KATHOLIEKE UNIVERSITEIT LEUVEN

Faculteit Psychologie en
Pedagogische Wetenschappen
Onderzoeksgroep voor Stress,
Gezondheid en Welzijn

HYPERVENTILATION INDUCED HYPOCAPNIA

PSYCHOLOGICAL CAUSES AND CONSEQUENCES

Proefschrift aangeboden tot het verkrijgen van de graad van
Doctor in de Psychologische Wetenschappen

door
Ilse Van Diest

o.l.v.
Prof. Dr. O. Van den Bergh, promotor
Prof. Dr. K. P. Van de Woestijne, co-promotor

2003

Ilse Van Diest

In dierbare herinnering aan Karel Kuipers

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Promotor: Prof. Dr. Omer Van den Bergh

Hyperventilation is a breathing pattern in excess of metabolic needs, leading to hypocapnia (a lowered CO_2 pressure in the blood). A first part of the present thesis (studies 1-6) aimed to study situational and dispositional factors triggering hyperventilation induced hypocapnia. A second part (studies 7-9) focused on psychological consequences of hyperventilation.

Although hyperventilation induced hypocapnia has been hypothesized to play an important role in a variety of pathologies (e.g., Ley, 1985; Leznoff, 1997; Klein, 1993), its critical triggers remain poorly understood. A review of studies on situational and dispositional factors associated with hyperventilation (Van Diest, Stegen, Van de Woestijne, & Van den Bergh, 1999) concluded that hyperventilation is typically observed under conditions characterized by high state anxiety, but that no studies have been carried out measuring PCO_2 responses during emotions other than fear or anxiety. This was the aim of our first study in which an emotional imagery paradigm was used to study the occurrence of hyperventilation responses within the two-dimensional affective space formed by valence and arousal (Van Diest et al., 2001a). Results showed that hyperventilation occurred not only during fearful imagery, but also during imagery of pleasant, highly arousing situations. These findings were replicated in a second study in which the emotional scripts used did no longer contain suggestions of autonomic responses (Van Diest et al., 2001b). In a third imagery study (Van Diest, Vos, Devriese, Wellens, Van de Woestijne, & Van den Bergh, submitted,a) the relevance of the emotional dimension of dominance, suggested risk of suffocation and physical confinement for the triggering of hyperventilation was explored. The major finding was that participants scoring high on NA responded with particularly strong PCO_2 decreases when imagining a claustrophobic situation that implied a risk of suffocation.

Studies 4-5 aimed to clarify the inconsistent findings reported in literature on the association between dispositional anxiety (or related concepts, such as negative affectivity or NA) and resting PCO_2 (Van Diest et al., in press). In study 4, no association between NA and PCO_2 was observed when controlling for hormonal influences upon PCO_2. Study 5 aimed to test our interpretation previously given (see Van Diest, et al. 1999) to a controversial finding of Dhokalia, Parsons and Anderson (1998). The latter found a positive association between NA and PCO_2, measured while participants were completing a questionnaire. In study 5, PCO_2 of high and low NA participants was studied under various conditions; it was found that filling out questionnaires was associated with a PCO_2 increase in high NA participants only. Study 6 explored the within-subject variability in breathing parameters during relaxation and during anxious imagery in participants scoring high and low for NA. Results indicated that inter-, but not intraindividual differences in anxiety were negatively related to the variability in some, but not all breathing parameters.

Study 7 examined the association strength of NA with a variety of individual symptoms (Van Diest, De Peuter, Eertmans, Notebaert, Victoir & Van den Bergh, submitted,b). It was found that the extent to which a particular symptom (1) refers to a specific location in the body ('vagueness'), (2) is likely to be a physiological manifestation of anxiety, and (3) may refer to both a physical condition and a negative emotion, were significant predictors for the association strength of a symptom with NA in women. In men, only 'vagueness' was a significant predictor. In an explorative factor analysis on the symptom checklist, two symptom factors were extracted. The first factor grouped hyperarousal symptoms typically associated with fight/flight tendencies; the second factor clustered systemic and sickness symptoms possibly stemming from a functional system promoting recuperative behavior in response to stress. Study 8 investigated the extent to which the association of a symptom with NA could be predicted by its typicality for hyperventilation induced hypocapnia. Results indicated that typicality for hyperventilation was not a significant predictor.

A last study (study 9) aimed to test whether the subjective symptoms of cognitive impairment associated with hypocapnia were mirrored in concomitant, objective cognitive performance deficits (Van Diest, Stegen, Van de Woestijne, Schippers, & Van de Woestijne, 2000). To this end, participants performed a Stroop-like task following hypocapnic and normocapnic overbreathing. The latter served as a within control condition of the former. Cognitive performance deficits following hypocapnic overbreathing were observed in a subgroup of participants who showed post-hyperventilation apneas. The pattern of results suggested that hypoxia, resulting from post-hyperventilation apneas, may account for the observed cognitive performance deficits.

Dankuwel

Iemand die dit proefschrift gelezen heeft, zal zich misschien verbazen over het feit hoeveel verklaard kan worden vanuit situationele factoren, en hoe weinig vanuit dispositionele of persoonlijkheidsfactoren. Dit geldt evenzeer voor de totstandkoming van dit proefschrift, waaraan talrijke mensen direct of indirect een bijdrage hebben geleverd.

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Chapter 1

Hyperventilation induced Hypocapnia: Physiological Aspects

The homeostasis of the pressure of CO_2 (PCO_2) in the arterial blood is necessary for the functioning of many, pH-regulated physiological processes in the body, such as nerve conduction and smooth muscle contractility (Gilbert, 1999). This can be obtained by the virtue of respiratory timing and volume parameters changing in accordance with the production of CO_2. Under normal circumstances, healthy subjects succeed in regulating arterial PCO_2 tightly and to keep it within narrow limits. As a consequence, a normal breathing pattern is characterized by little variability in PCO_2 (Shea, 1997), relative to the variability in respiratory timing and volume parameters (Bruce & Daubenspeck, 1995). This central notion regarding respiration will be elaborated in greater detail in subsequent paragraphs. First, respiratory parameters relevant to our research and their measurement will be briefly introduced. Next, some key concepts of breathing regulation will be treated. This background information will enable us to describe and understand the phenomenon of hyperventilation induced hypocapnia in a last part.

