of the Depression Anxiety Stress Scales (Lovibond & Lovibond, 1995), and both the STICSA State scale ($r = .67$) and the STICSA Trait scale ($r = .68$) (Gros et al., 2007).

Process Measures

Anxiety Sensitivity Index (*ASI;* Reiss et al., 1986). The ASI is a 16-item self-report measure that assesses fear of bodily sensations that are associated with arousal. This type of fear differs from state or trait anxiety (McNally, 1994) and is believed to amplify preexisting anxiety and place an individual at an increased risk for panic attacks. Each item is rated on a 5-point scale ranging from 0 (*very little*) to 4 (*very much*). Higher scores reflect higher levels of anxiety sensitivity. An example of an item is "When I cannot keep my mind in a task, I worry that I might be going crazy." The ASI is a widely used measure, and has demonstrated adequate test-

retest reliability for women (r = .74; Reiss et al., 1986) and high internal consistency reliability (α = .88; Peterson & Hellbronner, 1987). Moreover, it has demonstrated discriminant validity from other anxiety measures (Peterson et al., 1987).

Discomfort Intolerance Scale (*DIS*; Schmidt et al., 2006). The DIS is a 5-item, self-report measure of the degree to which individuals tolerate physical discomfort, including pain (e.g., I take extreme measures to avoid feeling physically uncomfortable). Participants rate each question on a scale from 0 (*not at all like me*) to 6 (*extremely like me*). Higher scores are indicative of a greater inability to tolerate discomfort. In a non-clinical sample, internal consistency reliability was found to be average (α = .60). In a clinical sample it was found to be somewhat higher (α = .70) (Schmidt et al., 2006). In terms of criterion validity, the DIS was moderately related to measures of anxiety and anxiety-related symptoms (Schmidt et al., 2006).

Distress Tolerance Scale (*DTS;* Simons & Gaher, 2005). The DTS is a 15-item questionnaire examining the degree to which individuals experience negative emotions as intolerable (e.g., I can't handle feeling distressed or upset). Items are rated on a Likert scale ranging from 1 (*strongly agree*) to 5 (*strongly disagree*). Lower scores indicate a tendency to have a lower tolerance for emotional distress. The internal consistency of the DTS was found to be α = .82 (Leyro et al., 2010). Moreover, this scale showed good convergent, discriminant and criterion validity, as it was negatively correlated with measures of affective distress and dysregulation, alcohol and marijuana (Simons & Gaher, 2005).

Panic Reactivity Measures (appendix E)

Panic reactivity was measured at baseline and after each inhalation (room air and CO_2). Regrettably, no gold standard exists concerning how to measure challenge-induced panic reactivity. Following other researchers (see Rassovsky & Kushner, 2003), the current study used self-reported panic symptomatology (i.e., a checklist of panic attack symptoms) and subjective

anxiety ratings as the main measures of panic reactivity. In addition, participants were asked whether they believed they have had a panic attack after each inhalation (room air and CO_2). This is also consistent with other researchers (see Rassovsky & Kushner, 2003).

Acute Panic Inventory (*API;* Liebowitz et al., 1984). The API is a 17-item self-report questionnaire that assesses the symptoms of physical and cognitive arousal associated with spontaneous panic attacks. Participants rate the severity of each symptom from 0 (*absent*) to 3 (*severe*) (e.g., do you feel faint?). The API has been used extensively as a measure of CO_2 reactivity in panic provocation studies (e.g., Goetz, Klein, Papp, Martinez, & Gorman et al., 2001; Gorman et al., 1990; Harrison et al., 1989; Schmidt et al., 2008). It is given to participants at baseline and immediately after each inhalation (room air and CO_2). To measure reactivity continuously using the API, total symptom scores (TSS) are obtained and change in TSS from room air to CO_2 is calculated. To measure reactivity categorically (e.g., panic attack or not), a count is made of the number of items that increased post-CO_2 relative to room air. Reactivity is then defined as whether at least four items increased (regardless of the intensity of the increase, i.e., number of points increased within a single item). Participants reporting an increase of fewer than four symptoms are deemed to have not reacted. The cut-off number of four corresponds to DSM-IV panic attack criteria (e.g., Goetz et al., 2001; Gorman et al., 1990).

Subjective Units of Distress Scale (*SUDS;* Wolpe, 1973). The SUDS is a visual analogue scale for anxiety (VAS-A). It is used to measure the degree of subjective intensity of current anxiety on a continuum ranging from *0* (*no anxiety at all*) to *100* (*the worst anxiety imaginable*). This scale is used as a measure of reactivity in CO_2 challenge studies (e.g., what was the highest level of fear you experienced during the breathing experiment?). It is given to participants at baseline and immediately after each inhalation (room air and CO_2). VAS-A scores are obtained and change in VAS-A from room air to CO_2 is measured. This change is considered

to be a continuous measure of reactivity. To assess reactivity using the SUDS categorically, reactivity is said to occur if an increase of ≥ 26 points in anxiety from room air to CO_2 is present. Change scores below 26 are considered to be no reactivity. A research group that is well known for its CO_2 studies (Battaglia & Perna, 1995) identified this cut-score. Battaglia and Perna (1995) conducted a receiver operating characteristics (ROC) statistical analysis to determine that 26 was the point that differentiated people with and without PD in their reactivity to CO_2.

Subjective Panic Attack Scale (*SPAS*). Dr. Kristin Vickers developed this 10-item questionnaire for use in her dissertation at Harvard University. Following each inhalation (room air and CO_2), participants are asked about various sensations and perceptions that they may or may not have experienced during the breathing experiments. Several questions provide a *yes* or *no* response, and other questions provide more qualitative data regarding how participants reacted to the challenge. Question 9 (in your opinion, did you just have a panic attack during the experience?) was used in this study as an additional measure of categorical, self-reported panic reactivity.

Procedure

Community Participants

Advertisements in the online classifieds, the Metro newspaper, and university campuses in Toronto included contact information for the study. Interested participants contacted the researcher by telephone or email. The researcher gave them further details of the study and invited them to complete a screening assessment over the telephone to determine their eligibility. Following verbal consent to undergo the assessment, they were asked about all exclusionary criteria on the Medical History Questionnaire followed by screening questions from the M.I.N.I. for the following disorders: Mood Disorders, Social Phobia, Panic Disorder, Agoraphobia, and Eating Disorders. They were also asked the screening question for Specific Phobias from the

SCID. Depression status (which was not exclusionary, except for Premenstrual Dysphoric Disorder) was assessed in all participants to ensure that current suicide risk was absent. Lastly, participants were asked about any family history of PD. If any exclusion criteria were endorsed at any point during a screening assessment, the researcher informed the participant that she was not eligible for the study. She was invited to enter her name into a draw to win $50 and was informed that she would be contacted via email if selected as a winner. If the participant did not endorse any exclusion criteria, the researcher invited her to complete the study in a single lab visit (approximately 1.5 hours).

The lab visit occurred as follows: The researcher asked all participants to read and subsequently sign a statement of informed consent (see appendix C for *Informed Consent for Community Participants*), which outlined the general purpose and procedure of the study and potential risks or discomforts that may arise. Since the screening assessment was conducted over the telephone, it was necessary for participants to complete the Medical History Questionnaire in paper form. There were two reasons for this: (1) as a precautionary measure (e.g., an additional medical check required by the Research Ethics Board of Ryerson University), and (2) to collect the full range of information provided by the questionnaire (not only the exclusion criteria). The full M.I.N.I. was then conducted, and subsequently participants were asked to complete several self-report questionnaires. They first completed the BDI-II to ensure, again, the absence of current suicide risk (i.e., a score > 1 on question 9, *suicidal thoughts or wishes*), followed by a questionnaire package that was presented to them in Qualtrics, a secure online survey software. This package included the following: Demographic Questions, the Eating Disorders Diagnostic Scale (EDDS), the Eating Disorder Inventory (EDI), the State-Trait Inventory for Cognitive and Somatic Anxiety (STICSA) – State Version and Trait Version, the Anxiety Sensitivity Index (ASI), the Discomfort Intolerance Scale (DIS) and the Distress Tolerance Scale (DTS). After this,

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participants engaged in the breathing experiments (described below) and were subsequently

debriefed about the study (see Appendix E for *Debriefing for Community Participants*) and

compensated. If at any point during the visit participants endorsed any exclusion criteria, they

were informed of their ineligibility and were compensated appropriately.

Procedure for SONA Participants

Introductory Psychology students at Ryerson University had the opportunity to view a

description of the study on the online SONA system. Those who were interested in completing

the study were able to sign up as participants for lab visit 1 through the online system. Lab visit 1

(approximately 45 minutes) consisted of the screening assessment to determine eligibility for the

study. Following written informed consent to undergo the assessment (see appendix C for

Informed Consent for SONA Participants – Visit 1), participants completed the full medical

history questionnaire in writing and completed the BDI-II. The full M.I.N.I. was then conducted,

in addition to the SCID screening question for Specific Phobias. Participants were also asked

about any family history of PD. They were subsequently debriefed (see appendix E for

Debriefing for SONA Participants – Visit 1), and course credit was granted. Note that the SONA

requirement dictates one course credit to equal approximately 45 minutes to 1 hour of study

participation. For this reason, SONA participants completed several measures at visit 1 that were

not included in the telephone screening for community participants, but were administered with

these participants during their single study visit. These measures included the full Medical

History Questionnaire, the full M.I.N.I., and the BDI-II. If any exclusion criteria were endorsed at

any point during the visit, the researcher informed the participant that she was not eligible to

complete lab visit 2. If no exclusion criteria were met, the researcher invited her to complete the

study in a separate session (lab visit 2; approximately 45 minutes) within 7 days of the first visit.

Lab visit 2 occurred as follows: Informed consent was first obtained, similar to that for the community participants (see appendix C for *Informed Consent for SONA Participants – Visit 2*). Following consent, participants completed the questionnaire package presented in Qualtrics (identical to that described for the community participants), and then engaged in the breathing tests. Lastly, the researcher debriefed participants about the study and course credit was granted (see appendix E for *Debriefing for SONA Participants – Visit 2)*.

Breathing Experiments

Each participant was on a breathing circuit (described later) and completed the breathing procedure. First, participants took one vital capacity breath of normal room air (the placebo inhalation). Second, participants took one vital capacity breath of 35% CO_2-enriched air (balance, or 65% oxygen; the experimental inhalation). These inhalations were not counterbalanced; rather, the placebo inhalation always occurred first. Similar to other CO_2 challenge studies (e.g., Perna, Casolari, et al., 2004), the research proceeded this way so that participants who did not like the placebo inhalation would have a chance to stop participating before the experimental inhalation that is much more likely to provoke discomfort.

The breathing circuit consisted of a disposable 30 mm ID (inner diameter) mouthpiece (single-participant use) fixed to a bacterial/viral filter (Pulmoguard; single-participant use) that was connected to transparent plastic tubing. The tubing connected into a gas-mixing chamber, which then connected to a respiratory flowhead, also called a pneumotach (a device that measures tidal volume). The pneumotach connected to a two-way non-rebreathing valve, one side of which is exclusively expiration, the other side of which is exclusively inspiration. The inspiratory port connected to a manual stopcock with two ports: one port fed room air (and was used for the baseline and placebo inhalations), and the second port connected to a gasbag filled with CO_2 -

enriched air (35% CO_2; 65% O_2; used exclusively for the experimental CO_2-enriched air inhalation).

The specific protocol for the breathing experiments was as follows: In preparation for a participant's arrival to the lab, the researcher disconnected the gas bag (Hans Rudolph, non-diffusing gas collection bag [15 liters] and a 4-way stopcock, 2500 series) from the breathing circuit and filled it with CO_2-enriched air from the gas tank. The researcher then reconnected the circuit and attached a new (sealed in plastic) Pulmoguard filter to the tubing connected to the gas-mixing chamber, and then attached a new mouthpiece onto the other end of the Pulmoguard filter.

When a participant arrived at the lab, she sat in a comfortable chair and was connected to a clinical vital signs monitor (Criticare Systems Inc., Model 5060DXNT, USA). The monitor's blood pressure cuff was attached to her non-dominant arm and its oxygen saturation finger clip sensor was connected to her non-dominant hand. She was given a new (single-participant use) nose clip. She put on the nose clip and placed the mouthpiece in her mouth. She was informed that throughout the session, oxygen saturation would be measured and blood pressure would be taken automatically each minute. To establish baseline measures, the researcher asked the participant to breathe normally on the breathing circuit (stopcock feeding room air) for 3 minutes. During this time, the researcher measured the participant's vital capacity by asking her to exhale as big a breath of room air as possible, inhale and hold this breath for 4 seconds, then exhale fully (recorded by AD Instruments, PowerLab System 8/30, with Chart Pro Modules). This vital capacity measure was used as a comparison for the later two experiments; specifically, only placebo or CO_2-enriched air vital capacity inhalations that were at least 80% of the room air vital capacity were considered valid. Following this, the researcher asked the participant to complete several questionnaires (the SUDS and the API). The two experimental breathing conditions then occurred. The instructions given for both breathing experiments were identical to those given at

baseline to measure vital capacity. The placebo inhalation was conducted first (stopcock turned to room air). This inhalation was simply a repeat of the previous vital capacity measurement. A recovery period followed, during which time the participant breathed as she wished off of the circuit and completed a set of questionnaires again (SUDS, API, and SPAS). Next, the experimental carbon dioxide-enriched air inhalation occurred (stopcock turned to carbon-dioxide enriched air). As the participant exhaled following the inhalation, the researcher turned the stopcock back to room air. A final recovery period followed, during which time the participant breathed as she wished off the circuit and completed the same questionnaire set (SUDS, API, and SPAS). After this final recovery period, the researcher instructed the participant that the experiment was over and that she could get up from the circuit.

The session ended immediately if any of the following conditions occurred: (1) if the participant wished to stop at any point; (2) if the participant's systolic blood pressure reached 170 or above; (3) if the participant's diastolic blood pressure reached 110 or above; (4) if the participant's systolic blood pressure decreased to 90 or below; (5) if the participant's diastolic blood pressure decreased to 50 or below; (6) if the participant's systolic blood pressure had a fall of 20 mmHg or more in a 1-minute period or in a 3-minute period; or (7) if the participant's diastolic blood pressure had a fall of 10mmHg or more in a 1-minute period or in a 3-minute period. The Research Ethics Board (REB) at Ryerson University approved these criteria to ensure that the study would stop if any abnormal blood pressure response occurred. Two participants were withdrawn from the study during the breathing experiments due to abnormal blood pressure levels ($n = 2$).

Results

Data Cleaning

Data from several participants ($n = 3$) who completed the study were not analyzed for the following reasons. One participant met criteria for BN-NP on the EDDS; the study considered only individuals with BN-P. Another participant's tidal volume during the CO_2 inhalation was less than 80% of her baseline tidal volume measure. Lastly, the single participant with PD that was recruited was also not included in any analyses. Data from 46 participants were analyzed.