1.1 Respiratory Parameters and their Measurement

1.1.1 Parameters

PCO_2

In normal lungs, alveolar partial pressure of CO_2 ($PACO_2$) is a valid approximation of arterial PCO_2 ($PaCO_2$), and can, in turn, reliably be estimated by measuring the

amount of CO_2 at the end of the expiration ($ETCO_2$; Gardner, 1996; Pahn, Tremer, Lee, & Barker, 1987). The latter can be expressed in pressure ($PETCO_2$, in mmHg or Torr) or in percentage ($FETCO_2$). $ETCO_2$ can be measured with a capnograph, an infrared CO_2 monitor that samples and analyses the expired air. A value of 40 mmHg has been proposed as a normal, resting $PETCO_2$ for healthy subjects (West, 1990). An individual's mean resting PCO_2 is rather stable, varying within a 2 h period by only 1-2 mmHg. Day-to-day variability is somewhat larger, with a mean range of 4 mmHg over one month (Shea, 1997).

Men have higher values of PCO_2 than women (Tatsumi, Moore, & Hannhart, 1995) and resting PCO_2 is known to decline with age (Dhokalia, Paterson, & Anderson, 1998). Women's progesterone levels are negatively associated with PCO_2 (England & Farhi, 1976; Takano, 1984). Progesterone levels are typically increased during the luteal phase of the menstrual cycle, during pregnancy, and also when using oral contraceptives. Because of these influences, PCO_2 is more variable in women than in men.

Time and volume parameters

The respiratory cycle can be described by its frequency and amplitude, or, by its time and volume components, respectively. The total cycle time (Ttot, in seconds) can be divided into inspiratory time (Ti, in seconds) and expiratory time (Te, in seconds). Between the end of expiration and the start of a new inspiration, an end-expiratory pause may occur. Some authors treat such respiratory pause as a third, separate component of the breathing cycle (e.g., Wientjes, 1993; Han, 1995), whereas others add it to Te. We will follow the latter option.

Inspiratory (Vi) and expiratory volume (Ve) are expressed in ml; we will use Vi as measurement of tidal volume (V_T, in ml), which is the volume that is displaced during each breath. Four important parameters can be calculated out from Ti, Te and V_T:

(1) Respiratory Rate (RR) or breathing frequency (f) is the number of respiratory cycles per minute: $f = (Ti + Te)/60$

(2) The inspiratory flow or drive (V_T/Ti, in ml per second) is thought to reflect the central inspiratory drive mechanism, which determines the intensity of the inspiration (Gautier, 1980)

(3) The duty cycle time (Ti/Ttot) is the percentage of Ttot that was spent to Ti. This parameter is thought to reflect the central time mechanism with which the inspiratory drive mechanism is switched on and off (Gautier, 1980)

(4) Minute ventilation (V'_E, in ml or l/min) is the product of f and mean V_T over one minute, reflecting the total amount of air that is being replaced during one minute: $V'_E = f \times V_T$

A small proportion of V'_E does not actually reache the alveoli, but remains in the "dead space" formed by the nose, mouth, throat, trachea and bronchi. Dead space refers to the fact that no actual gas exchange is taking place in these parts of the respiratory tract. A measure of physiologically effective ventilation is alveolar ventilation (V'_A, in ml or l/min); it refers to the amount of air that is involved in gas exchange. V'_E equals the sum of alveolar and dead space ventilation. The proportion of dead space ventilation in V'_E varies as a function of the relative contributions of V_T and f to the respiratory cycle: the proportion of dead space ventilation will be greater in a rapid, shallow breathing pattern than in a slow breathing pattern with large volumes.

1.2 Measurement techniques

Two important respiratory measurement devices and techniques used in our own studies will be discussed briefly: pneumotachography and inductive plethysmography.

In pneumotachography, airflow is derived from pressure changes over a fixed resistance constituted by a bundle of parallel capillary tubes (Fleisch type) or a

metal screen (Lilly type). Volume is obtained from analogue or digital integration of the flow signals. The pneumotachograph is designed such that, for a given flow range, a direct proportionality between flow and pressure drop over the resistance is ensured (Ritz et al., 2002). In our studies, a Fleisch No. 2 was used; this type is known to keep linearity for flow ranges of normal, spontaneous breathing (Ritz et al., 2002). Calibration of the integrated flow is typically performed using a gas syringe with a known volume. Pneumotachography enables very reliable and valid volume measurements. However, an important disadvantage is its intrusiveness: participants have to breathe in a closed face-mask or via a mouthpiece (with nose-clip) to which the pneumotachograph is connected. Indeed, several studies report alterations of the spontaneous breathing pattern by such devices (Askanazi, Silverberg, Forster, Hyman, & Milic-Emili, 1980; Gilbert, Auchincloss, Brodsky, & Boden, 1972; Han, Stegen, Cauberghs, & Van den Woestijne, 1997a; Western & Patrick, 1988).

This does not apply for inductive plethysmography, in which chest and abdominal wall movements are measured in order to derive airflow or volume. To this end, two coils are strapped over the chest and the upper abdomen. The change in mean cross-sectional area of the coil caused by chest and abdominal wall displacement modifies the inductance of the coil (Ritz et al., 2002). Calibration is performed by simultaneous pneumotachography. Off-line multiple regression analyses yield the regression coefficients of the chest and abdominal signals to be used for the reconstruction of the volume out of the chest and abdominal signals (Strömberg, Dahlbäck, & Gustafsson, 1993). It is evident that these regression coefficients are reliable only if the participant does not change posture or position from the calibration to the measurement period.

1.2. Metabolic and Behavioral Control of Breathing

Parts of the subsequent paragraphs have been copied from Van Diest, Han, Van de Woestijne, Devriese, Winters, & Van den Bergh (2002). Chinese Journal of Tuberculosis and Respiratory Diseases, 25 (2), 299-301.

1.2.1 Metabolic control

The metabolic control of breathing is relatively well understood. The main structures involved are both the central and peripheral chemoreceptors and the respiratory centers in the brain stem. Metabolic control of breathing rests upon reflexive responding and feedback loops: an error signal in a controlled variable precedes any change in ventilation (Shea, 1996). For instance, a perturbation in $PaCO_2$ is an error signal that gives rise to changes in ventilation counteracting the initial perturbation. Central chemoreceptors are very sensitive to changes in $PaCO_2$ (and pH); peripheral receptors are located in the carotid bodies and respond mainly to changes in PaO_2, and to a lesser degree also to $PaCO_2$ (Cunningham, Robbins, & Wolff, 1986; Gallego, Nsegbe & Durand, 2001). Figure 1 depicts the ventilation versus $PETCO_2$ response curve to inspired CO_2. At the lower end of the curve, there is a discontinuity, or the so-called "dog-leg", suggesting a cessation of chemoreceptor activity at lower levels of PCO_2. In normal, quiet, unstimulated breathing, ventilation is located just on the dogleg near the junction of the discontinuity with the steeper part of the curve (Cunningham et al., 1986; Gardner, 1996).

Several observations indicate that metabolic control cannot fully account for the regulation of breathing (Gallego et al., 2001; Shea, 1996). First, blood gases of healthy humans do show a lack of variability. In awake humans, measured with noninvasive equipment under strictly defined conditions of relaxation, an individual's mean resting $PaCO_2$ is rather stable, varying within a 2 h period by

only 1-2 mmHg (Shea, 1997). On the other hand, ventilation itself displays much variability. When subjects open their eyes to read, breathing is increased rapidly by an average of 6% (Shea, Walter, Pelley, Murphy and Guz, 1987) without any preceding perturbation in $PaCO_2$ or PaO_2. Similarly, ventilation is increased in a characteristic way during mental arithmetic. Although the breathing pattern is altered - generally by causing a more rapid breathing - changes in $PaCO_2$ are hardly observed.

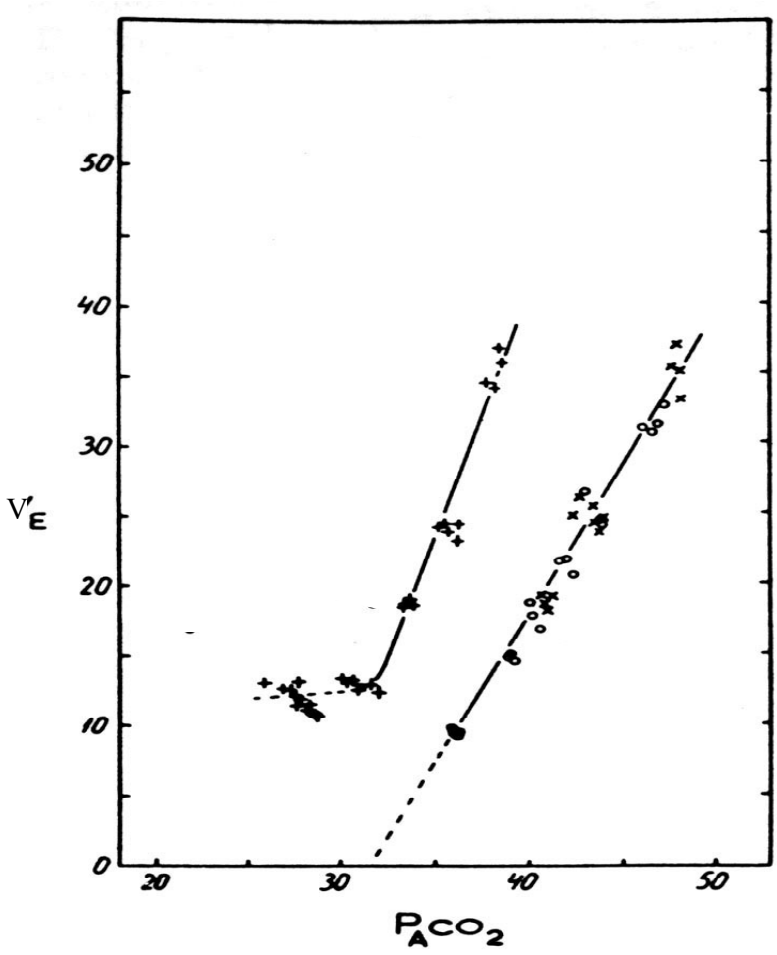


Figure 1. Ventilation in function of $PACO_2$ at steady PAO_2 of 47 (+), 110 (o), and 169 (x) Torr. From: Cunningham et al. (1986), p. 496.

A second observation concerns patients suffering from Congenital Central Hypoventilation Syndrome (CCHS). Such patients lack chemoreceptor control of breathing and seriously hypoventilate during non-REM sleep, requiring mechanical ventilation. However, during wakefulness and during REM sleep, many of those patients breathe adequately. In most situations, and despite changes in metabolism, they manage to keep blood gas tensions rather stable (Shea, 1997).

A third observation that cannot be explained by metabolic control is what happens at the onset of exercise. In many subjects, ventilation is increased before any change in $PaCO_2$ occurs (Somjen, 1992). Tobin, Perez, Guenther, D'Alonso, & Dantzker (1986) observed that the exercise hyperpnea precedes muscle recruitment. As a consequence, exercise hyperpnea cannot be induced by a neurogenic or humoral stimulus. More recently, brain-imaging studies have proved the involvement of the motor cortex in exercise hyperpnea (Fink et al., 1995).

Summarizing, $PaCO_2$ (or PaO_2) cannot always be the driving stimulus for changes in ventilation, as it remains within normal resting limits. Somjen (1992) concludes that homeostatic negative feedback fails to explain the lack of variability in blood gas tensions and he derives that the central nervous system must be capable of *anticipating* present and future needs, reflecting a *feedforward* behavioral control, rather than the well-studied feedback metabolic control of breathing.

1.2.2 Behavioral control

Behavioral control of breathing refers to the modulation of the breathing pattern that is not primarily related to metabolic requirements, e.g., voluntary changes in breathing patterns, such as during speech, and involuntary changes caused by variations in vigilance, emotions and cognitive activity (Gallego et al., 2001). The hypothalamus, the limbic system and the cortex are structurally involved in the behavioral control of breathing (Gallego et al., 2001; Shea, 1996). These brain structures are newer in evolutionary perspective than those involved in metabolic

control. Some authors suggest that also ontogenetically, behavioral control of breathing may develop thanks to metabolic control. Somjen (1992) proposed that behavioral control is learned at an early age on the basis of experience. In early infancy, environmental or internal changes presumably do perturb controlled variables, but later on, the respiratory system would learn to anticipate such perturbations. Because of this anticipatory nature, Somjen (1992) uses explicitly the term "feedforward" control for behavioral control, to contrast it with the feedback responding of metabolic control (see also Dworkin, 1993). An ontogenetic development of behavioral control of breathing could easily be understood within the psychological theory of associative learning, or, classical conditioning. Perturbations in arterial blood gases are viewed as unconditioned stimuli (US) and internal or external stimuli entailing a predictive value for such perturbations would function as conditioned stimuli (CS). Although its role in the development of behavioral control of ventilation has not been confirmed directly, studies both in humans (Gallego & Perruchet, 1991; Stegen, De Bruyne, Rasschaert, Van de Woestijne, & Van den Bergh, 1999; Van den Bergh, Kempynck, Van de Woestijne, Baeyens, & Eelen 1995) and animals (Orem & Netcik, 1986; Martin & Mitchell, 1993; Nsegbe, Vardon, Dauger, Perruchet, Gaultier, & Gallego, 1998; Nsegbe, Vardon, Perruchet, & Gallego, 1997) have shown that respiratory behavior can be modified by classical conditioning procedures. Both external stimuli (e.g., a sound, Gallego & Perruchet, 1991; an odor, Van den Bergh et al., 1995) and internal stimuli (thoughts or mental images, Stegen et al., 1999) may function as CS's in the conditioning of human respiratory behavior. Because the planning or anticipation of a behavior is, by definition, a process of mental imagery, such CS's may play a particularly important role in the behavioral control of breathing. Indirect support may be found in the observation that mental imagery of exercise increases ventilation, without any associated movement (Gallego, Denot-Ledunois, Vardon, & Perruchet, 1996).