The data were then screened for missing values. Missing values were carefully scrutinized; it was determined that less than ten percent of the data (e.g., individual questionnaire items) were not completed; specifically, only 0.56 % of the entire data matrix was missing. It was also determined that a single participant contributed only one, if that, item missing per questionnaire, consistent with missing-at-random data. With this careful examination completed, it was decided to fill in these missing data by pro-rating. Specifically, a participant's responses for all items in a particular scale were averaged, and this average was used to fill in the missing value.

Next, outliers were examined carefully, and whether transformations should be applied to the data in subsequent analyses was considered. Across all participants, no outliers were found in scores on the BDI-II, STICSA – state, STICSA – trait, ASI, DTS, DIS, and EDI. One outlier was found at the low end of the distribution of SUDS scores after the room air inhalation. Two additional outliers were found: one at the low end of the distribution of SUDS scores and one at the low end of the distribution of API scores, both after the CO_2 inhalation. These outliers described individuals who reported feeling less anxious after the inhalations, compared to baseline. Examination of these outliers revealed that there was no pattern among them; each value was derived from a different individual, and could therefore be attributed to random

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variability across different panic measures and participants. For this reason, all values were retained. Furthermore, data transformations were not required, as all variables that would serve as dependent variables in subsequent analyses based on the general linear model (GLM; Pedhauzer, 1982) approximated the normal distribution.

Demographics and Psychological Characteristics of the Sample

Participants ranged in age from 18 to 45 years ($M = 24.41$, $SD = 6.13$). Most participants reported their ethnicity as Caucasian (39.1%), followed by East Asian (19.6%), East Indian (10.9%), West Indian (8.7%), Latin American/Hispanic (6.5%), African (4.3%), North American Indian (2.2%), South East Asian (2.2%), Middle Eastern (2.2%), and Other (4.3%). In total, 15.2% of the sample endorsed a history of unexpected panic attacks. Participants were assessed for Axis-I clinical diagnoses as per the DSM-IV-TR criteria (APA, 2000). All participants in the BN group (100%) met diagnostic criteria for BN-P according to two methods: the M.I.N.I. interview and the self-reported EDDS. On the EDDS, these participants reported an average of 5.4 (SD = 4.6) binges per week over the past 3 months, and 4.8 (SD = 5.0) purges per week over the past 3 months.

The M.I.N.I. was used to assess Axis-I disorders that did not constitute exclusion criteria. In total, 13.0% of the sample reported symptoms consistent with at least one other psychological diagnosis. Among this subsample ($n = 6$), the following mood and anxiety disorders were endorsed: Major Depressive Disorder ($n = 3$), Post Traumatic Stress Disorder ($n = 3$), and Obsessive-Compulsive Disorder ($n = 1$). Note that one participant endorsed both MDD and PTSD. No participants endorsed diagnostic criteria consistent with alcohol or substance use disorders or psychotic disorders.

Self-report measures were used to assess various clinical characteristics. Depressive symptoms were assessed with the BDI-II. Across all participants, the mean BDI-II score was

13.07 (SD = 13.26). State and trait anxiety were measured by the STICSA – State Version and Trait Version. Across all participants, the mean STICSA State score was 33.02 (SD = 11.14), and the mean STICSA Trait score was 35.26 (SD = 12.55). Three additional psychological factors were measured: anxiety sensitivity (by the ASI), distress tolerance (by the DTS) and discomfort intolerance (by the DIS). Across all participants, the mean ASI score was 19.67 (SD = 13.40), the mean DTS score was 48.54 (SD = 15.14), and the mean DIS score was 13.00 (SD = 4.60).

Table 1 describes the demographic and psychological characteristics of the two study groups. No significant differences were found between the two groups on the above-stated demographics and Axis-I diagnoses. Specifically, a t-test was not significant for age, t (44) = -0.86, ns, r_{pb} = .13. Chi-squares were not significant for ethnicity, χ^2 (9) = 10.38, ns, ϕ = .48, or the presence/absence of major depressive disorder, χ^2 (1) = 1.69, ns, ϕ = .19, or anxiety disorders (post-traumatic stress disorder and obsessive-compulsive disorder), χ^2 (1) = .60, ns, ϕ = .11. The presence/absence of unexpected panic attacks (not a DSM diagnosis but an important variable in panic research; Perna et al., 1995) also did not vary between the two groups as revealed by a non-significant chi-square analysis, χ^2 (1) = 2.26, p = .13, ϕ = .22.

Scores on the following continuous variables were normally distributed within each group. BDI-II scores were significantly higher in participants with BN compared to those without BN, t (44) = -5.74, p < .001, r_{pb} = .65. STICSA – State scores were also significantly higher in participants with BN compared to those without BN, t (44) = -2.81, p < .01, r_{pb} = .39, as were STICSA – Trait scores, t (44) = -2.74, p < .01, r_{pb} = .38.

Table 1

Sample Demographics and Psychological Characteristics Separated by Study Group

	BN participants (*n* = 15)	Control participants (*n* = 31)
Age in years - *M* (*SD*)	25.53 (7.13)	23.87 (5.63)
Ethnicity - Frequency (%)		
Caucasian	7 (46.6%)	11 (35.5%)
North American Indian	0 (0%)	1 (3.2%)
East Indian	1 (6.7%)	4 (12.9%)
West Indian	1 (6.7%)	4 (12.9%)
African	0 (0%)	2 (6.5%)
South East Asian	0 (0%)	1 (3.2%)
East Asian	3 (20%)	5 (16.1%)
Middle Eastern	0 (0%)	1 (3.2%)
Latin American/Hispanic	3 (20%)	0 (0%)
Other Ethnicity	0 (0%)	2 (6.5%)
Diagnoses[a] – Frequency (%)		
Major Depressive Disorder	2 (13.3%)	1 (3.2%)
Post Traumatic Stress Disorder	2 (13.3%)	1 (3.2%)
Obsessive Compulsive Disorder	0 (0%)	1 (3.2%)
Bulimia Nervosa	15 (100%)	0 (0%)
Panic History – Frequency (%)		
History of unexpected panic attacks	4 (26.7%)	3 (9.7%)
No history of unexpected panic attacks	11 (38.9%)	28 (90.3%)

	BN participants (*n* = 15)	Control participants (*n* = 31)
BDI-II scores – *M (SD)**	25.40 (11.86)	7.10 (9.23)
STICSA State scores – *M (SD)***	39.20 (10.02)	30.03 (10.54)
STICSA Trait scores – *M (SD)***	42.07 (11.11)	31.97 (12.02)
ASI scores – *M (SD)*	23.07 (12.65)	18.03 (13.64)
DTS scores – *M (SD)*	42.67 (12.98)	51.39 (15.47)
DIS scores – *M (SD)*	12.40 (5.30)	13.29 (4.25)

Note. BDI-II = Beck Depression Inventory-II; STICSA = State Trait Inventory for Cognitive and Somatic Anxiety; ASI = Anxiety Sensitivity Index; DTS = Distress Tolerance Scale; DIS = Discomfort Intolerance Scale.

[a] One participant endorsed 2 co-morbid disorders: MDD and PTSD. All other participants endorsed one co-morbid disorder.

* significant differences were found between groups at $p < .001$ (2-tailed)

** significant differences were found between groups at $p < .01$ (2-tailed)

Hypothesis 1: Comparison of Panic Reactivity in Participants With and Without BN

All participants rated their anxiety on a SUDS scale (from 0 – 100) at baseline, after the room air inhalation, and after the CO_2 inhalation. All participants also rated their panic symptomatology on the API at baseline and after each inhalation. Moreover, all participants rated their subjective experience of a panic attack on the SPAS after the room air inhalation and after the CO_2 inhalation. To determine whether a participant exhibited a panic reaction or not, both the SUDS scores and the API scores were analyzed in two ways: (1) as continuous variables – change scores from the room air inhalation to the CO_2 inhalation; or (2) as categorical variables – measures of yes or no panic reactivity. As previously mentioned, for the SUDS, a 'yes' was indicated by an increase of $\geq$ 26 in the SUDS score (e.g., Perna, Casolari, et al., 2004). For the API, a 'yes' was indicated by an increase of any intensity (i.e., score) in $\geq$ 4 items (e.g., Goetz et al., 2001). The SPAS can only be analyzed categorically, as participants simply responded to this question by a yes or no response. Table 2 displays participants' raw scores on the SUDS and API measured at baseline, after the room air inhalation, and after the CO_2 inhalation.

1.1. Panic Reactivity to the Room Air Inhalation

Table 3 displays frequencies, means and standard deviations of panic reactivity to room air, separated by study group. Chi-squares and t-tests were performed to examine whether panic reactivity occurred from baseline to the room air inhalation, based on the panic reactivity measures. Chi-square results showed no significant difference between the two groups in reactivity to room air, according to the categorical measures of the SUDS, χ^2 (1) = 1.01, *ns*, ϕ = -.15, and the API, χ^2 (1) = .60, *ns*, ϕ = .11. T-tests showed similar findings; reactivity to room air was not significantly different between the two groups, according to the continuous measures of the SUDS, *t* (44) = 1.87, *ns*, r_{pb} = -.27, and the API, *t* (44) = 0.37, *ns*, r_{pb} = -.06. Moreover,

participants were asked, in their opinion, if they had a panic attack after the room air inhalation (SPAS, question 9) and no participants indicated that they experienced a panic attack.

1.2. Panic Reactivity to the CO_2 Inhalation

Considering that this study measures panic reactivity using five approaches, Table 4 displays the correlations between these five measures of panic reactivity to CO_2.

Chi-squares were performed to examine the proportions of participants within each group (control, BN) categorized by yes/no panic reactivity when reactivity was measured categorically. Table 3 displays the frequencies of yes/no panic reactivity, separated by study group.

According to the SUDS, there was a significant association between diagnostic group and whether or not panic reactivity occurred, χ^2 (1) = 4.32, $p < .05$, $\phi = .31$. The proportion of participants with BN who exhibited panic reactivity was significantly greater than those without BN. According to the API, there was a significant association between diagnostic group and whether or not panic reactivity occurred, χ^2 (1) = 8.08, $p < .01$, $\phi = .42$. The proportion of participants with BN who exhibited panic reactivity was significantly greater than those without BN. According to the SPAS, there was also a significant association between diagnostic group and panic reactivity, χ^2 (1) = 4.32, $p < .05$, $\phi = .31$, with a greater proportion of participants in the BN group endorsing the experience of a panic attack.

T-tests were performed to examine the *levels* of panic reactivity within each group (BN, non-BN) when reactivity was measured continuously. Table 3 displays the means and standard deviations of panic reactivity, separated by study group.

The SUDS percentages of change scores from the room air inhalation to the CO_2 inhalation (i.e., SUDS score after CO_2 minus SUDS score after room air) were normally distributed within groups. According to the SUDS, participants with BN had a significantly greater increase in SUDS scores from the room air condition to the CO_2 condition compared to

those without BN, $t (44) = -3.56, p < .01, r_{pb} = .47$. The API percentages of change scores were also normally distributed across groups. According to the API, participants with BN had a significantly greater increase in API scores compared to those without BN, $t (44) = -3.90, p < .001, r = .51$.

In order to demonstrate whether having a history of unexpected panic attacks influenced categorical panic reactivity to CO_2, the panic responses of participants with a panic history were visually inspected. Of the participants without BN with a panic history ($n = 3$), none displayed categorical reactivity according to all panic measures. Of the participants with BN with a panic history ($n = 4$), two displayed categorical reactivity: 1 according to the API only, and 1 according to the API and SPAS.

Categorical panic reactivity in those with an MDD diagnosis and a PTSD diagnosis were also visually inspected. The single participant without BN with an MDD diagnosis displayed categorical reactivity according to the API only. Of the participants with BN ($n = 2$), only one displayed categorical reactivity. This was also only according to the API. No participants with a PTSD diagnosis (BN; $n = 2$, non-BN; $n = 1$) displayed categorical reactivity.

1.3. Associations Between STICSA State Scores, STICSA Trait Scores, and Measures of Panic Reactivity

Correlations were conducted between the 4 main panic reactivity measures and STICSA state and trait scores. These relationships were examined within the total sample and within each group. Table 5 displays all correlations. Participants with BN were coded as 1, and participants without BN were coded as 0. Findings revealed that STICSA state and trait scores were significantly correlated only with the API categorical measure when examined in the non-BN group alone; $r_{pb} = .42, p < .05$ and $r_{pb} = .43, p < .05$, respectively. No other significant

correlations were revealed. A Bonferroni correction was then applied to decrease the alpha. With this new alpha in place ($p < .002$), results were no longer significant.

1.4. Association Between BDI-II Scores and Measures of Panic Reactivity

Correlations were also conducted between the 4 main panic measures and BDI-II scores within the total sample and within each group. Table 5 displays all correlations. Depressive symptoms were correlated with panic reactivity only according to the API categorical measure when examined within the total sample ($r = .34$, $p < .05$) and within the non-BN group alone ($r = .42$, $p < .05$). No other significant correlations were revealed.

Table 2

Means and Standard Deviations of Panic Reactivity Scores Separated by Study Group (Raw Scores)

	BN participants ($n = 15$)	Control participants ($n = 31$)
Baseline Inhalation		
SUDS	20.27 (19.31)	8.58 (12.48)
API	3.33 (3.66)	2.23 (3.60)
Room Air Inhalation		
SUDS	17.0 (18.71)	9.97 (15.49)
API	3.53 (2.67)	2.71 (4.59)
Carbon Dioxide Inhalation		
SUDS	24.87 (23.76)	8.10 (13.29)
API	6.4 (4.45)	2.48 (3.21)

Note. SUDS = Subjective Units of Distress Scale; API = Acute Panic Inventory.
Note. This table provides means and standard deviations of the SUDS and API raw scores. Raw categorical frequencies of yes/no panic do not exist; these frequencies derive from a comparison of panic reactivity scores from one inhalation to another inhalation.
Note. The SPAS was not completed at baseline. This measure was only completed after the room air inhalation and after the carbon dioxide inhalation.

Table 3

Frequencies, Means, and Standard Deviations of Categorical and Continuous Panic Reactivity Separated by Study Group (Change Scores)

	BN participants (*n* = 15)	Control participants (*n* = 31)
Room Air Inhalation		
Categorical – Frequency (%)		
SUDS	0 (0%)	2 (6.5%)
API	2 (13.3%)	2 (6.5%)
SPAS	0 (0%)	0 (0%)
Continuous – *M (SD)*		
SUDS	-3.27 (6.71)	1.39 (8.33)
API	.20 (2.91)	.49 (2.23)

	BN participants (*n* = 15)	Control participants (*n* = 31)
Carbon Dioxide Inhalation		
Categorical – Frequency (%)		
SUDS	2 (13.3%)	0 (0%)
API	5 (33.3%)	1 (3.2%)
SPAS	2 (13.3%)	0 (0%)
Continuous – *M (SD)*		
SUDS	7.78 (10.41)	-1.87 (7.76)
API	2.87 (2.36)	-.23 (2.59)

Note. SUDS = Subjective Units of Distress Scale; API = Acute Panic Inventory; SPAS = Subjective Panic Attack Scale.

Note. Baseline change scores are not reported because they do not exist; the change scores derive from a comparison of panic reactivity from one inhalation to another inhalation.