It is unclear yet how metabolic and behavioral control interact and how each contributes to changes in time and volume parameters. With respect to the latter,

both Rafferty and Gardner (1996) and Gallego et al. (1996) suggest that the respiratory timing parameters are weakly controlled by the chemical drive, allowing for non-metabolic functions of breathing (e.g., speech), whereas V_T would be controlled dominantly by the chemical drive. This is in line with several observations reported in literature. In a study on the influence of exercise and CO_2 inhalation on the breathing pattern, it was found that the relative contribution of f in the total increase of ventilation was less during CO_2 inhalation than during exercise (Askanazi, Milic-Emili, & Broell, Hyman, & Kinney, 1979). This difference may be due to a conditioned increase in f during exercise. Such a feedforward regulation can be ruled out during CO_2 inhalation, since it is very unlikely that participants had had, in contrast with exercise, prior experiences with CO_2 inhalation. Yet another observation lends indirect support to the idea that metabolically controlled changes in the breathing pattern are preferably associated with changes in V_T, and, conversely, behavioral control with changes in f. During exercise, the ventilation of low state anxious subjects is increased by an increase in V_T only, whereas both f and V_T are increased in high state anxious subjects (Masaoka & Homma, 1999). Again, this suggests that the feedforward influence of anxiety upon breathing is related to f, and that metabolic changes are rather associated with changes in V_T.

1.3. Hyperventilation: a Physiological Account

1.3.1 Definition

In hyperventilation, metabolic and behavioral components of breathing control are dissociated, leading to an anomaly in respiratory homeostasis. More specifically, hyperventilation is a breathing pattern in excess of metabolic requirements (Gardner, 1996). Because more CO_2 is being exhaled than produced by the body, PCO_2 (arterial, alveolar and end-tidal) is substantially lowered, or, hypocapnia occurs.

Obvious increases in f or V_T do not necessarily lead to hypocapnia. For example, a large V_T can be associated with a low f, with no change in the total alveolar ventilation or $PaCO_2$. Panting may lead to a dramatic increase in expired ventilation, but not necessarily to hypocapnia. This is due to a relatively high degree of dead space ventilation in the total ventilation (V'_E): if breathing is very rapid and shallow, only a minor proportion of the ventilated air actually reaches the alveoli where gas exchange occurs.

At the start of hyperventilation, there is a dramatic reduction of PCO_2 (Gardner, 1996). However, the washout of CO_2 does not continue endlessly. After a few hours, a compensating mechanism is installed that recovers blood pH to normal levels (Gilbert, 1999; Huey & West, 1983). As a result, blood pH is normal, but $PaCO_2$ remains low. This new balance can easily be maintained without manifest overventilation by occasional sighing or one deep breath at regular intervals (Gardner, 1996). Chronic hyperventilation refers to such a compensated condition. The buffer capacity for pH-changes in the arterial blood of chronically hyperventilating individuals is severely compromised. In such condition, even a modest increase in ventilation, e.g., by sighing, can rapidly produce an alkalotic state and its associated symptoms (Ley, 1985).

When PCO_2 is low, there is no chemical drive to breathe any longer (Cunningham et al., 1986; Gardner, 1996; see figure 1). As a consequence, respiratory pauses (apneas) easily occur, especially when behavioral influences that may drive breathing are weakened as well, e.g., during sleep or anesthesia (Bainton & Mitchell, 1966; Corfield, Morrell, & Guz, 1995; Mangin, Krieger, Kurtz, 1982; Meah & Gardner, 1994). However, feedforward controlled influences upon breathing still operate under hypocapnia in awake subjects and may further maintain hypocapnia. Several authors report that anxious subjects recover more slowly from voluntary hyperventilation than non-anxious subjects (Han et al, 1997b; Hardonk & Beumer, 1979; Wilhelm, Gerlach & Roth, 2001), which suggests that anxiety constitutes an important feedforward operating influence that drives breathing under hypocapnia. When the symptoms associated with

hypocapnia inflate anxiety, a positive feedback loop may easily ensue, in which hypocapnia and anxiety maintain and enhance each other in a spiraling-like process. Psychological feedforward influences that may trigger or maintain hyperventilation will be dealt with extensively in the next chapter. Secondary physiological changes and symptoms associated with hypocapnia will be treated first.

1.3.2 Secondary physiological changes and symptoms

Hypocapnia induces respiratory alkalosis (or: an increased blood pH), with notable consequences for the body (Gilbert, 1999). The $PaCO_2$ at which symptoms typically occur in normal subjects is 20 mmHg with an outside range of 14 to 29 mmHg (Rafferty, Saisch, & Gardner, 1992).

Central changes

Cerebral blood flow is linearly related to $PaCO_2$ and reductions in cerebral blood flow have been described under hypocapnia (Gardner, 1996; Gotoh, Meyer, & Takagi, 1965; Kastrup, Dichgans, Niemeier, & Schabet, 1998; Mathew & Wilson, 1990; Mountz, Modell, Wilson, & Curtis, 1989). Not surprisingly, lightheadedness and dizziness are typically experienced under hypocapnic conditions, but also more severe symptoms, such as loss of consciousness, visual disturbances, headache, tremor, tinnitus, hallucinations and unilateral somatic symptoms on the left more than the right may occur (Gardner, 1996). Some older studies suggest that hypocapnia is also associated with impaired problem solving and other performance tasks (e.g., Gellhorn & Joslyn, 1937). Clinically, typical complaints are: a ‘spacey feeling’, impaired thinking, things or the self not feeling real, etc. (Gilbert, 1999).

Peripheral changes

Hypocapnia is associated with an increased neuronal excitability, giving rise to paresthesiae (tingling sensations) in hands, feet, face or limbs. It also promotes

smooth muscle constriction (Gilbert, 1999), which may induce symptoms in several visceral systems, such as cramps in the gastro-intestinal tract and cold hands or feet. Also coronary arteries narrow in response to hypocapnia, which can cause chest pain, especially when an underlying coronary heart disease is present (Gardner, 1996). Hypocapnia is also associated with vagal suppression and an increased cardiac output, which may lead to symptoms of a rapid or stronger heartbeat (Gardner, 1996).

Besides the listed symptoms, hyperventilation is associated with symptoms that are not specific for hypocapnia. Particularly anxiety and respiratory symptoms have been found to occur in a similar degree during normocapnic and during hypocapnic overventilation (Hornsveld & Garssen, 1996; Van Diest, Stegen, Van de Woestijne, Schippers, & Van den Bergh, 2000).

Chapter 2

Psychological Triggers of Hyperventilation

Based on: Van Diest, Stegen, Van de Woestijne, & Van den Bergh (1999). Gedrag & Gezondheid, 27(6), 290-303.

Although the clinical-diagnostic entity of the Hyperventilation Syndrome (HVS) as conceptualized in the seventies and eighties may be problematic (Hibbert & Pilsbury, 1988; 1989; Hornsveld, Garssen, Dop, van Spiegel, & de Haes 1996), hyperventilation induced hypocapnia is a common psychophysiological stress response that remains relevant for both clinical and non-clinical populations. Hyperventilation has been hypothesized to play a role in various pathologies, including asthma, chronic fatigue syndrome, multiple chemical sensitivity, panic, somatization, functional cardiac disorder, chronic muscle pain, and in psychosomatic complaints in the general population (Bazelmans, Bleijenberg, Vercoulen, van der Meer, & Folgering, 1997; Hibbert & Pilsbury, 1988; Ley, 1985; Leznoff, 1997; Papp, Klein, & Gorman, 1993; Salkovskis & Clark, 1990; Sharpe & Bass, 1992; Stegen et al., 1999; Van den Bergh, Stegen & Van de Woestijne, 1997; Wientjes & Grossman, 1994; Wilhelm, Gevirtz, & Roth, 2001b). Nonetheless, the critical triggers for hyperventilation responses remain poorly understood. This chapter aims to review the psychological conditions under which acute and chronic hyperventilation have been observed.

2.1 Acute Hyperventilation

Most often, acute hyperventilation is conceived of as part of a fight/flight response, allowing an organism to react adequately to the stressor (e.g., Wilhelm et al., 2001b). A rapid decrease in the arterial PCO_2 can be considered a feedforward response that compensates for the expected increase in PCO_2 due to the action implied in fighting or fleeing. However, when no such physical action follows, which is typically the case in contemporary, human stressful situations, this respiratory response is dysfunctional. Unlike the good face validity of this conceptualization of hyperventilation, it does not allow for accurate predictions of its occurrence. It is clear that "stress" is too vague a concept in specifying the critical triggers for the occurrence of this psychophysiological stress response. Compared with cardiovascular psychophysiology, relatively little research exists sketching respiratory behavior under stress. Also, relatively little efforts have been made to study respiratory stress responses from a broader, general psychophysiological theoretical framework. For example, no studies have been conducted in order to investigate $ETCO_2$ responses with respect to the theoretical distinction between defensive action and defensive attention (Lang, Davis, & Öhman, 2000), or, between fear and anxiety (Bouton, Mineka, & Barlow, 2001).

We aimed to review studies that have investigated $ETCO_2$ responses of non-clinical samples to different kinds of emotional stressors and attentional load. More specifically, we searched in the literature for (1) studies that have measured $ETCO_2$ responses during emotions or stress and (2) studies describing $ETCO_2$ responses associated with attentional processes. From a psychophysiological perspective (e.g., Frijda, 1999), it can be expected that ventilation would reflect the general action tendency of an organism. This would predict an increased ventilation and a decreased $ETCO_2$ during highly aroused affective states in general, but not during calm affects, nor during conditions of cognitive or attentional load.

2.1.1. Emotions and stress

Although quite some studies have investigated f and V_T responses associated with stress and emotions (for an excellent review: see Boiten, Frijda, & Wientjes, 1994), relatively few studies have incorporated also $ETCO_2$ measures. Table 2A summarizes them.

It can be concluded from table 2A that anticipation of an uncontrollable threat and an inescapable, aversive (e.g., painful) stimulus seem to constitute the prototypical stressors triggering hyperventilation responses. For example, in the study of Suess, Alexander, Smith, Sweeney and Marion (1980), participants performed a difficult perceptual judgment task; they were told that every 10th error they would make, would result in a painful electric shock. The experimenter manipulated the feedback regarding the number of errors made in such way that the participants were expected to assume for several minutes that one more error would produce an electric shock.

In another study, Ley & Yelich (1998) found that a math test was associated with a decrease in $ETCO_2$ in test-anxious children, but not in children without test anxiety. More controllable stressors, such as the shock avoidance task in the study of Allen, Sherwood and Obrist (1986) were not associated with hyperventilation.

In the study of Moynihan & Gevirtz (2001), the "psychologic" stressor consisted of two parts. First, participants performed a 1-minute Stroop test pronouncing aloud their answers. The participant telling a recent personally stressful event followed this for another minute. The more stressful of both periods, defined as the strongest response on the electrodermal and heart rate variables, was used as "psychologic stress" induction. A strong drop in $ETCO_2$ was observed (see table 2A). However, because $ETCO_2$ was being measured using a nose cannula that sampled expired air while participants were speaking, it is likely that the measurements were unreliable and have fairly underestimated the true $ETCO_2$. Therefore, we are reluctant to draw conclusions from these results.

Table 2A. Studies Investigating $PETCO_2$ Responses to Stress in Non-Clinical Samples

Authors	Participants	Devices	Manipulation	$PETCO_2$
Moynihan & Gevirtz (2001)	31 N	NI nose cannula	recounting a stressful event/Stroop task	-14.31
Ley & Yelich (1998)	16 TA 16 N	NI nose cannula	math test	-1.83 in TA
Allen et al. (1986)	22 N	I mouthpiece	RT shock avoidance	0
			cold pressor test	-3.7
Garssen (1980)	15 N 3 men	NI nose cannula	anticipation exam	-2.3
Suess et al. (1980)	29 N 16 men	I mask	task under threat of shock	-3.0
Morgan et al. (1979)	19 N	blood sample	painful arterial punction	-1.1 ($PaCO_2$)
Dudley (1969)	10 N 1 tbc patient	NI	AO-behavior during hypnotically induced emotions	-7.1
			hypnotic suggestion of pain	-10.7
Dudley et al. (1965)	21 N, 5 lung disease	NI	short term AO-behavior (pain)	-9.9
Beckmann (1915)	10	?	clinical demonstration	-2.3
	6		anticipation exam	-2.9

Note: NI = non-intrusive measurement; I = intrusive measurement; RT = reaction time; AO = action-oriented; N = normal population; TA = test anxious

Dudley & Pitts-Poarch (1980) suggest that respiratory hyperfunction generally reflects the preparation for action. From this perspective, it can be expected that hyperventilation responses may also occur during positive affective states. Unfortunately, we found no studies in the literature that measured $ETCO_2$ responses during pleasant emotional states.