Table 4

Correlations Between Measures of Panic Reactivity to CO_2

	Categorical Measures			Continuous Measures	
Categorical Measures	SUDS	API	SPAS	SUDS	API
SUDS	--				
API	.23[a]	--			
SPAS	.48[a]**	.55[a]**	--		
Continuous Measures					
SUDS	.62[b]**	.43[b]**	.36[b]*	--	
API	.20[b]	.62[b]**	.46[b]**	.56[c]**	--

Note. SUDS = Subjective Units of Distress Scale; API = Acute Panic Inventory; SPAS = Subjective Panic Attack Scale.
[a] correlation = phi (ϕ)
[b] correlation = point-biserial (r_{pb})
[c] correlation = pearson (r).
** $p < 0.01$ (2-tailed)
* $p < 0.05$ (2-tailed)

Table 5

Correlations Between the BDI-II, STICSA State, STICSA Trait, and Measures of Panic Reactivity

	BDI-II	STICSA – State	STICSA – Trait
Total Sample			
Categorical (r_{pb})			
SUDS	.14	-.05	.03
API	.34*	.21	.29
Continuous (r)			
SUDS	.26	.10	.06
API	.23	.14	.10
BN Group Only			
Categorical (r_{pb})			
SUDS	-.13	-.35	-.19
API	-.10	-.23	-.04
Continuous (r)			
SUDS	-.16	-.31	-.20
API	.11	-.13	-.17
Control Group Only			
Categorical (r_{pb})			
SUDS	--	--	--
API	.42*	.42*	.43*
Continuous (r)			
SUDS	-.003	.01	-.13
API	-.31	-.04	-.23

Note. BDI-II = Beck Depression Inventory-II; STICSA = State Trait Inventory for Cognitive and Somatic Anxiety; SUDS = Subjective Units of Distress Scale; API = Acute Panic Inventory.

* $p < .05$ (2-tailed)

Hypothesis 2

2.1. Association between Group and Measures of Anxiety Sensitivity, Discomfort Intolerance, and Distress Tolerance

Table 1 displays the mean scores of AS, DI, and DT within each group. ASI scores in the BN group and in the non-BN group did not significantly differ from each other, $t(44) = 1.20$, ns, $r_{pb} = .18$. DTS scores also did not significantly differ between groups, $t(44) = 1.88$, ns, $r_{pb} = -.27$, nor did DIS scores, $t(44) = .61$, ns, $r_{pb} = -.09$.

2.2. Association between Panic Reactivity to CO_2 and Measures of Anxiety Sensitivity, Discomfort Intolerance, and Distress Tolerance

Correlations were performed among ASI, DIS and DTS scores within the total sample and within each group in relation to panic reactivity. Discomfort Intolerance was negatively correlated with only the SUDS categorical measure of panic reactivity ($r_{pb} = -.31$, $p < .05$) within the total sample. No other findings were significant (see Table 6 for all correlations).

2.3. Potential Mediators of the Relationship between Group and Panic Reactivity to CO_2

Proposed mediators of the relationship between BN and panic reactivity included: AS, DI, and DT. As proposed by Baron and Kenny (1986), three criteria are necessary in order to perform a mediation analysis: 1) a significant association between the proposed mediator and the outcome variable (panic reactivity); 2) a significant association between the main predictor (diagnostic group) and the outcome variable; and 3) a significant association between the main predictor and the proposed mediator. In the current study, the first criterion was met only with the DIS (proposed mediator) and the SUDS categorical measure (outcome variable). The second criterion was also met; diagnostic group significantly predicted the SUDS categorical measure. The third criterion, however, was not met; a significant association was not found between diagnostic group and DIS scores. Therefore, a mediational analysis was not performed.

Table 6

Correlations Between Anxiety Sensitivity, Distress Tolerance, Discomfort Intolerance, and Measures of Panic Reactivity

	Anxiety Sensitivity	Distress Tolerance	Discomfort Intolerance
Total Sample			
Categorical (r_{pb})			
SUDS	.05	-.09	-.31*
API	.20	-.22	-.25
Continuous (r)			
SUDS	.11	-.10	-.09
API	.16	-.09	-.24
BN Group Only			
Categorical (r_{pb})			
SUDS	-.02	-.01	-.45
API	.05	-.07	-.36
Continuous (r)			
SUDS	.11	.05	-.16
API	.38	-.22	-.22
Control Group Only			
Categorical (r_{pb})			
SUDS	--	--	--
API	.30	-.21	-.06
Continuous (r)			
SUDS	-.02	.18	.02
API	-.04	.16	-.04

Note. SUDS = Subjective Units of Distress Scale; API = Acute Panic Inventory.
* $p < .05$ (2-tailed)

Hypothesis 3

3.1. Relationship between Panic Reactivity to CO_2 and EDI Scores

An exploratory analysis was performed to investigate the relationship between CO_2 reactivity and EDI subscale scores only in the participants with BN (see Table 7 for all correlations). EDI – Bulimia scores and EDI – Drive for thinness scores were not significantly correlated with any of the panic measures. Only one significant correlation was found amongst the remaining 6 EDI subscale scores and the panic measures. Specifically, a significant positive association was found between Perfectionism and API continuous scores ($r = .52, p < .05$). To minimize Type I error, a Bonferroni correction was applied to the data to decrease the alpha. With this value in place ($p < .002$), the relationship between Perfectionism and API continuous scores was no longer significant.

3.2. Relationship between Panic Reactivity to CO_2 and Binge/Purge Frequency

The frequencies of binges and purges endorsed by participants with BN were examined. These frequencies were derived from three items on the Eating Disorder Diagnostic Scale: The number of times each participant endorsed being engaged in 1) bingeing, 2) vomiting and 3) laxative use per week over the past 3 months. Vomiting and laxative use scores were combined to derive at a total number of purges per week. No significant associations were found between frequencies of binges and purges on the one hand and panic reactivity on the other, according to the categorical and continuous measures of panic (see Table 8 for all correlations).

Table 7

Correlations Between EDI Subscale Scores and Measures of Panic Reactivity in the BN Group

	Categorical Measures of Panic Reactivity (r_{pb})		Continuous Measures of Panic Reactivity (r)	
EDI Subscale	SUDS	API	SUDS	API
Drive for thinness	-.06	-.25	-.06	-.03
Bulimia	-.42	-.17	-.34	-.09
Ineffectiveness	-.17	-.31	-.12	-.11
Body dissatisfaction	.42	-.12	.20	.04
Perfectionism	-.08	.46	.16	.52*
Interpersonal Distrust	-.25	-.46	-.38	-.24
Interoceptive Awareness	-.31	-.20	-.20	-.12
Maturity Fears	-.35	-.35	-.22	-.23

Note. EDI = Eating Disorder Inventory; SUDS = Subjective Units of Distress Scale; API = Acute Panic Inventory.
* $p < .05$ (2-tailed)

Table 8

Correlations Between EDDS Binge and Purge Frequency and Measures of Panic Reactivity in the BN Group

	Categorical Measures of Panic Reactivity (r_{pb})		Continuous Measures of Panic Reactivity (r)	
	SUDS	API	SUDS	API
Binges	-.21	-.03	-.18	-.17
Purges	-.04	-.30	-.21	-.48

Note. SUDS = Subjective Units of Distress Scale; API = Acute Panic Inventory.
* $p < .05$ (2-tailed)

Discussion

Although theorists originally posited challenge-induced panic as a specific marker for PD (e.g., Verburg, Pols, de Leeuw, & Griez, 1998), more recent findings, including those of the current investigation, are more consistent with the hypothesis that panic reactivity to CO_2 may not, in fact, be limited to individuals with panic Disorder. Accordingly, the purported specificity of CO_2-panic warrants continued investigation, with the ultimate goal of determining underlying vulnerabilities shared by persons who exhibit panic reactivity to CO_2 (e.g., Vickers & McNally, 2004). The current study aimed to further this line of inquiry by investigating CO_2-panic amongst individuals with bulimia nervosa, a clinical group that has received little attention in this research area, yet is known to possess characteristics that predict reactivity in other clinical groups and non-clinical groups (e.g., relatively elevated anxiety sensitivity, serotonin deficiencies). Because of recruitment difficulties, the current study could not compare reactivity in individuals with BN to those with PD. As such, it was posited that participants with a diagnosis of BN would display significantly greater panic reactivity to CO_2 compared to participants without BN. Findings in this sample supported this hypothesis.

No significant differences were found between the two groups in panic reactivity to the room air inhalation, according to both the SUDS and the API measured categorically and continuously. Additionally, when asked directly if they experienced a panic attack from the room air inhalation, no participant responded 'yes.' Upon examining the frequencies of yes/no panic, two observations were made. The first observation was that in the BN group, the mean SUDS continuous change score from room air to CO_2 was negative. This implies that some participants with BN reported feeling less anxious after the room air inhalation compared to the baseline measure; why some participants reported feeling this way is unclear. One possible explanation is that some participants with BN may have been especially anxious before the room air inhalation

because they did not know whether they would be inhaling CO_2 enriched-air or normal room air, and they feared the bodily symptoms that can be produced by CO_2-enriched air as discussed thoroughly during the informed consent process. Accordingly, after the room air inhalation, some participants in this group might have felt less anxious, now knowing that the inhalation did not produce bodily symptoms. The second observation was that in the non-BN group, more participants panicked to room air than to CO_2, according to both the SUDS and API categorical measures. (It should be noted that no participant without BN self-reported that she had experienced a panic attack after the room air inhalation). This finding of more participants panicking to room air than to CO_2 (according to the API and SUDS categorical measures) in those without BN is not a typical finding; in other words, some participants in this group did not react as participants typically do to room air in CO_2 studies (regardless of diagnostic group). The explanation for this surprising finding is decidedly unclear. It is predicted that with a larger sample, the percentage of people without BN or PD who display panic reactivity in response to room air will decrease.

Significant differences were found between the two groups in panic reactivity to the CO_2 inhalation, as stated above. Specifically, according to the four main measures of panic reactivity (i.e., categorical and continuous measures of the SUDS and the API), participants with BN exhibited greater panic reactivity to CO_2 than did participants without BN. Moreover, when asked directly if they experienced a panic attack from the CO_2 inhalation, a significantly greater proportion of participants with BN indicated 'yes' compared to participants without BN. In sum, diagnostic group (BN or non-BN) was a significant factor in determining whether or not participants reacted to CO_2. These results were consistent with prediction.

The current study excluded individuals who had some factors known to increase reactivity (e.g, PMDD, Harrison et al., 1989). However, participants with other factors known to increase

reactivity were included due to difficulties with recruitment. Specifically, several individuals recruited into this study had a history of unexpected panic attacks, which previous research has demonstrated augments panic reactivity to CO_2 (e.g., Perna et al, 1995). Findings in the current study, although based on a small sample, indicated that panic history alone could not account for the significant relationship between diagnostic group and panic reactivity, since only two of the participants with a history of unexpected panic attacks evinced panic reactivity and five did not evince panic reactivity. Similarly, this study included participants with PTSD, a diagnosis shown in one but not another study to increase panic reactivity (Muhtz et al., 2011; Talesnik et al., 2007). In the current study, no participants with a PTSD diagnosis displayed reactivity, consistent with the hypothesis that the inclusion of participants with PTSD cannot itself account for the relationship between the BN diagnosis and enhanced panic reactivity. However, these conclusions are clearly preliminary, as the small sample size prevented statistical analyses from being performed on participants with and without a history of unexpected panic and with and without PTSD.

The current study considered depression by two means: 1) depression diagnosis (yes/no), and 2) level of depressive symptoms. Previous research has shown that a diagnosis of depression is not associated with panic reactivity (Perna et al., 1995); however this finding may differ in cases of depression co-morbid with another disorder. For instance, a co-morbid depressive disorder actually increased vulnerability to panic reactivity in people with PD (Verburg, Klaasen, Pols, & Griez, 1998), and, in the study that found enhanced panic reactivity in people with PTSD, many participants (6 out of 10) had co-morbid depression (Muhtz et al., 2011). The previous study that used a sample of participants with eating disorders excluded those with a depression diagnosis (Perna, Casolari, et al., 2004), preventing these researchers from examining whether co-morbid depression and BN augments panic reactivity. The current study did include

individuals with co-morbid depression and BN but was unable to test whether co-morbid

depression and BN enhanced panic reactivity or whether depression by itself affected panic

reactivity due to the small sample size. However, two observations should be noted: 1) the single

person in the non-BN group that displayed API panic reactivity had a diagnosis of MDD;

conversely, no participant in the non-BN group without MDD displayed categorical panic

reactivity; and 2) of the two participants in the BN group with MDD, one displayed categorical

panic reactivity according to the API. The larger sample size that will result from ongoing data

collection will enable a conclusion to be reached regarding how those with co-morbid BN and

depression react to CO_2.

    With respect to the continuous measure of depressive symptomatology, depressive

symptoms were found to be significantly higher in participants with BN compared to participants

without BN. In fact, moderate levels of depression characterized participants with BN while

minimal levels of depression characterized participants without BN (Beck et al., 1996). This

finding is consistent with the high rates of depression reported in people with BN (e.g., Godart et

al., 2003). Indeed, researchers have posited that BN may be driven in some individuals by

negative affect (e.g., Stice, Bohon, Marti, & Fischer, 2008; Stice & Fairburn, 2003). Depressive

symptoms were not related to panic reactivity in participants with BN. It should be noted that the

previous study using a sample of participants with eating disorders did not assess level of

depressive symptoms (Perna, Casolari, et al., 2004). However, in the current study, depressive

symptoms were related to panic reactivity in participants without BN, as assessed by the API

categorical measure. Possibly, then, depressive symptoms in those without BN or PD are, in fact,

related to panic reactivity. This unexpected finding clearly needs replication with a larger sample

of individuals without BN or PD.

Measures of state and trait anxiety were also included in this study since neither construct has been examined in a BN sample with respect to CO_2-panic. Participants with BN reported greater state and trait anxiety compared to participants without BN. According to past research, it is not clear how state and trait anxiety might affect panic reactivity in anxiety disorder groups and individuals without an Axis-I diagnosis because of conflicting findings (for a review, see Zvolensky & Eifert, 2001). In the current study, a relationship was not found between these two constructs and panic reactivity. No conclusions should be drawn from this finding without replication.

Various studies have demonstrated that certain psychological constructs predict panic reactivity to CO_2 in both non-clinical and clinical participant groups. These constructs include: AS (e.g., Eifert et al., 1999), DT (e.g., Kutz et al., 2010), and DI (e.g., Schmidt et al., 2007). Measures of these three constructs were included in the current study. It was hypothesized that these constructs would be correlated with panic reactivity, regardless of group. Indeed, considering that some control participants exhibited CO_2 reactivity (according to the API categorical measure), perhaps these psychological constructs could account for that finding. Results did not support this prediction. Only DI when looked at within the total sample was associated with the SUDS categorical measure of reactivity. This finding of a relationship between DI and panic reactivity suggests that participants with high levels of an inability to tolerate discomfort were less likely to panic from the CO_2 challenge. None of the other constructs were associated with any of the panic reactivity measures when examined within the total sample and within each group. The mediating role of discomfort intolerance in the association between diagnostic status and panic reactivity could not be examined, as there was no association between diagnostic status (the independent variable) and level of discomfort intolerance (the mediator) (see Baron & Kenny, 1986). Thus, despite largely consistent findings in other studies that AS and

DT are associated with panic reactivity (e.g., Kutz et al., 2010), this hypothesis was not supported in the current study. One plausible explanation for this null result may be that the sample size was small; accordingly, analyses might have lacked power to find differences between groups on these variables. More data collection will enhance the chance of attaining significant findings.