2.1.2. Attention

Following Obrist (1981), a reduction in muscle activity is one of the most reliable features of an attentive posture. A concomitant decrease in supplies serving physical activity has been hypothesized to underlie the heart rate deceleration that is typically observed under attentional orienting. Since the respiratory and the cardiovascular system are highly interdependent and primarily serve metabolic functions, it can be expected that such a decrease in supplies for physical activity would be reflected in a decreased ventilation as well. This is in line with observations of an inhibited breathing pattern in humans that showed up more frequently in the workplace and in social situations (Anderson, Austin, & Haythornthwaite, 1993; Haythorntwaite, Anderson, & Moore, 1992). In rats, an inhibited ('strained') breathing pattern has been described, which would typically occur in situations where inhibitory control and attention are crucial. This strained breathing pattern was characterized by a prolonged initial stage expiration and a higher PCO_2 (Fokkema, 1999).

Such a decreased duty cycle time (Ti/Ttot) and a higher PCO_2 may be functional for attentional processes also more directly in that it induces an increased oxygen supply to the brain via the cerebrovascular dilating effect of CO_2 (Kastrup, et al., 1998). In line with this, Flexman, Demaree and Simpson (1974) found that signals in a visual signal detection task presented during exhalation were detected more frequently than those presented during inhalation. However, Gallego, Perruchet and Camus (1991) did not confirm this finding. In a study in which PCO_2

was artificially altered by manipulating inspired CO_2 during mechanical ventilation, it was found that despite discrete changes in EEG, acute $PETCO_2$ increases of 7-10 mmHg above baseline did not affect the latency or amplitude of the P3 event-related potential (Bloch-Salisbury, Lansing, & Shea, 2000). However, it is unclear to which extent the mechanical ventilation and the artificially induced $PETCO_2$ increases are representative for naturally occurring increases in $PETCO_2$. Given the fact that chemoreceptor sensitivity is particularly high just above normal resting PCO_2, it can be expected that such naturally occurring increases would be rather modest and short-lived. Therefore, we argue that it is unlikely that substantial tonic increases in $ETCO_2$ would occur in a similar way as hypocapnia can occur over longer periods of time (see table 2A). Studying naturally occurring phasic $ETCO_2$ responses in a S1-S2 paradigm may be a more fruitful approach to investigate the hypothesized functionality of $ETCO_2$ increases for attentional processes.

Table 2B. Studies Measuring $ETCO_2$ during Attentional Load

Authors	Participants	Devices	Task	$PETCO_2$
Ley & Yelich (1998)	16 TA 16 N	NI	math test	-1.83 in TA
Chin et al. (1996)	8 N men	NI	tetris video game (t) vs. watching tv	t<tv
Schleifer & Ley (1994)	11 N	NI	data-entry task	-2.1
Wientjes et al. (1993)	10 N 10 PS	NI	Shiffrin & Schneider task	0
Rigg et al. (1977)	19 N 13 men	?	mental arithmetic	-.16 kPa

Note: TA = test anxious; N = normals; NI = non-intrusive measurement; I= intrusive measurement; PS = people with many psychosomatic complaints.

Unfortunately, up till now, only studies measuring $ETCO_2$ over longer time periods during different kinds of attentional or cognitive load have been carried out (see table 2B for an overview). It is clear from table 2B that no tonic increases in $ETCO_2$ under attentional load have been observed. Two studies even report significant decreases in $ETCO_2$. This may be due to the fact that the attentional tasks used may have induced considerable stress and anxiety as well. In that case, the reported findings in table 2B are not unambiguously attributable to attentional or cognitive processes. Denot-Ledunois, Vardon, Perruchet and Gallego (1998) explicitly took into account the distinction between cognitive and emotional load. The experimenter personally knew all the children who participated in the experiment and the experiment took place at the experimenter's house, where all children had been before. Also, 7 out of the 10 children were very familiar with the video game they had to perform. The authors found that cognitive load was associated with a decreased ventilation (a decreased f without any change in V_T). Unfortunately, and again, no $ETCO_2$ measures were applied.

Summarizing, although some studies point to an association of attentional load with breathing inhibition, no experimental evidence exists up till now showing that transient, phasic increases in $ETCO_2$ may accompany or promote attentional processes. The few studies that have measured responses in $ETCO_2$ over longer time periods under conditions of cognitive load have not controlled for the potential confounding of concomitant emotional load.

2.1.3. Integrative summary

A hallmark of most studies cited in tables 2A and 2B is their empiristic approach. Few studies have made an attempt to frame their findings within a broader theoretical framework of psychophysiological responding. We think it may be a fruitful approach trying to define respiratory responses along the defensive continuum of Lang, Bradley and Cuthbert (1997), because this would allow

studying the effects of both cognitive load and stress or anxiety within the same theoretical framework. Lang et al. (1997) describe an aversive motivational circuit, which, with increasing arousal, triggers reactions ranging from orientation (OR) to defense (DR). The underlying neurophysiological circuit is largely subcortical and the core structures involved are the amygdala, the thalamus, the hypothalamus and the central gray area (for a more detailed description, see Lang et al., 1997). Behaviorally, it involves a progression from immobility to a triggering of overt reactions to threat.

Based on the studies reviewed above, it can be hypothesized that hyperventilation responses occur when an organism is motivationally at the DR-side of the defensive continuum but the action tendency underlying the DR is not carried out. For example, Dudley, Masuda, Martin and Homes (1965) applied increasingly painful stimuli to participants, until the point that they indicated that they could not bear the pain any longer (see table 2A). It is very likely that this rather cruel manipulation has elicited a DR and it was found to lead to strong decreases in $ETCO_2$.

Also strained breathing in rats (Fokkema, 1999) and the observed inhibited breathing pattern in humans (Anderson et al., 1993; Haythorntwaite et al., 1992) may, in our view, be linked to the defensive cascade model of Lang. Following Fokkema (1999), strained breathing may be functional in that it prevents the organism from hyperventilation. The high breathing frequency, which typically occurs during physical action, can be easily blocked or regulated by slowing expiration by means of upper airway resistance, leading to the strained breathing pattern. Such a break on respiration can be released immediately when physical action requires a higher respiratory rate. This corresponds quite well to what Lang et al. (1997) would call a switch from an attentive defensive set to a defense reaction with overt action.

Also the findings of Masaoka and Homma (1999) fit well a model that assumes a continuum of respiratory responding ranging from inhibited (strained) breathing at the attention side to overbreathing at the overt defense side of the

continuum. They report that participants with low state anxiety responded with a significant increase in $ETCO_2$ to a 73 dB stimulation, whereas the $ETCO_2$ of participants with high state anxiety significantly decreased. This may reflect an attentive (orientation and/or strained breathing) response in the former, and a DR-like response in the latter, which would be consistent with Lang's et al. (1997) model of a progression from attentive to more action-oriented defensive responses with increasing arousal (i.e. anxiety).

However, the outlined speculative integration clearly assumes hyperventilation to be a defensive response. In line with suggestions of Dudley & Pitts-Poarch (1980), hyperventilation may show up under action-oriented, pleasant affects as well. We feel that this is a theoretically important question that should be dealt with first.

2.2 Chronic Hyperventilation

Chronic hyperventilation may underlie the physical symptoms experienced by anxious and depressive persons. After several hours of hyperventilation, a normal pH is restored. However, the buffer capacity to tolerate pH changes (e.g. from breath holding, exercise, sighing) is reduced because of this compensation, giving rise to a more rapid development of the symptoms of acidosis (air hunger) and alkalosis (cerebral vasoconstriction; Gilbert, 1999).

In order to look for evidence for chronic hyperventilation in anxious and depressive persons, studies comparing baseline $ETCO_2$ of people with anxiety or depressive disorders with non-clinical samples will be reviewed. In a subsequent part, also studies investigating the association of resting $ETCO_2$ with trait negative affectivity in non-clinical samples will be dealt with.

In advance, however, we would like to draw the reader's attention to some potential methodological confoundings that apply particularly when the association of $ETCO_2$ and anxiety is studied on an interindividual level. As discussed in chapter

one, $ETCO_2$ is influenced by gender, age and by the phase in the menstrual cycle and the use of oral contraceptives in women. Ideally, interindividual associations should be controlled for these biological influences, which has not been the case in the studies reviewed below. Therefore, all findings listed below should be considered and interpreted with great caution. Another methodological issue concerns the variety in the respiratory measurement equipment used, ranging from very intrusive (mouthpiece and nose clip or closed face-masks) over less intrusive (open masks) to minimally intrusive devices (only a nose cannula). Han et al. (1997a) compared intrusive with non-intrusive techniques and report that the use of a mouthpiece influences the breathing pattern more strongly in anxious persons. Particularly in anxiety patients, $ETCO_2$ progressively decreases during breathing via a mouthpiece (Han et al., 2000). Since most studies reviewed below remained rather vague about the technical details of the measurements, it is difficult to say to which extent this aspect may have contributed to the reported results.

2.2.1 Clinical depression

In line with a general psychophysiological perspective on emotional responding, Boiten et al. (1994) expect that depressive feelings would be associated with a lowered respiratory activity, whereas tenseness and anxiety would be associated with an increased ventilation. This was partially confirmed by the findings of Damas-Mora, Grant, Kenyon, Patel and Jenner (1976). Compared with a non-clinical control group, these authors found a lower $ETCO_2$ in agitated and reactive depressions, but a marginally significant higher $FETCO_2$ in 'retarded endogenous depressions'. The group with agitated depression scored higher on the STAI-state than the retarded depressive group. In another study, Damas-Mora, Souster en Jenner (1982) found a lower $ETCO_2$ in reactive than in endogenous depressions. These findings seem to emphasize the importance of the overall activation level, which is decreased in endogenous, but increased in reactive depressions. We argue

that it would be particularly interesting to make within-person comparisons in a bipolar affective disorder group between depressed and manic episodes.

2.2.2 Anxiety disorders

Since the symptoms of panic and hyperventilation show considerable overlap, relatively much research has focused on the role it may entail in panic disorder. Whereas cognitive theories on panic (e.g., Clark, 1986; Salkovskis & Clark, 1990; Salkovskis, Jones, & Clark, 1986) consider hyperventilation as one of the many possible physiological manifestations of fear and anxiety, more biologically inspired theories on panic adhere a more prominent role to it. Following Klein's (1993) suffocation alarm theory, panic patients have a dysfunctional suffocation alarm in the brain and chronically hyperventilate to keep PCO_2 low. Also the core assumption of Ley's (1985; 1989) hyperventilation theory of panic is that high anxious subjects slightly overbreathe chronically. Such subjects would be particularly at risk to develop panic disorder because the mild, chronic hyperventilation is associated with the fear provoking sensation of dyspnea, which would be the ultimate trigger of a first full-blown panic attack (Ley, 1985; 1989). Ley (1992) proposed a comprehensive model of panic heterogeneity, in which he accounted for both cognitively and physiologically based panics. The Type 1 panic attack is the classic or respiratory attack, marked by hypocapnia. The Type 3 is the cognitive subtype, in which only weak physiological responses can be detected. The Type 2 panic attack falls between both other types and would be an evolved Type 1 panic attack, in which the originally spontaneous respiratory panic attacks have been associated with predictive internal/external cues eliciting anticipatory fear. Summarizing, both Klein (1993) and Ley (1985; 1989) assume chronic hyperventilation in at least a considerable proportion of panic disorder patients, which should be reflected in lower resting values of $ETCO_2$.

Table 2C focuses on baseline differences between clinically anxious and non-clinical samples.

Table 2C. Studies Measuring Resting $ETCO_2$ in Clinically Anxious Patients

Authors	Participants	Devices	Effect
Kroeze & Van den Hout (2001)	18 PD 19 N	I face mask	$ETCO_2$: PD = N state anxiety: PD > N
Wilhelm et al. (2001c)	16 PD 15 GAD 19 N	NI nose cannula	$ETCO_2$: PD < N SUD: PD = GAD > N
Han et al. (2000)	117 PD 127 OA 477 SD 159 N	I mouthpiece	$ETCO_2$ men: (PD, OA) < N $ETCO_2$ women: PD = OA = N
Hegel & Ferguson (1997)	17 PD 18 GAD 20 N	I mask	$ETCO_2$: PD < GAD, N state anxiety: PD = GAD > N
Papp et al. (1997)	59 PD 39 N	I	$ETCO_2$: PD < N
Abelson et al. (1996)	16 PD/PD&Ag 16 N	I mouthpiece	$ETCO_2$: PD < N
Stein & Asmundson (1994)	24 PD 26 N	NI nose cannula	$ETCO_2$: PD = N state anxiety: PD > N
Lee et al. (1993)	5 PD 5N	I mouthpiece	$ETCO_2$: PD < N situational distress PD > N
Margraf (1993)	60 patients: PD, D, asthma	blood sampling	$PaCO_2$: PD = D = asthma
Munjack et al. (1993)	64 PD/PD&Ag 48 GAD 24 N	blood sampling	venous PCO_2: PD < GAD < N
Papp et al. (1993)	18 PD 20 SocPh 23 N	blood sampling	venous PCO_2: SocPh > N PD = N SocPh = N