It was surprising that participants with BN and participants without BN did not differ in terms of AS and DT considering the research linking high levels of these two constructs to BN (e.g., Anestis et al., 2007; Anestis et al., 2008). Possibly, people with BN in the current study were higher functioning than those in previous studies investigating AS and DT in BN (Anestis et al., 2007; Anestis et al., 2008). More specifically, the current study required participants to be both free from any psychotropic medication and physically healthy, not requirements in the previous studies linking AS and DT to BN.

Finally, eating disorder characteristics among participants with BN were investigated in an attempt to explain why panic reactivity to CO_2 occurred in these participants. However, panic reactivity was not associated with any features of eating disorders according to the EDI (e.g., level of bulimic symptoms, level of drive for thinness), or frequency of bingeing and purging.

In sum, this study found a significant relationship between diagnostic status (BN or non-BN) and panic reactivity to CO_2. AS, DT and DI could not be tested as mediators of the relationship. AS and DT were not significantly associated with panic reactivity, and criteria for a mediation analysis (Baron & Kenny, 1986) were not met with DI. Moreover, specific eating disorder features and frequency of BN symptoms were not associated with the relationship. Therefore, the conclusion most consistent with the findings from the current study is that diagnostic status (BN or non-BN) accounts for the differences in panic reactivity to CO_2.

Speculation can be made regarding the link between BN and enhanced panic reactivity. First and foremost, an important consideration is that when panic reactivity was examined as a

categorical measure of yes/no panic, there was clearly heterogeneity within the BN group. On average as a group, participants with BN were more reactive than were controls, but within the group only a certain proportion reacted. Thus, the statement that individuals with BN displayed panic reactivity should be understood to mean that despite the higher reactivity of participants in the BN group on average, many participants with BN did not show panic reactivity. The question of the factors differentiating those with BN who panicked and those with BN who did not panic is an important issue to receive attention in future data collection and analysis.

Another important consideration is that in order to properly answer the question of whether the effects of the CO_2 challenge are specific to PD, the reactivity of participants with BN needs to be compared with that of participants with PD. Indeed, although those with BN displayed panic reactivity compared to those without BN, they may still display less reactivity compared to those with PD. Although a PD comparison group was not included in the current study, it is possible to estimate effect sizes from past studies that utilized the same measures of panic reactivity. Unfortunately, because of unreported frequency data in some studies and different percentages of CO_2 used in other studies, effect size estimates could be calculated only for the SUDS continuous panic measure. The effect size of panic reactivity comparing PD participants and a non-clinical group in a past study, computed based on published means and standard deviations, was large (Cohen, 1992), $r = .67$ (Perna et al., 2004). The effect size comparing those with and without BN in the current study was smaller but is still considered as a large effect ($r = .47$). Thus, perhaps participants with BN displayed greater reactivity than participants without BN but would display less reactivity compared to those with PD.

The heterogeneity within the BN group in terms of panic reactivity suggests that another factor (aside from diagnostic status) might be distinguishing those with BN who displayed panic reactivity from those with BN who do not display reactivity. Indeed, a much larger proportion of

participants with BN would be expected to panic if serotonin abnormalities could fully explain the link between BN and panic reactivity. Further complicating matters, the fact that people with depression have serotonin deficiencies and yet do not react to CO_2 suggests that a serotonergic deficiency hypothesis may be insufficient to account for panic reactivity to CO_2.

Perhaps another biological factor may explain the panic reactivity shown by some participants with BN. Along those lines, people with PD and people with BN appear to be similar not only in serotonergic dysfunction, but also in noradrenergic dysfunction. In PD, the development of panic attacks and fear, in part, result from increased noradrenergic neuronal activity (McNally, 1994). Tricyclic antidepressants (TCAs) modulate the noradrenergic system in addition to affecting the reuptake of serotonin (Bakker, Balkom, & Spinhoven, 2002). Various TCAs that affect noradrenergic pathways (in addition to serotonergic pathways) are effective in the treatment of PD (e.g., imipramine), as are newer antidepressants (selective noradrenergic agents) that act predominantly on noradrenergic pathways (e.g., reboxetine; Versiani et al., 2002). In BN, greater than normal noradrenergic activity contributes to binge eating (Fava, Copeland, Schweiger, & Herzog, 1989), in addition to other factors that contribute to binge-eating. Binge-eating reduces the functioning of noradrenaline, as evidenced by reduced noradrenergic activity in normal-weight bulimic women during abstinence from bingeing (Kaye et al., 1990). TCAs that act on both serotonergic and noradrenergic pathways (e.g., imipramine, desipramine) reduce the frequency of bingeing and purging and improve mood (Kaye et al., 1990; Kruger & Kennedy, 2000). Importantly, reboxetine, which as previously mentioned is thought to act primarily on noradrenergic pathways, has the same effect (Fassino, Daga, Boggio, Garzaro, & Piero, 2004). The possible role of the noradrenergic system in CO_2-panic has been tested in participants with PD. One study found that imipramine and two SSRIs (paroxetine and sertraline) were similarly effective at reducing reactivity to CO_2 after 7 days of treatment (Bertani, Perna, Arancio,

Caldirola, & Bellodi, 1997). A more recent study found that both an SSRI (paroxetine) and reboxetine resulted in decreased panic reactivity to CO_2 after 7 days of panic treatment, but the decrease was significantly stronger in those treated with paroxetine (Perna, Casolari, et al., 2004). While these results indicate that the noradrenergic system affects CO_2-panic, they also suggest that the serotonergic system might be more important than the noradrenergic system in the treatment of PD. However, it is likely that both serotonergic and noradrenergic pathways are implicated in CO_2-panic. Considering the aforementioned similarities in noradrenergic function between people with BN and people with PD, it is possible that increased noradrenergic function could account for the panic reactivity shown by some people with BN in the current study.

Perhaps other psychological factors that are associated with both PD and BN and have been shown to increase panic reactivity to CO_2 may explain the panic reactivity shown by participants with BN. Coping, an important mediator between stress and health, is one such factor. Maladaptive coping strategies have been found among persons with PD. Indeed, individuals with PD engage in maladaptive coping strategies (Feldner, Zvolensky, & Leen-Feldner, 2004), such as emotion-focused coping (i.e., managing the distressing emotions that accompany the problem) instead of problem-focused coping (i.e., using strategies to manage or reduce the problem itself). One study found that avoidance-oriented coping (a type of emotion-focused coping, defined as avoiding or denying the problem) predicted CO_2-panic in non-clinical participants (Spira, Zvolensky, Eifert, & Feldner, 2004). Another study found an association between emotion-focused coping and panic reactivity (specifically, subjective anxiety ratings) in a sample of participants with PD (Schmidt, Eggleston, Trakowski, & Smith, 2005). Therefore, emotion-focused coping may predict panic reactivity in CO_2 challenge studies of people with PD. Maladaptive coping strategies are also prevalent in persons with BN (Yager, Rorty, & Rossotto, 1995). A psychological explanation for bingeing and purging is that these behaviours are used to

cope with emotions that accompany a problem, as opposed to using more adaptive coping behaviours to deal with the problem itself. Therefore, perhaps the participants with BN who displayed panic reactivity in the current study engaged in various emotion-focused coping strategies to a greater extent than the other participants.

Another psychological factor that may explain panic reactivity displayed by participants with BN is emotion dysregulation. Emotion dysregulation refers to an inability to modulate one's emotional responses. Emotional responses include acceptance or avoidance (suppression) of anxiety-provoking states. Although related to maladaptive coping strategies described above, emotion dysregulation relates to the expression of emotions (or lack thereof) more generally. This construct is associated with anxiety disorders, including PD (e.g., Levitt, Brown, Orsillo, & Barlow, 2003), and eating disorders (e.g., Harrison, Sullivan, Tchanturia, & Treasure et al., 2010). Emotional avoidance in particular has been tested in CO_2 challenge studies using several repeated inhalations of 20% CO_2 enriched air (e.g., Feldner, Zvolensky, Eifert, & Spira, 2003; Karekla, Forsyth, & Kelly, 2004; Levitt et al., 2003). In these studies, researchers questioned whether emotional avoidance would relate to anxious and fearful responses to the body sensations induced by CO_2. This hypothesis received support in studies of non-clinical participants and participants with PD, such that those high in emotional avoidance displayed greater panic reactivity in terms of panic symptoms, anxiety, and emotional distress during the challenge (Feldner et al., 2003; Karekla et al., 2004).

Yet another explanation that could account for the enhanced panic reactivity of some participants with BN in the current study is the effect that experiencing adverse events (AE) has on panic reactivity to CO_2. Indeed, a recent study found that early experience of AE was associated with enhanced panic reactivity in people with and without panic attacks or PD (Ogliari et al., 2010). The types of AE included: parental loss, stressful events (e.g., marital difficulties),

major life events (e.g., life-threatening accidents), and events of suffocative nature (e.g., near-drowning in water) (Ogliari et al., 2010). Moreover, other research has linked these types of AE to increased susceptibility to develop panic attacks or PD (Manfro et al., 1996). Unfortunately, the variable of lifetime frequency of AE was not assessed in the current study.

Research about the mechanisms that link the occurrence of early AE to enhanced panic reactivity to CO_2 is in its early stages (Oligari et al., 2010). It is known that stressful events (such as childhood maltreatment) can alter the neurobiological systems that moderate responses to stressors, which, in term, can have long-term effects upon physiology (e.g., MacMillan et al., 2009; Watts-English, Fortson, Gibler, Hooper, & DeBellis, 2006). For instance, the autonomic branch of the sympathetic nervous system (i.e., the fight-or-flight response) may become more sensitive (in some people) after exposure to stressors, and this increased sensitivity may lead to augmented heart rate, blood pressure, and vigilance. Furthermore, the serotonergic system may become less effective after exposure to stressors, which is thought to lead to cognitive and behavioural deficits such as learning and memory deficits, aggression, and mood disturbances. The release of cortisol, a hormone released by the adrenal gland in response to stress, becomes dysregulated, which may increase vulnerability to physical and psychological problems (see Watts-English et al., 2006, for a review).

How stress alters physiology has been most investigated with respect to childhood maltreatment (e.g., MacMillan et al., 2009), which is known to characterize many persons with bulimia (Rorty, Yager, & Rossotto, 1994; Steiger et al., 2001). The effect of childhood maltreatment per se upon CO_2 reactivity has not been investigated yet. Instead, researchers have focused on how another type of AE – early separation-related experiences – affects CO_2 reactivity. These investigations (e.g., Oligari et al., 2010) have revealed that separation anxiety in particular is linked to PD through genetic determinants. Furthermore, separation anxiety is a

precursor for PD (Battaglia et al., 2009) and is also associated with enhanced panic reactivity to CO_2 (Battaglia et al., 2009; Oligari et al., 2010).

Animal models have been used to investigate the possible association between separation-related early experiences and reactivity to CO_2. It should be noted that the animal analogue used is not equivalent to the experience of human separation anxiety, and therefore generalizability of the results to human separation anxiety may be questioned. In the study, outbred mice were repeatedly cross-fostered to adoptive mothers for their first 4 postnatal days and CO_2 sensitivity was tested with 6% CO_2 (Amato et al., 2011). Cross-fostered mice that experienced early interference in their infant-mother interactions showed significant greater reactivity to CO_2 than did normally-reared mice. It is possible that participants in the BN group of the current study experienced early separation-related AE (e.g., Oligari et al., 2010). Indeed, many studies link BN and the experience of AE, including early separation anxiety (e.g., Troisi et al., 2006). The current study did not examine a history of separation anxiety.

A final possibility that must be considered is the following. Perhaps there is no underlying commonality between PD and BN that can explain the CO_2-panic in this study. Symptom similarities do exist between these disorders: Acute and short-lived clinical manifestations characterize both disorders; namely panic attacks in people with PD, and bingeing and purging in those with BN (Kendler et al., 1995). However, symptom similarity does not necessarily require similar determinants (e.g., Vickers & McNally, 2004); consequently, it is possible that those with BN and those with PD show enhanced panic reactivity for different reasons.

The current research has several strengths. This is the first known study that used a sample of eating disordered individuals with BN only to test the specificity of the CO_2 challenge. Perna, Casolari, et al. (2004) utilized an ED sample consisting of both BN and AN. However, psychological and physiological differences exist between these two eating disorders (e.g., Kaye

et al., 1998), which make it difficult to interpret the non-significant findings of the Perna, Casolari, et al. (2004) study.

Another strength of the current research was that risk factors known to enhance reactivity to the CO_2 challenge were taken into account. These include: specific Axis-I disorders (i.e., Social Anxiety Disorder, Situation-Specific Phobias, Premenstrual Dysphoric Disorder), and first and second-degree relatives with PD. Such factors have been consistently demonstrated across studies to be associated with reactivity to CO_2, and thus individuals with these factors were excluded from participating in the current study. Moreover, the current study examined other variables as potential predictors of panic reactivity that researchers have studied with respect to CO_2-panic – depression, state and trait anxiety – but that had not been examined specifically with respect to individuals with BN. Consideration of many factors previously studied in respect to reactivity to the CO_2 challenge is a major strength of the current study, enabling the (tentative) conclusion that diagnostic group, not these other factors, predicted panic reactivity in those with BN.

Although the current study considered the aforementioned factors, possible psychological risk factors (such as emotional avoidance) suggested in recent CO_2 research that are related to BN were not considered, as discussed earlier. Therefore, it was impossible to determine whether these factors were associated with panic reactivity. In addition, some risk factors for panicking to CO_2 were not exclusionary criteria (e.g., unexpected panic attacks) due to recruitment difficulties. It would have been beneficial to have a true non-clinical sample and a pure BN sample, without any additional Axis-I disorders. A true non-clinical sample would also be more consistent with past CO_2 studies. This was a limitation of the current study.

Several additional limitations to the current study are noteworthy. A major limitation was the small sample size, particularly that of participants with BN. Consequently, some of the

analyses conducted were low in statistical power, particularly those in which only the BN subset of the sample was analyzed. Additionally, some of the chi-square analyses conducted had low expected counts. A larger sample size is needed to allow more confidence in the results found.

Another major limitation of this study was the lack of a PD group for comparison. While findings of this study demonstrated significant differences between participants with BN and those without, an essential unanswered question is how participants with BN compare to participants with PD in terms of reactivity to CO_2. It may be that those with BN react more than those without BN, but still less than those with PD. Inclusion of a clinical comparison group with PD when examining panic reactivity is essential and constitutes an important part of this ongoing study's goals. Unfortunately, to date only one participant with PD has been tested due to recruitment difficulties for this group. To illustrate, 10 individuals who screened into the PD group subsequently became ineligible due to the following: asthma ($n = 1$), high blood pressure ($n = 1$), heart murmur ($n = 1$), taking psychotropics ($n = 3$), and retracting decision to participate in the breathing experiments ($n = 4$). While statistical analyses cannot yet include the single PD participant and obviously no conclusions can be derived from this one person's data, she reported reactivity to CO_2 on all measures of panic. Data collection for the PD study group will continue.

A third issue worthy of consideration pertains to the study of CO_2-panic more generally and concerns the aforementioned lack of a single, consensual definition of 'reactivity' in CO_2 challenge studies (Rassovsky & Kushner, 2003). This issue was pointed out over two decades ago (Sanderson & Wetzler, 1990), but researchers continue to diverge in how they operationalize the construct, with post-challenge changes in anxiety and/or self-reported bodily symptoms and/or a participant self-reporting a panic attack commonly all used as definitions. Obviously, the way in which reactivity is defined in CO_2 challenge studies impacts the rates of reactivity that are obtained. Accordingly, the need for a PD group within the current study is made even more

salient; the current study enables the conclusion that people with BN on average show higher reactivity to CO_2 than do participants without BN, but cannot address the comparison of BN and PD reactivity.

In light of the ongoing debate about the proper definition of panic reactivity, the current study utilized both categorical and continuous measures that have been used by other researchers. Significant correlations were found amongst most measures of panic reactivity utilized in this study. However, the SUDS categorical measure was not significantly correlated with the API, categorical or continuous measure. The limitations inherent to using categorical measures of reactivity may partially account for these differential findings across reactivity measures. Although categorical analyses were performed, emphasis was placed on findings from the analyses using the continuous panic reactivity measures, following other researchers (e.g., Griez et al., 1990). The reason for emphasizing the continuous measures of reactivity as outcomes is that it allows for the capture of possible small differences in reactivity that might distinguish different groups of participants without PD. In addition, whether the SUDS is really a good measure of panic reactivity is questionable, as this scale is actually a measure of subjective anxiety. This may account for the current study's finding of a greater percentage of participants indicating panic reactivity according to the API compared to the SUDS categorical data. However, the SUDS has been consistently used in studies of CO_2 reactivity as a measure of CO_2 reactivity, not simply that of anxiety (e.g., Perna et al., 2004) and as such it was included in the current study.

Researchers who have elected not to rely on the SUDS alone have tended to administer a symptom checklist to participants that corresponds to the *DSM* panic attack symptoms. The current study used the Acute Panic Inventory in accord with the extant research. However, it should be noted that even researchers using the API have diverged in how they assess panic

reactivity: as a category (yes/no reactivity) based on whether a specified cut-off number of API symptoms was endorsed, or as a category if and only if the cut-off number of symptoms on the API included a cognitive symptom. The current study used a cut-off score of at least four symptoms (of any type), which is consistent with previous studies (e.g., Goetz et al., 2001; Gorman et al., 1990). The presence of an additional cognitive symptom (e.g., fear of losing control) is necessary for some researchers (e.g., Papp et al., 1993; Perna et al., 1994); it was not necessary in the current study, nor was it necessary in many other studies as noted above, where 4 symptoms could be of any type. Researchers requiring a cognitive symptom maintain that this additional criterion helps to differentiate between the presence of mere somatic symptoms (experienced by many after CO_2) and the presence of a panic attack. The cognitive symptoms, therefore, hold an interpretative dimension, as the majority of PD patients report such symptoms during panic attacks (Barlow et al., 1985). A final limitation that should be mentioned regarding how reactivity was measured concerns the exclusive reliance on self-report. The study could have benefited from behavioural, clinician-rated, and physiological measures of reactivity.

Considering the findings, strengths and limitations of this study, future directions for this research may be considered. First and foremost, it is crucial that people with BN be compared to those with PD in terms of panic to CO_2. Second, it is necessary to recruit a larger sample of participants to enhance power. If differences are still found between participants with BN and those without BN with a larger sample size, the current study's hypotheses will be supported. In addition, if participants with BN react similar to those with PD, the current study's hypotheses will be supported. Moreover, it will be important to understand if some facet of BN, aside from actual diagnosis, can help explain this reactivity. Despite these limitations, preliminary findings suggest that a BN diagnosis is important in CO_2 reactivity.

Appendix A – Recruitment Materials

Advertisements for Craigslist.com and Kijiji.com

PANIC AND EATING BEHAVIOURS STUDY – Female Participants Needed! (Toronto)

Do you suffer from Bulimia Nervosa?
                    OR
Do you suffer from Panic Disorder or Panic Attacks?

You may be eligible to participate in a research study in the Psychology Department at Ryerson University about the relationship between panic and eating behaviours.

Participants must be:
-   physically healthy (e.g., no asthma, diabetes, head injury)
-   between ages 18 - 45

This study involves a 15-minute telephone screen to determine eligibility, then one visit to Ryerson University for approximately 60-90 minutes.

* You will be compensated for your participation *

For more information, please contact: 416-979-5000 ext. 4985 or prlab@psych.ryerson.ca

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PANIC AND EATING BEHAVIOURS STUDY – Female Participants Needed! (Toronto)

Have you NEVER suffered from any of the following?

Panic Disorder   Premenstrual Dysphoric Disorder
Bulimia Nervosa   Situation-Specific Phobias
Social Anxiety Disorder

Participants must be:
-   physically healthy (e.g., no asthma, diabetes, head injury)
-   between ages 18 - 45

You may be eligible to participate in a research study in the Psychology Department at Ryerson University about the relationship between panic and eating behaviours.

This study involves a 15-minute telephone screen to determine eligibility, then one visit to Ryerson University for approximately 60-90 minutes.

* You will be compensated for your participation *

For more information, please contact: 416-979-5000 ext. 4985 or prlab@psych.ryerson.ca

FEMALE PARTICIPANTS NEEDED!

Panic and Eating Behaviours Study

Do you suffer from **BULIMIA NERVOSA?**
OR
Do you suffer from **PANIC DISORDER or PANIC ATTACKS?**

Are you physically healthy? (e.g., no asthma, diabetes, head injury)

Are you between 18 and 45 years old?

You may be eligible to participate in a research study.

Participants must have NO recent illegal drug use.

This study involves a 30-minute telephone screen to determine eligibility, then one 60-90 minute visit to Ryerson University. Participants will fill out questionnaires and engage in two breathing experiments.

You will be compensated for your participation.

For more information please contact
Phone: (416) 979-5000 ext. 4985
Email: prlab@psych.ryerson.ca

All queries are confidential.

FEMALE PARTICIPANTS NEEDED!

Panic and Eating Behaviours Study

Have you NEVER suffered from any of the following:

Panic Disorder   **Premenstrual Dysphoric Disorder**
Bulimia Nervosa   **Situation-Specific Phobia**
Social Anxiety Disorder

Are you physically healthy? (e.g., no asthma, diabetes, head injury)

Are you between 18 and 45 years old?

You may be eligible to participate in a research study.

Participants must have NO recent illegal drug use.

This study involves a 30-minute telephone screen to determine eligibility, then one 60-90 minute visit to Ryerson University. Participants will fill out questionnaires and engage in two breathing experiments.

You will be compensated for your participation.

For more information please contact
Phone: (416) 979-5000 ext. 4985
Email: prlab@psych.ryerson.ca

All queries are confidential.

Appendix B – Screening Materials

Telephone Screen (for Community Participants)

SECTION I: Hi, my name is _____ and I am a researcher in the Psychophysiology Lab at Ryerson University. I am contacting you because you had expressed interest in participating in our study entitled Anxiety, Panic, and Eating Behaviours.

In order to see if you would be eligible to participate in the study, I have to ask you some questions over the telephone. These questions are about your medical status, thoughts, emotions and behaviours, and will take between 15 to 30 minutes. You will not be compensated for answering these questions–we are simply trying to find out if you are eligible to do the Anxiety, Panic, and Eating Behaviors study and if you are, then you would get compensation for being in the study.

"Would you like to proceed?"

YES_____ NO_____

If YES, continue. If NO, stop.

"Do you have some time right now?"
Yes _____ No _____

IF NO, ask, "When would be a good time to call back?"

    Date/time to call back _____

IF YES, PROCEED.

I'll first tell you briefly what this study is about. The purpose of this study is to learn about the relationship between panic and eating behaviours. The experiment will involve one visit to our laboratory at Ryerson University, located at 105 Bond Street. The total time commitment in the laboratory will be approximately 1 – 1.5 hours. During the visit, you will complete several questionnaires that ask about your thoughts, emotions and behaviours, and you will engage in two breathing experiments.

"Would you like to proceed?"
Yes _____ No _____

IF YES, PROCEED to SECTION II below.

Everything you disclose in this study will remain completely confidential and will only be known to myself, the principal investigator of the study, and my research supervisor, Dr. Kristin Vickers. This includes information regarding any psychological disorder you may have, including an eating disorder. However, as part of this study, we are obligated to inform everyone that there are five cases in which we might need to break confidentiality:

(1) if you intend to harm yourself;

(2) if you intend on harming someone else;

(3) if there is reasonable suspicion that a child up to the age of 16 years is at risk of neglect or abuse, we are required by law to report this to the Children's Aid Society right away;

(4) if our files are subpoenaed by the courts (records can be opened by a specific court order);

(5) if a regulated health professional has engaged in inappropriate sexual behavior toward you and you provide us with the name of this individual, we are obligated to report them to their regulatory body.

Would you like to continue?   Yes _____   No _____

If **YES**:

To see if you're eligible,

I will first ask you some questions about your **Medical History.**

When did you have your most recent physical exam?
MONTH and YEAR: _____

STOP if no physical exam within the past year.

Did this most recent physical exam indicate that you are in good physical health?
Yes / No / Don't Know

STOP if answer is NO or DON'T KNOW or NOT SURE
CONTINUE only if answer is YES

1. I will list several medical conditions. Please indicate whether you have ever been diagnosed by a physician as having any of these medication conditions by responding YES or NO. If you are NOT SURE, please explain.

- head injury   Yes / No / Not Sure
- brain tumor   Yes / No / Not Sure
- cerebral aneurysm   Yes / No / Not Sure
- cerebal hemorrhage   Yes / No / Not Sure
- stroke   Yes / No / Not Sure
- transient ischemic attack   Yes / No / Not Sure
- heart attack   Yes / No / Not Sure
- heart disease   Yes / No / Not Sure
- coronary artery disease   Yes / No / Not Sure
- congestive heart failure   Yes / No / Not Sure
- mitral valve prolapse   Yes / No / Not Sure
- diabetes   Yes / No / Not Sure
- vasovagal syncope (fainting episodes)   Yes / No / Not Sure
- renal problems (kidney problems)   Yes / No / Not Sure
- heart murmur   Yes / No / Not Sure
- cardiac arrhythmia   Yes / No / Not Sure
- respiratory disease   Yes / No / Not Sure
- lung disease   Yes / No / Not Sure
- basilar artery migraine   Yes / No / Not Sure
- asthma   Yes / No / Not Sure
- epilepsy   Yes / No / Not Sure
- hemiplegic migraine   Yes / No / Not Sure
- seizures   Yes / No / Not Sure
- liver disease   Yes / No / Not Sure
- kidney disease   Yes / No / Not Sure
- opthalmoplegic migraine   Yes / No / Not Sure
- hypertension (high blood pressure)   Yes / No / Not Sure
- cerebrovascular accident   Yes / No / Not Sure

STOP if any symptoms in #1 are answered YES or NOT SURE.

2. Has any biological family member (first degree relative) ever been diagnosed with:

- cerebral aneurysm   Yes / No / Not Sure
- cerebral hemorrhage   Yes / No / Not Sure
- hemiplegic migraine   Yes / No / Not Sure

STOP if any symptoms in #2 are answered YES or NOT SURE.

3. Please tell me Yes, No, or Not Sure to the following.
- Are you currently pregnant?   Yes / No / Not Sure
- Do you have a history of fainting?   Yes / No / Not Sure
- Are you taking any medication that affects your heart rate?   Yes / No / Not Sure
  (e.g. beta-blockers, calcium channel blockers, and tricyclic antidepressants)
- Are you in poor physical health?   Yes / No / Not Sure
- Have you been told to limit physical activity?   Yes / No / Not Sure
- Have you ever been dizzy or passed out during or after exercise?   Yes / No / Not Sure
- Are there any restrictions on your daily behaviour due to a medical
  condition?   Yes / No / Not Sure

STOP if any symptoms in #3 are answered YES or NOT SURE.

4. Have you ever been diagnosed by a physician with:

- Allergies   Yes / No / Type _____
- Cancer   Yes / No / Type _____
- Psychological Disorders   Yes / No / Type _____

STOP if YES to a latex allergy, any anaphylactic allergy, or cancer, or if YES to any of the following psychological disorders: Social Anxiety Disorder, Situational-Specific Phobias, Premenstrual Dysphoric Disorder

5. Have you ever been diagnosed by a physician as having a condition that I have not yet asked you about?   Yes / No

If YES: What condition(s)?

_____

6. Do you get headaches? Yes / No
a) Did paralysis of one side of your body ever occur? Yes / No

STOP if A is answered YES.

b) Did any of the following ever occur in the context of your headaches:
- feeling that the world was revolving or like you were revolving in space? Yes / No
- tingling sensations on both sides of your body? Yes / No
- double vision? Yes / No
- ringing in your ears? Yes / No
- paralysis of both sides of your body? Yes / No
- difficulty speaking? Yes / No
- visual symptoms in both eyes' visual fields near your nose and ears? Yes / No
- decreased hearing? Yes / No
- decreased level of consciousness? Yes / No
- lack of coordination? Yes / No

STOP if 2 symptoms in B are answered YES.

c) Did paralysis of the nerves needed for eye movement ever occur, leading to a dropped eyelid, double vision, or excessive dilation of the pupil of your eye? Yes / No

STOP if C is answered YES.

7. What medications are you currently taking?

_____

_____

STOP if using medications that can significantly affect heart rate (e.g., beta-blockers, calcium channel blockers, tricyclic antidepressants) or psychotropic medications (except for benzodiazepines less than 2x/week).

8. Do you use nicotine?   Yes / No

9. Do you drink caffeine?   Yes / No

If YES to nicotine and/or caffeine: Would you be able to refrain from nicotine and/or caffeine for 4 hours prior to participating in this study?   Yes / No

STOP if answer is NO

10. Do you use alcohol?   Yes / No

11. You may choose whether or not you would like to answer the following question: Do you use substances other than nicotine and alcohol?

Yes / No / No Response

STOP if YES

If eligible based on Medical Criteria, continue.

I will now ask you some questions about your thoughts, emotions and behaviours.

1) Have you been consistently depressed or down, most of the day,
nearly every day, for the past two weeks?   No   Yes

2) In the past two weeks, have you been much less interested in
most things or much less able to enjoy the things you used to
enjoy most of the time?   No   Yes

3) Have you felt sad, low or depressed most of the time for the
last two years?   No   Yes

4) In the past month did you think that you would be better off
dead or wish you were dead?   No   Yes

5) During the past year, were most of your menstrual periods
preceded by a period lasting about one week when your mood
changed significantly?**   No   Yes

6) Have you ever had a period of time when you were feeling 'up'
or 'high' or 'hyper' or so full of energy or full of yourself that you
got into trouble, or that other people thought you were not your
usual self? (Do not consider times when you were intoxicated on
drugs or alcohol.)   No   Yes

7) Have you ever been persistently irritable, for several days, so that
you had arguments or verbal or physical fights, or shouted at people
outside your family? Have you or others noticed that you have been
more irritable or over reacted, compared to other people, even in
situations that you felt were justified?   No   Yes

8) Have you, on, more than one occasion, had spells or attacks when
you suddenly felt anxious, frightened, uncomfortable, or uneasy,
even in situations where most people would not feel that way?

Did the spells surge to a peak, within 10 minutes of starting?   No   Yes

75

9) Do you feel anxious or uneasy in places or situations where you might have a panic attack or panic-like symptoms, or where help might not be available or escape might be difficult: like being in a crowd, standing in a line, when you are away from home or alone at home, or when crossing a bridge, traveling in a bus, train or car?   No Yes

10) In the past month, were you fearful or embarrassed being watched, being the focus of attention, or fearful of being humiliated? This includes things like speaking in public, eating in public or with others, writing while someone watches, or being in social situations.   No Yes

11) Are there any other things that you have been especially afraid of, like flying, seeing blood, getting a shot, heights, closed places, or certain kinds of animals or insects?   No Yes

12) How tall are you?   _____

13) What was your lowest weight in the past 3 months?   _____

Height (ft in) 4'9   4'10   4'11   5'0   5'1   5'2   5'3   5'4   5'5   5'6   5'7
Weight (lbs) 81   84   87   89   92   96   99   102   105   108   112
Height (ft in) 5'8   5'9   5'10   5'11   6'0   6'1   6'2   6'3
Weight (lbs) 115   118   122   125   129   132   136   140

14) In the past 3 months, did you have eating binges or times when you ate a very large amount of food within a 2-hour period?   No Yes

15) In the last 3 months did you have eating binges as often as twice a week?   No Yes

**If needed:
Y. PREMENSTRUAL DYSPHORIC DISORDER

Y1 During the past year, were most of your menstrual periods preceded by a period lasting about one week when your mood changed significantly? No Yes

Y2 During these periods, do you have difficulty in your usual activities or relationships with others, are you less efficient at work, or do you avoid other people? No Yes

Y3 During these premenstrual episodes (but not at in the week after your period ends) do you have the following problems most of the time:

 a Do you feel sad, low, depressed, hopeless, or self-critical? No Yes

 B Do you feel particularly anxious, tense, keyed up or on edge? No Yes

 C Do you often feel suddenly sad or tearful, or are you particularly sensitive to others' comments? No Yes

 D Do you feel irritable, angry or argumentative? No Yes

ARE **1** OR MORE **Y3** ANSWERS CODED **YES**?

 E Are you less interested in your usual activities, such as work, hobbies or meeting with friends? No Yes

 F Do you have difficulty concentrating? No Yes

 G Do you feel exhausted, tire easily, or lack energy? No Yes

 h Does your appetite change, or do you overeat or have specific food cravings? No Yes

 i Do you have difficulty sleeping or do you sleep excessively? No Yes

 j Do you feel you are overwhelmed or out of control? No Yes

 k Do you have physical symptoms such as breast tenderness or swelling, headaches, joint or muscle pain, a sensation of bloating, or weight gain? No Yes

ARE **5** OR MORE **Y3** ANSWERS CODED **YES**? IF **YES,** DIAGNOSIS MUST BE CONFIRMED BY PROSPECTIVE DAILY RATINGS

Diagnoses:

- Panic Disorder   Yes / No

    o   Unexpected panic attacks   Yes / No

    o   To your knowledge, has anyone in your biological family – including cousins, aunts, uncles and grandparents – ever been diagnosed with Panic Disorder? Yes / No

- Bulimia Nervosa   Yes / No

- Social Phobia   Yes / No

- Situational Specific Phobias   Yes / No

- Premenstrual Dysphoria   Yes / No

Eligible to participate?   Yes / No   –   Reason: _____

If **NO:**
Thank you for answering these questions. Unfortunately, you are not eligible to participate in this study. However, you could have your name entered into a draw to win $50. If you want to do this, I will have to write down your full name and your email address, so that we'll be able to later contact whoever wins the draw. Would you like to give this information and then be entered into a draw to win $50?

If **YES**:
Thank you for answering these questions. You are eligible to participate in this study. Would you like to set up an appointment to come to the lab on Ryerson Campus to complete the study?
You will be compensated $20 if you complete the study. If you do not complete the study, you will be compensated for the amount of time you participated, which is $10 per hour and includes the time you spent answering these questions over the telephone. Please remember to refrain from any nicotine and caffeine for 4 hours prior to arriving at the lab.

Laboratory appointment day/time: _____

Appendix C – Informed Consent Forms

<u>Informed Consent for Community Participants</u>

Ryerson University: Informed Consent Agreement

Title of Study: Panic and Eating Behaviours Study

You are being asked to participate in a research study. Before you give your consent to be a volunteer, it is important that you read the following information and ask as many questions as necessary to be sure you understand what you will be asked to do.

Investigators:

Andrea Woznica, B.A., Graduate Student, Department of Psychology, Ryerson University

Kristin Vickers, Ph.D., Department of Psychology, Ryerson University

Purpose of the Study: The purpose of this study is to learn about the relationship between panic and eating behaviours. About 90 women (all physically healthy who are 18 to 45 years old) will take part in this study. Some of the women in this study will have symptoms consistent with Bulimia Nervosa (an eating disorder); other women in this study will have symptoms consistent with Panic Disorder and suffer from panic attacks (intense bursts of fear accompanied by bodily symptoms) in the past; and other women in this study will have neither diagnosis.

Description of the Study: The experiment will involve one visit to the Psychophysiology Lab (room SBB220) at the Psychology Research and Training Centre at Ryerson University, located at 105 Bond Street. The total time commitment will be approximately two hours (including both the phone call and laboratory visit).

- For 4 hours before your first lab visit, it is preferred that you do NOT use any products containing nicotine or caffeine.

- After signing this Consent Form if you choose to participate, you will be asked some questions about your emotions and your medical history. You will then complete several paper-and-pencil questionnaires. This part of the lab visit will take about 1 – 1.5 hours.

- Then, in the second part of the lab visit, which is estimated to take about 30 minutes, you will engage in breathing experiments. These experiments will make it harder to breathe for a short while, but the symptoms will go away quickly. Before and after these experiments, you will be asked to fill out several brief questionnaires. You may see all of the questionnaires ahead of time. During each experiment, your heart rate, oxygen saturation, blood pressure and breathing will be measured by equipment attached to your arm, your ear, your hand and your mouthpiece. Throughout the experiments, which will last about 30 minutes in total, you will wear a mouthpiece in your mouth and a nose clip. You will breathe through a tube connected to the mouthpiece. You will breathe normal room air throughout the 30-minute session except for during one of the two experiments, which will last 30 seconds. In this experiment, you will receive one inhalation of room air that is mixed with larger than normal concentration of carbon dioxide (35% carbon dioxide mixed with 65% oxygen). In the other of the two experiments, you will receive one inhalation of room air. These breathing experiments will each last only 30 seconds. They may cause you to feel breathless. At any time, you may stop your participation by

signaling to the researcher or by removing the mouthpiece that you are wearing. After you complete the questionnaires following the second breathing experiment, you will have the opportunity to learn more about this study in a 10-minute discussion with Andrea Woznica. Then your participation in this study will be finished.

What is Experimental in this Study: None of the procedures or questionnaires used in this study is experimental in nature. The only experimental aspect of this study is the gathering of information for the purpose of analysis.

Risks or Discomforts:

- Temporary physical and psychological discomfort may be caused at those times when you are breathing room air that is mixed with larger than normal concentrations of carbon dioxide.

- The physical effects of breathing carbon dioxide-enriched room air may include racing heart sensations, increased breathing rate, shortness of breath, and dizziness. These effects are entirely harmless and painless. They are expected to disappear quickly when returning to breathing normal room air.

- Breathing air that contains more carbon dioxide than normal room air may result in you feeling anxious or fearful. This feeling is entirely harmless and temporary.

- Breathing air that contains more carbon dioxide than normal room air may also result in you having a panic attack, which is an intense burst of fear accompanied by bodily symptoms. If you were to have a panic attack, you would feel extremely afraid and have bodily symptoms such as shortness of breath and dizziness. This panic feeling is harmless and temporary.

- If at any point while you are doing the breathing experiments you begin to feel uncomfortable, you can stop your participation (either temporarily or permanently) immediately by removing your mouthpiece or signaling to Andrea Woznica, who will be in the room with you at all times.

- Answering questions about your moods and personal history, because of the personal nature of the questions asked, may result in you reflecting on unpleasant memories while responding to the questionnaires or interview. If you begin to feel uncomfortable, you may discontinue participation, either temporarily or permanently. In addition, you may skip any question that you do not want to answer at any point.

Benefits of the Study: The results of this study will not benefit you directly, but the knowledge gained may help the researcher and others to understand the relationship between panic and eating behaviours. I cannot guarantee, however, that you will receive any benefits from participating in this study.

Confidentiality: Everything you disclose in this study will remain completely confidential and will only be known to the principal investigator of the study, Andrea Woznica, and her research supervisor, Dr. Kristin Vickers. This includes information regarding any psychological disorder you may have, including an eating disorder. However, as part of this study, we are obligated to inform everyone that there are five cases in which we might need to break confidentiality:

(1) if you intend to harm yourself;

(2) if you intend on harming someone else;

(3) if there is reasonable suspicion that a child up to the age of 16 years is at risk of neglect or

abuse, we are required by law to report this to the Children's Aid Society right away;

(4) if our files are subpoenaed by the courts (records can be opened by a specific court order);

(5) if a regulated health professional has engaged in inappropriate sexual behavior toward you and you provide us with the name of this individual, we are obligated to report them to their regulatory body.

This informed consent agreement and all data that identify you will be stored in a locked storage space in the Psychophysiology Lab (room SBB220) and access to collected data will be limited to Andrea Woznica, Dr. Kristin Vickers, any other graduate student in the Psychophysiology Lab, and any undergraduate student working directly on this study. You will complete some questionnaires by paper and pencil, and others by entering your responses into a secure computer program. We do need to tell you that the secure computer program stores its data on a server in the United States. This is mentioned because the Patriot Act means the U. S. government can monitor all electronic data. All of your data is kept completely confidential, however. An ID number as opposed to your name will be used on all forms you complete (both paper and electronic), on the interviews that you take part in, and in all computer files that will contain the data you generate during the study. The paper data you generate while participating in this study will be kept in a locked file cabinet, separate from this consent agreement and any other data that identifies you. No videotapes or audiotapes are used in this study.
If you care to know more about the Patriot Act, please visit the link provided - http://epic.org/privacy/terrorism/hr3162.html. If you would like to see the Patriot Act website now, before going any further, please let the researcher know and she will show you this site on the computer.
Your consent form and all data will be kept for seven years after the publication of the results of this research. Your confidentiality will be protected to the full extent allowed by law. Only group findings will be reported in publications and presentations arising from this research.

Incentives to Participate: You will receive a total of $20 for the telephone screen and lab visit. You will still receive $10 if you choose to stop participation before the end of the lab visit.

Costs and/or Compensation for Participation: There are no costs associated with your participation in this study. You are asked to transport yourself to Ryerson University on one occasion.

Voluntary Nature of Participation: Participation in this study is voluntary. Your choice of whether or not to participate will not influence your future relations with Ryerson University. If you decide to participate, you are free to withdraw your consent and to stop your participation at any time without penalty or loss of benefits to which you are allowed. Your right to withdraw your consent also applies to our use of your data. If you decide that you do not want us to keep or analyze data that you have provided during the course of your participation in this study, please feel free to notify us. At any particular point in the study, you may refuse to answer any particular question or stop participation altogether.

Questions about the Study: If you have any questions about the research now, please ask. If you have questions later about the research, you may contact:

Andrea Woznica		Dr. Kristin Vickers
416-979-5000 ext 4985	or	416-979-5000 ext 7727
awoznica@psych.ryerson.ca		kvickers@ryerson.ca

If you have questions regarding your rights as a human subject and participant in this study, you may contact Nancy Walton at the Ryerson University Research Ethics Board for information.

Nancy Walton
Chair, Research Ethics Board
Ryerson University, POD 470B
350 Victoria Street
Toronto, Ontario, Canada M5B 2K3
Phone: (416) 979-5000 Ext. 6300
Email: nwalton@ryerson.ca, Web: http://www.ryerson.ca/research

Agreement:

Your signature below indicates: (1) that you have read the information in this agreement and have had a chance to ask any questions you have about this study; (2) that you agree that information collected from you during the telephone screen for this study can be retained and analyzed and (3) that you agree to be in this study (as described in this consent form) and have been told that you can change your mind and withdraw your consent to participate at any time. You have been given a copy of this agreement. You have been told that by signing this consent agreement you are not giving up any of your legal rights.

_____
Name of Participant (please print)

_____   _____
Signature of Participant   Date

_____   _____
Signature of Investigator   Date

Ryerson University: Informed Consent Agreement

Title of Study: Panic and Eating Behaviours Study

You are being asked to participate in a research study. Before you give your consent to be a volunteer, it is important that you read the following information and ask as many questions as necessary to be sure you understand what you will be asked to do.

Investigators:

Andrea Woznica, B.A., Graduate Student, Department of Psychology, Ryerson University

Kristin Vickers, Ph.D., Department of Psychology, Ryerson University

Purpose of the Study: In this study, we are seeking to find people with certain types of emotions, thoughts and behaviours in order for them to participate in a second study that will investigate people's reactions to several breathing experiments. Eligible participants, based on this study, will then be invited to the second study. They can then choose whether or not they want to participate. About 90 women (all physically healthy who are 18 to 45 years old) will take part in this study.

Description of the Study: The experiment will involve one visit to the Psychophysiology Lab (room SBB220) at the Psychology Research and Training Centre at Ryerson University, located at 105 Bond Street. The total time commitment will be approximately one hour.

- After agreeing to this Consent Form if you choose to participate, you will undergo an interview with the researcher. You will be asked a variety of questions about your medical history and then about your emotions, thoughts and behaviours. This will take approximately 1 hour.

What is Experimental in this Study: None of the interviews/questionnaires used in this study is experimental in nature. The only experimental aspect of this study is the gathering of information for the purpose of analysis.

Risks or Discomforts:
- Answering questions about your moods and personal history, because of the personal nature of the questions asked, may result in you reflecting on unpleasant memories while responding to the questionnaires or interview. If you begin to feel uncomfortable, you may discontinue participation, either temporarily or permanently. In addition, you may skip any question that you do not want to answer at any point.

Benefits of the Study: The results of this study will not benefit you directly, but the knowledge gained may help the researcher and others to understand the relationship between panic and eating behaviours. I cannot guarantee, however, that you will receive any benefits from participating in this study.

Confidentiality: Everything you disclose in this study will remain completely confidential and will

only be known to the principal investigator of the study, Andrea Woznica, and her research supervisor, Dr. Kristin Vickers. This includes information regarding any psychological disorder you may have, including an eating disorder. However, as part of this study, we are obligated to inform everyone that there are five cases in which we might need to break confidentiality:

(1) if you intend to harm yourself;

(2) if you intend on harming someone else;

(3) if there is reasonable suspicion that a child up to the age of 16 years is at risk of neglect or abuse, we are required by law to report this to the Children's Aid Society right away;

(4) if our files are subpoenaed by the courts (records can be opened by a specific court order);

(5) if a regulated health professional has engaged in inappropriate sexual behavior toward you and you provide us with the name of this individual, we are obligated to report them to their regulatory body.

This informed consent agreement and all data that identify you will be stored in a locked storage space in the Psychophysiology Lab (room SBB220) and access to collected data will be limited to Andrea Woznica, Dr. Kristin Vickers, any other graduate student in the Psychophysiology Lab, and any undergraduate student working directly on this study. All of your data is kept completely confidential, however. An ID number, as opposed to your name, will be marked on the paper data that you generate from the interviews that you take part in. This data will be kept in a locked file cabinet, separate from this consent agreement and any other data that identifies you. No videotapes or audiotapes are used in this study.

Your consent form and all data will be kept for seven years after the publication of the results of this research. Your confidentiality will be protected to the full extent allowed by law. Only group findings will be reported in publications and presentations arising from this research.

Incentives to Participate: If you are currently an **Introductory Psychology student** in PSY 102/202 at Ryerson University, you will receive 1% of course credit in research, which will cover the time for the lab visit. You will still receive 1 course credit point if you choose to stop participation before the end of the lab visit.

Costs and/or Compensation for Participation: There are no costs associated with your participation in this study. You are asked to transport yourself to Ryerson University on one occasion.

Voluntary Nature of Participation: Participation in this study is voluntary. Your choice of whether or not to participate will not influence your future relations with Ryerson University. If you decide to participate, you are free to withdraw your consent and to stop your participation at any time without penalty or loss of benefits to which you are allowed. Your right to withdraw your consent also applies to our use of your data. If you decide that you do not want us to keep or analyze data that you have provided during the course of your participation in this study, please feel free to notify us. At any particular point in the study, you may refuse to answer any particular question or stop participation altogether.

Questions about the Study: If you have any questions about the research now, please ask. If you have questions later about the research, you may contact:

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awoznica@psych.ryerson.ca		kvickers@ryerson.ca

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Email: nwalton@ryerson.ca, Web: http://www.ryerson.ca/research

Agreement:

Your signature below indicates: (1) that you have read the information in this agreement and have had a chance to ask any questions you have about this study; (2) that you agree that information collected from you during the telephone screen for this study can be retained and analyzed and (3) that you agree to be in this study (as described in this consent form) and have been told that you can change your mind and withdraw your consent to participate at any time. You have been given a copy of this agreement. You have been told that by signing this consent agreement you are not giving up any of your legal rights.

_____
Name of Participant (please print)

_____   _____
Signature of Participant   Date

_____   _____
Signature of Investigator   Date

Ryerson University: Informed Consent Agreement

Title of Study: Breathing, Panic and Eating Behaviours Study

You are being asked to participate in a research study. Before you give your consent to be a volunteer, it is important that you read the following information and ask as many questions as necessary to be sure you understand what you will be asked to do.

Investigators:

Andrea Woznica, B.A., Graduate Student, Department of Psychology, Ryerson University

Kristin Vickers, Ph.D., Department of Psychology, Ryerson University

Purpose of the Study: The purpose of this study is to learn about the relationship between panic and eating behaviours. About 90 women will take part in this study (all physically healthy who are 18 to 45 years old and all of whom previously completed the Panic and Eating Behaviours study and met eligibility criteria to participate in this study). Some of the women in this study will have symptoms consistent with Bulimia Nervosa (an eating disorder); other women in this study will have symptoms consistent with Panic Disorder and suffer from panic attacks (intense bursts of fear accompanied by bodily symptoms) in the past; and other women in this study will not have symptoms consistent with either diagnosis.

Description of the Study: The experiment will involve one visit to the Psychophysiology Lab (room SBB220) at the Psychology Research and Training Centre at Ryerson University, located at 105 Bond Street. The total time commitment will be approximately one hour.

- For 4 hours before your lab visit, it is preferred that you do NOT use any products containing nicotine or caffeine.

- After signing this Consent Form if you choose to participate, you will be asked to complete a questionnaire about your medical history. You will then complete several questionnaires, both on paper and the computer. This part of the lab visit will take approximately 30 minutes.

- In the second part of the lab visit, which is estimated to take about 30 minutes, you will engage in two breathing experiments. These experiments will make it harder to breathe for a short while, but the symptoms will go away quickly. Before and after these experiments, you will be asked to fill out several brief questionnaires on the computer. You may see all of the questionnaires ahead of time. During each experiment, your heart rate, oxygen saturation, blood pressure and breathing will be measured by equipment attached to your arm, your ear, your hand and your mouth. Throughout the experiments, which will last about 30 minutes in total, you will wear a mouthpiece in your mouth and a nose clip. You will breathe through a tube connected to the mouthpiece. You will breathe normal room air throughout the 30-minute session except for during one of the two experiments, which will last 30 seconds. In this experiment, you will receive one inhalation of room air that is mixed with a greater than normal concentration of carbon dioxide (35% carbon dioxide mixed with 65% oxygen). In the other of the two experiments, you will receive one inhalation of room air. These breathing experiments will each last only 30 seconds. They may cause you to feel breathless. At any time, you may stop your participation by signaling to the researcher or by removing the mouthpiece

that you are wearing. After you complete the questionnaires following the second breathing experiment, you will have the opportunity to learn more about this study in a 10-minute discussion with Andrea Woznica. Then your participation in this study will be finished.

What is Experimental in this Study: None of the procedures or questionnaires used in this study is experimental in nature. The only experimental aspect of this study is the gathering of information for the purpose of analysis.

Risks or Discomforts:

- Temporary physical and psychological discomfort may be caused at those times when you are breathing room air that is mixed with greater than normal concentrations of carbon dioxide.

- The physical effects of breathing carbon dioxide-enriched room air may include racing heart sensations, increased breathing rate, shortness of breath, and dizziness. These effects are entirely harmless and painless. They are expected to disappear quickly when returning to breathing normal room air.

- Breathing air that contains more carbon dioxide than normal room air may result in you feeling anxious or fearful. This feeling is entirely harmless and temporary.

- Breathing air that contains more carbon dioxide than normal room air may also result in you having a panic attack, which is an intense burst of fear accompanied by bodily symptoms. If you were to have a panic attack, you would feel extremely afraid and have bodily symptoms such as shortness of breath and dizziness. This panic feeling is harmless and temporary.

- If at any point while you are doing the breathing experiments you begin to feel uncomfortable, you can stop your participation (either temporarily or permanently) immediately by removing your mouthpiece or signaling to Andrea Woznica, who will be in the room with you at all times.

- Answering questions about your moods and personal history, because of the personal nature of the questions asked, may result in you reflecting on unpleasant memories while responding to the questionnaires or interview. If you begin to feel uncomfortable, you may discontinue participation, either temporarily or permanently. In addition, you may skip any questions that you do not want to answer at any point.

Benefits of the Study: The results of this study will not benefit you directly, but the knowledge gained may help the researcher and others to understand the relationship between panic and eating behaviours. I cannot guarantee, however, that you will receive any benefits from participating in this study.

Confidentiality: Everything you disclose in this study will remain completely confidential and will only be known to the principal investigator of the study, Andrea Woznica, and her research supervisor, Dr. Kristin Vickers. This includes information regarding any psychological disorder you may have, including an eating disorder. However, as part of this study, we are obligated to inform everyone that there are five cases in which we might need to break confidentiality:

(1) if you intend to harm yourself;

(2) if you intend on harming someone else;

(3) if there is reasonable suspicion that a child up to the age of 16 years is at risk of neglect or abuse, we are required by law to report this to the Children's Aid Society right away;

(4) if our files are subpoenaed by the courts (records can be opened by a specific court order);

(5) if a regulated health professional has engaged in inappropriate sexual behavior toward you and you provide us with the name of this individual, we are obligated to report them to their regulatory body.

This informed consent agreement and all data that identify you will be stored in a locked storage space in the Psychophysiology Lab (room SBB220) and access to collected data will be limited to Andrea Woznica, Dr. Kristin Vickers, any other graduate student in the Psychophysiology Lab, and any undergraduate student working directly on this study. You will complete some questionnaires by paper and pencil, and others by entering your responses into a secure computer software program. We do need to tell you that the secure computer program stores its data on a server in the United States. This is mentioned because the Patriot Act means that the U.S. government can monitor all electronic data. All of your data is kept completely confidential, however. An ID number as opposed to your name will be used on all forms you complete (both paper and electronic), on the interviews that you take part in, and in all computer files that will contain the data you generate during the study. The paper data you generate while participating in this study will be kept in a locked file cabinet, separate from this consent agreement and any other data that identifies you. No videotapes or audiotapes are used in this study.
If you care to know more about the Patriot Act, please visit the link provided - http://epic.org/privacy/terrorism/hr3162.html. If you would like to see the Patriot Act website now, before going any further, please let the researcher know and she will show you this site on the computer.
Your consent form and all data will be kept for seven years after the publication of the results of this research. Your confidentiality will be protected to the full extent allowed by law. Only group findings will be reported in publications and presentations arising from this research.

Incentives to Participate: If you are currently an **Introductory Psychology student** in PSY 102/202 at Ryerson University, you will receive 1% of course credit in research, which will cover the time for the lab visit. You will still receive 1 course credit point if you choose to stop participation before the end of the lab visit.

Costs and/or Compensation for Participation: There are no costs associated with your participation in this study. You are asked to transport yourself to Ryerson University on one occasion.

Voluntary Nature of Participation: Participation in this study is voluntary. Your choice of whether or not to participate will not influence your future relations with Ryerson University. If you decide to participate, you are free to withdraw your consent and to stop your participation at any time without penalty or loss of benefits to which you are allowed. Your right to withdraw your consent also applies to our use of your data. If you decide that you do not want us to keep or analyze data that you have provided during the course of your participation in this study, please feel free to notify us. At any particular point in the study, you may refuse to answer any particular question or stop participation altogether.

Questions about the Study: If you have any questions about the research now, please ask. If you have questions later about the research, you may contact:

Andrea Woznica   Dr. Kristin Vickers
416-979-5000 ext 4985   or   416-979-5000 ext 7727
awoznica@psych.ryerson.ca   kvickers@ryerson.ca

If you have questions regarding your rights as a human subject and participant in this study, you may contact Nancy Walton at the Ryerson University Research Ethics Board for information.

Nancy Walton
Chair, Research Ethics Board
Ryerson University, POD 470B
350 Victoria Street
Toronto, Ontario, Canada M5B 2K3
Phone: (416) 979-5000 Ext. 6300
Email: nwalton@ryerson.ca, Web: http://www.ryerson.ca/research

Agreement:

Your signature below indicates: (1) that you have read the information in this agreement and have had a chance to ask any questions you have about this study; (2) that you agree that information collected from you during the telephone screen for this study can be retained and analyzed and (3) that you agree to be in this study (as described in this consent form) and have been told that you can change your mind and withdraw your consent to participate at any time. You have been given a copy of this agreement. You have been told that by signing this consent agreement you are not giving up any of your legal rights.

_____
Name of Participant (please print)

_____   _____
Signature of Participant   Date

_____   _____
Signature of Investigator   Date

Appendix D – Medical History Questionnaire

ID NUMBER_____

1. Have you ever been diagnosed by a physician as having any of the following? If you are NOT SURE, please explain.

CONDITION	NO	NOT SURE (IF NOT SURE, PLEASE	YES
Head Injury			
Brain Tumor			
Cerebral Aneurysm			
Cerebral Hemorrhage			
Stroke			
Transient Ischemic Attack			
Heart Attack			
Heart Disease			
Coronary Artery Disease			
Congestive Heart Failure			
Mitral Valve Prolapse			
Diabetes			
Vasovagal syncope (fainting episodes)			

2. Have you ever been diagnosed by a physician as having any of the following? If you are NOT SURE, please explain.

CONDITION	NO	NOT SURE (IF NOT SURE, PLEASE	YES
Heart Murmur			
Cardiac Arrhythmia			
Respiratory Disease			
Lung Disease			
Basilar Artery Migraine			
Asthma			
Epilepsy			
Hemiplegic Migraine			
Seizures			
Liver Disease			
Kidney Disease			
Ophthalmoplegic Migraine			
Hypertension (High Blood			
Cerebrovascular Accident			
Renal Problems (Kidney Problems)			

3. Has any family member (first degree relative) ever been diagnosed with any of the following?

CONDITION	NO	NOT SURE (IF NOT SURE, PLEASE	YES
Cerebral Aneurysm			
Cerebral Hemorrhage			
Hemiplegic Migraine			

4. Please check YES, NO, or NOT SURE for each of the questions below: If you are NOT SURE, please explain:

QUESTION	NO	NOT SURE (IF NOT SURE, PLEASE	YES
Are you currently pregnant?			
Do you have a history of fainting?			
Are you taking any medication that affects your heart rate? Examples include: beta-blockers, calcium channel blockers, and tricyclic antidepressants.			
Are you in poor physical health?			
Have you been told to limit physical activity?			
Have you ever been dizzy or passed out during or after exercise?			
Are there any restrictions on your daily behavior due to a medical condition?			

5. Have you ever been diagnosed by a physician with any of the following? If YES, please explain the type.

CONDITION	NO	YES	IF YES, PLEASE EXPLAIN THE TYPE
Allergies			
Cancer			
Psychological Disorder			

6a. Have you ever been diagnosed by a physician as having a condition that has not been asked about on this questionnaire?   **YES**   **NO**

6b. If you answered NO to question 6a above, please skip to question 7 (next page). If you answered YES to question 6a above, please list the condition/s and explain below in the table:

CONDITION	PLEASE EXPLAIN

7a. Do you get headaches?   **YES**   **NO**

If you answered NO to question 7a above, please skip to question 8 (on page 6). If you answered YES to question 7a above, please answer the questions in the HEADACHE SYMPTOMS table below (question 7b).

7b. Please answer each question in the HEADACHE SYMPTOMS table below with respect to the headaches you have had. Please consider each question as it relates to symptoms you may have had during your headache, after your headache has passed, or before your headache has started.

HEADACHE SYMPTOMS

QUESTION	NO	NOT SURE (IF NOT SURE, PLEASE	YES
Did paralysis of one side of your body ever occur?			
Did **two** (or more) of the following occur?: feeling that the world was revolving or like you were revolving in space; tingling sensations on both sides of your body; double vision; ringing in your ears; paralysis of both sides of your body; difficulty speaking; visual symptoms in both eyes' visual fields near your nose and ears; decreased hearing; decreased level of consciousness; lack of coordination?			
Did paralysis of the nerves needed for eye movement occur, leading to a drooping eyelid, double vision, or excessive dilation of the pupil of your eye?			

8. Please list previous hospitalizations for past medical problems:

DIAGNOSIS	DATES	TREATMENT

9a. Are you currently taking prescription medications?   **YES**   **NO**

9b. If you answered YES to question 9a above, please list the prescription medications you are taking and the condition each is treating.

PRESCRIPTION MEDICATION	FOR WHAT CONDITION?

10. When did you have your most recent physical exam?

MONTH and YEAR: _____

11. Did this most recent physical exam indicate that you are in good physical health?

YES   NO   DON'T KNOW

12a. Are you currently taking non-prescription medications? **YES**   **NO**

12b. If you answered YES to question 12a above, please list the non-prescription medications you are taking and the condition each is treating or the purpose of the non-prescription medication.

NON-PRESCRIPTION MEDICATION	FOR WHAT CONDITION OR PURPOSE?

13a. Are you currently taking vitamins, minerals or herbal supplements? **YES**   **NO**

13b. If you answered YES to question 13a above, please list the vitamins, minerals, or herbal supplements you are taking and the purpose of each. Herbal supplements include weight loss preparations such as ephedra (ma huang) and yohimbine.

VITAMIN, MINERAL, OR HERBAL SUPPLEMENT	FOR WHAT PURPOSE?

14a. Are you currently trying to become pregnant?   **YES**   **NO**

14b. Have you experienced a miscarriage or abortion in the past month? **YES**   **NO**

14c. Please list the date of your most recent pregnancy:

NEVER BEEN PREGNANT or   DATE:_____

15a. Are you currently taking birth control pills or using other hormonal means of contraception?
                                                          YES   **NO**

15b. If YES, please specify what type of hormonal contraception: TYPE:_____

16a. Do you smoke cigarettes?   **YES**   **NO**

16b. If YES, please specify number of cigarettes per day:

NUMBER OF CIGARETTES DAILY:_____

The next questions below (#17 & #18) are optional and you may choose NOT to answer either or both of them. These questions are for the purposes of data collection only.

17a. Do you drink alcohol?   **YES**   **NO**

17b. If YES, please specify number of drinks per week:

NUMBER OF DRINKS PER WEEK:_____

18a. Do you use substances other than nicotine or alcohol? **YES**   **NO**

18b. If YES, please specify the type of substance:

TYPE OF SUBSTANCE _____

We greatly appreciate you giving us this information. All information will be kept confidential. It is important that this form be accurate. Please print your id number below if you are have answered these questions to the best of your knowledge.

"I have read the questions on this form carefully and have answered each as accurately as possible."

_____   _____

(print id number)   (date)

Appendix E – Panic Reactivity Measures

Subjective Units of Distress Scale

On this scale, 0 means no anxiety, not disturbed at all, and 100 means extreme anxiety, the worst anxiety imaginable. Please rate your current level of anxiety by making a mark on the line below:

0_____100
no anxiety   *extreme anxiety*

<u>Acute Panic Inventory</u>

Please use the following rating scale to complete each item as you feel now:

not at all (0)   slight (1)   moderate (2)   severe (3)

1.   Do you feel faint?   _____

2.   Are you afraid of dying?   _____

3.   Are you generally fearful?   _____

4.   Do you have heart palpitations?   _____

5.   Do you have any difficulty in breathing, or are you breathing rapidly?   _____

6.   Do you have the urge to urinate?   _____

7.   Do you have the urge to defecate?   _____

8.   Do you feel dizzy or light-headed?   _____

9.   Do you feel confused?   _____

10.   Do you have a sense of unreality?   _____

11.   Do you feel detached from part or all of your body?   _____

12.   Is it difficult for you to concentrate?   _____

13.   Are you sweating?   _____

14.   Is it difficult for you to speak?   _____

15.   Would it be difficult for you to do a job?   _____

16.   Do you feel any shakiness, trembling, or twitching?   _____

17.   Do you feel nauseous?   _____

Subjective Panic Attack Scale

We are interested in your experiences during the experiment you just took part in. People have different sensations and perceptions. Please answer the questions on the next two pages.

1.   During the experiment, did you have an increase
        in bodily sensations?   no   yes

        If you answered "no" to question 1, please skip to question 3.

2.   If you answered yes to question 1, was this increase
        in bodily sensations sudden?   no   yes

3.   Were you afraid during the experiment?   no   yes

4.   Were you more excited than usual during the experiment?   no   yes

5.   Did you enjoy the experiment?   no   yes

6.   Was the experiment like any other experience
        you have had in your life?   no   yes

7. If you answered yes to question 6, please describe the experience that was similar to what you felt during the experiment.
_____
_____

8. Please describe any other sensations or feelings you had during the experiment.
_____
_____

Please continue answering the questions on the next page.

Please read the following definition:

A panic attack is a sudden increase in physiological sensations accompanied by fear.

Please answer the following questions:

9. In your opinion, did you just have a
   panic attack during the experiment?   no   yes

10. Besides your experiences in this study,
    have you ever had a panic attack?   no   yes

11. If you answered "yes" to question 10, please indicate *how similar* the experience you just had during the experiment was to the panic attacks you typically experience. Please rate how similar the experience you just had was to your typical panic attack on the following scale, where 0 means "not at all similar to my typical panic attack"; 4 means "somewhat similar to my typical panic attack"; and 8 means "identical to my typical panic attack."

   0   1   2   3   4   5   6   7   8
   not   somewhat   identical
   at all   similar
   similar

Debriefing for Community Participants

Ryerson University: Debriefing Form

Title of Study: Panic and Eating Behaviours Study

Thank you very much for participating in our study. In this study, we are investigating people's reactions to a mixture of 35% carbon dioxide and 65% oxygen. This concentration of carbon dioxide is greater than what you breathe in room air. You first completed several questionnaires related to your emotions, thoughts, and behaviours. You then completed 2 breathing experiments. In the first, you breathed normal room air. In the second, you breathed the 35% carbon dioxide mixture. You also completed questionnaires that asked about your reactions to the breathing experiments. These questionnaires will help us to better understand the relationship between anxiety, panic, and eating behaviours. Approximately 90 female participants will complete this study. This study will be available to female undergraduates in Introductory Psychology at Ryerson University, and to females from the Greater Toronto Area community.

This is a study about people's reactions to carbon dioxide. A mixture of 35% carbon-dioxide and 65% oxygen has been shown to incite symptoms that are comparable to natural panic attacks (intense bursts of fear accompanied by bodily symptoms). Therefore, this experimental model has been used in laboratories to study panic, as seen in individuals who have been diagnosed with Panic Disorder. However, recent research has revealed that some people without Panic Disorder or a history of panic also react to carbon-dioxide. This includes people with psychological disorders other than Panic Disorder (for example, social phobia), and even people without any psychopathology. This interesting finding led researchers to question why some people react to carbon dioxide while others do not. It is possible that certain psychological factors, aside from disorders, may affect reactivity to carbon dioxide. These factors include anxiety sensitivity, discomfort intolerance and distress tolerance. Researchers have attempted to answer this question by studying people's reactions to carbon dioxide in terms of physiology (e.g., heart rate, blood pressure) and psychology (questionnaires asking about emotions, thoughts and behaviours). One diagnostic group that has not been extensively looked at in terms of their carbon-dioxide reactivity is individuals with eating disorders. The present study, therefore, uses a sample of participants with symptoms consistent with Bulimia Nervosa to examine whether these individuals respond to carbon-dioxide enriched air similar to the Panic Disorder participants. Additionally, certain psychological factors were questioned across all participants (including those without any psychopathology) to determine the extent to which they predict an anxious response to the carbon-dioxide. These results will potentially contribute meaningfully to our understanding of the commonality between Panic Disorder and other diagnostic categories that have been shown to react to carbon dioxide. For more information, please contact Andrea Woznica.

If you are a student at Ryerson and are currently experiencing psychological distress and would like to discuss your concerns in a safe and confidential environment, the Ryerson Centre for Student Development and Counselling (CSDC) is a free resource located on campus. Staff provides support and guidance for a range of concerns including anxiety, low mood, and academic difficulties. The contact information for the CSDC is as follows:

Centre for Student Development and Counselling
Website: http://www.ryerson.ca/counselling/index.html
Email: csdc@ryerson.ca
Phone: 416-979-5195
Location: JOR-07C (Lower level of Jorgensen Hall, 380 Victoria Street)

If you are not a Ryerson student and are experiencing psychological distress, the city of Toronto also offers a free telephone hotline available 24 hours a day. Please call the Toronto Distress Centre:

416-408-HELP (4357)
Website: http://torontodistresscentre.com/

If you are a student at Ryerson and are extremely distressed, you can call this hotline number as well **416-408-HELP** (4357)

Once again, we would like to thank you very much for your participation. If you are interested in further information, you are encouraged to take a look at the references provided on the next page. Finally, if you have any further questions or concerns pertaining to this research, feel free to contact:

Andrea Woznica		Dr. Kristin Vickers, PhD
Department of Psychology		Department of Psychology
Ryerson University	or	Ryerson University
Email: awoznica@ryerson.ca		Email: kvickers@ryerson.ca
Phone: 416-979-5000 ext 4985		Phone: 416-979-5000 x 7727

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These journal articles and books are available for free via the Ryerson library, or please email Andrea Woznica to have the journal articles sent to you.

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Kutz, A., Marshall, E., Bernstein, A., & Zvolensky, M. J. (2010). Evaluating emotional sensitivity and tolerance factors in the prediction of panic-relevant responding to a biological challenge. *Journal of Anxiety Disorders, 24*, 16-22.

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Ryerson University: Debriefing Form

Title of Study: Panic and Eating Behaviours Study

Thank you very much for participating in our study. In this study, we are seeking to find people with certain types of emotions, thoughts, and behaviours in order for them to participate in a second study. Eligible participants, based on this study, will then be invited to the second study. They can then choose whether or not they want to participate. The second study will address the relationship between panic and eating behaviours. Specifically, the second study will investigate people's reactions to several breathing experiments. Please contact Andrea Woznica for more information.

In the study you did today, you completed several self-report interviews related to your emotions, thoughts, and behaviours. Approximately 90 female participants will complete this study. This study will be available to female undergraduates in Introductory Psychology at Ryerson University, and to females from the Greater Toronto Area community.

If you are an Introductory Psychology student at Ryerson and are currently experiencing psychological distress and would like to discuss your concerns in a safe and confidential environment, the Ryerson Centre for Student Development and Counselling (CSDC) is a free resource located on campus. Staff provides support and guidance for a range of concerns including anxiety, low mood, and academic difficulties. The contact information for the CSDC is as follows:

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The city of Toronto also offers a free telephone hotline available 24 hours a day. If you are experiencing psychological distress, please call the Toronto Distress Centre:
416-408-HELP (4357)   Website: http://torontodistresscentre.com/

Once again, we would like to thank you very much for your participation. If you are interested in further information, you are encouraged to take a look at the references provided below. Finally, if you have any further questions or concerns pertaining to this research, feel free to contact:

> Andrea Woznica   Dr. Kristin Vickers, PhD
> Department of Psychology   Department of Psychology
> Ryerson University   or   Ryerson University
> Email: awoznica@ryerson.ca   Email: kvickers@ryerson.ca
> Phone: 416-979-5000 ext 4985   Phone: 416-979-5000 x 7727

Reference: This journal article is available for free via the Ryerson library.

Sheehan, D. V., et al. (1998). The Mini-International Neuropsychiatric Interview (M.I.N.I): The development and validation of a structured psychiatric interview for DSM-IV and ICD-10. *Journal of Clinical Psychiatry, 59,* 22-23.

Ryerson University: Debriefing Form

Title of Study: Breathing, Panic and Eating Behaviours Study

Thank you very much for participating in our study. In this study, we are investigating people's reactions to a mixture of 35% carbon dioxide and 65% oxygen. This concentration of carbon dioxide is greater than what you breathe in room air. You first completed several questionnaires related to your emotions, thoughts, and behaviours. You then completed 2 breathing experiments. In the first, you breathed normal room air. In the second, you breathed the 35% carbon dioxide mixture. You also completed questionnaires that asked about your reactions to the breathing experiments. These questionnaires will help us to better understand the relationship between anxiety, panic, and eating behaviours.

Approximately 90 female participants will complete this study. This study will be available to female undergraduates in Introductory Psychology at Ryerson University, and to females from the Greater Toronto Area community. If you are an Introductory Psychology student, you have completed the first lab visit where you were asked questions about your emotions, thoughts, and behaviours and about your physical health. You were invited to this second lab visit if you were in good physical health, and endorsed symptoms that were either consistent with a diagnosis of Bulimia Nervosa (an eating disorder) *or* a diagnosis of Panic Disorder (an anxiety disorder with panic attacks, which are intense bursts of fear accompanied by bodily symptoms). Additional participants were invited if they had symptoms that were *not* consistent with either diagnosis. Please note that this is a research study only, and that the researcher is identifying symptoms that are consistent with particular psychological disorders but is not making a diagnosis. A diagnosis can only be determined by a mental health professional.

This is a study about people's reactions to carbon dioxide. A mixture of 35% carbon-dioxide and 65% oxygen has been shown to incite symptoms that are comparable to natural panic attacks (intense bursts of fear accompanied by bodily symptoms). Therefore, this experimental model has been used in laboratories to study panic, as seen in individuals who have been diagnosed with Panic Disorder. However, recent research has revealed that some people without Panic Disorder or a history of panic also react to carbon-dioxide. This includes people with psychological disorders other than Panic Disorder (for example, social phobia), and even people without any psychopathology. This interesting finding led researchers to question why some people react to carbon dioxide while others do not. It is possible that certain psychological factors, aside from disorders, may affect reactivity to carbon dioxide. These factors include anxiety sensitivity, discomfort intolerance and distress tolerance. Researchers have attempted to answer this question by studying people's reactions to carbon dioxide in terms of physiology (e.g., heart rate, blood pressure) and psychology (questionnaires asking about emotions, thoughts and behaviours). One diagnostic group that has not been extensively looked at in terms of their carbon-dioxide reactivity is individuals with eating disorders. The present study, therefore, uses a sample of participants with symptoms consistent with Bulimia Nervosa to examine whether these individuals respond to carbon-dioxide enriched air similar to the Panic Disorder participants. Additionally, certain psychological factors were questioned across all participants (including those without any psychopathology) to determine the extent to which they predict an anxious response to the carbon-dioxide. These results will potentially contribute meaningfully to our understanding of the commonality between Panic Disorder and other diagnostic categories that have been shown to react to carbon dioxide. For more information, please contact Andrea Woznica.

If you are an introductory Psychology student at Ryerson and are currently experiencing psychological distress and would like to discuss your concerns in a safe and confidential environment, the Ryerson Centre for Student Development and Counselling (CSDC) is a free resource located on campus. Staff provides support and guidance for a range of concerns including anxiety, low mood, and academic difficulties. The contact information for the CSDC is as follows:

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Once again, we would like to thank you very much for your participation. If you are interested in further information, you are encouraged to take a look at the references provided on the next page. Finally, if you have any further questions or concerns pertaining to this research, feel free to contact:

Andrea Woznica		Dr. Kristin Vickers, PhD
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