Table 2C. continued

Authors	Participants	Devices	Effect
Van den Hout et al. (1992)	15 PD 11GAD N	I	$ETCO_2$: PD = GAD < N situational distress PD = GAD
Gorman et al. (1990)	26 PD 22 SocPh 14 N	blood sampling	venous PCO_2: PD = SocPh = N
Bass et al. (1989)	23 PD & Ag 18 N	NI nose cannula	$ETCO_2$: PD < N subjective anxiety: PD > N
de Ruiter et al. (1989)	21PD 88 PD & Ag 11 GAD	I mouthpiece	$ETCO_2$: PD = PD &Ag = GAD
Holt & Andrews (1989)	50 PD/ Ag 29 SocPh/GAD 16 N	I mouthpiece	$ETCO_2$: PD = SocPh = GAD = N
Gorman et al. (1988)	31 PD/PD&Ag 25 Controls (12 OA, 13 N)	canopy	$PaCO_2$: PD < controls ($p < .08$)
Pain et al. (1988)	12 PD 12 N	I mouthpiece	$ETCO_2$: PD = N state anxiety: PD > N
Gorman et al. (1986)	76 PD/PD&Ag 22 N	blood sampling	venous pCO_2: PD/PD & Ag < N
Rapee (1986)	20 PD 13 GAD	?	$ETCO_2$: PD < GAD

Note: SUD = subjective units of distress; PD = panic disorder; GAD = generalized anxiety disorder; N = normal controls; OA= anxiety disorders other than panic disorder; NI = non-intrusive measurements; I = intrusive measurements; PD &Ag = panic disorder with agoraphobia; SocPh = social phobia.

From the 15 studies including both a panic disorder and a healthy control group, ten studies (66.7 %) report significantly lower resting $ETCO_2$ values in patients with panic disorder than in healthy controls. Two studies were not included in this proportion because of ambiguous findings. Han et al. (2000) found a lower

resting $ETCO_2$ in male but not in female panic patients. In the study of Gorman et al. (1988), panic patients only tended ($p < .08$) to have lower resting $ETCO_2$ levels than a control group. However, since the latter consisted for about 50 % of other anxiety patients (not panic disorder), one could question the appropriateness of the control group. Indeed, some studies in table 2C also report a lower resting $ETCO_2$ in anxiety disorders other than panic disorder compared to normals (e.g., in men: Han et al., 2000; Munjack, Brown, & McDowell, 1993; Van den Hout, Hoekstra, Arntz, Christiaanse, Ranschaert, & Schouten, 1992).

In contrast with what would be predicted from the theories of Klein (1993) and Ley (1985; 1989), only a minority of studies in table 2C do report a differentiation between different anxiety disorders: Three out of ten studies (30 %) found a lower $ETCO_2$ in panic disorder than in other anxiety disorder groups (Hegel & Ferguson, 1997; Munjack et al., 1993; Rapee, 1986).

Besides the methodological concerns already raised (see pp. 21-22), an important issue that may have played a role in the inconsistent findings is the way the participants may apprehend the experimental context. In many studies, the baseline during which the reported $ETCO_2$ values are measured is followed by a CO_2-inhalation, lactate infusion or voluntary hyperventilation. The method sections of these studies reveal little about how and when participants were informed about what would happen later on in the experiment. The expectation of a respiratory or any other challenge may induce more anticipatory anxiety in panic patients, leading to lower $ETCO_2$-values than in the other groups. Some studies attempt to control for differences in apprehensiveness of the laboratory context by measuring the state anxiety at the beginning of the experiment (Han et al., 2000; Hegel & Ferguson, 1997; Kroeze & Van den Hout, 2001; Pain, Biddle, & Tiller, 1988; Stein & Admundson, 1994) or ratings of subjective distress following each trial throughout the entire experiment (Bass, Lelliot, & Marks, 1989; Lee, Curtis, Weg, Abelson, Modell, & Campbell, 1993; Van den Hout et al., 1992; Wilhelm, Trabert, & Roth, 2001c). Group differences in state anxiety measured at the beginning of the experiment were not mirrored in any study in a similar pattern of group differences

in resting $ETCO_2$ (see table 2C). However, measuring state anxiety at the start of the experiment might have been too insensitive; differences between groups would possibly have shown up if subjective anxiety would have been assessed more frequently throughout the experiment, as was done in the studies of Bass et al. (1989), Lee et al. (1993), Van den Hout et al. (1992) and Wilhelm et al. (2001c). Except for the latter[1], group differences in subjective distress or anxiety were mirrored quite perfectly in $ETCO_2$ levels. In another study (Coplan et al., 1998) baseline $FETCO_2$ levels of panic patients who would panic during lactate infusion or CO_2 inhalation later on in the experiment were compared with those of panic patients who would not panic and healthy subjects. Patients who panicked in response to the challenge were found to have higher levels of self-reported fear and lower levels of $ETCO_2$ preceding the challenge than non-panickers or healthy controls. This may indicate that anticipatory anxiety is associated with a lower $ETCO_2$ and facilitates the occurrence of a panic attack during a subsequent challenge. Even more interestingly, Coplan et al. (1998) found that baseline scores of fear correlated inversely with $ETCO_2$. In the study of Margraf (1993), patients did not anticipate any respiratory or other challenge at the time of measurement. Under these conditions, no differences between panic patients, depressive patients or patients with bronchial asthma were found.

To summarize, evidence seems to suggest that lowered baseline levels of $ETCO_2$ in panic or other anxiety patients reflect higher levels of situational distress or anticipatory anxiety, rather than a trait-like tendency towards chronic hyperventilation in this group.

However, this matter should be sorted out in a repeated within measurement design in which both subjective anxiety and $ETCO_2$ are measured repeatedly during many different occasions in the same subjects.

[1] In the study of Wilhelm et al. (2001c), baseline $FETCO_2$ was measured after the participants had performed voluntary hyperventilation. The authors suggest themselves that the lower baseline $FETCO_2$ in panic patients as compared to normals may have been due to a slower recovery of $FETCO_2$ following hyperventilation in the former than in the latter.

2.2.3. Dispositional negative affectivity

Chronically reduced levels of $ETCO_2$ have been hypothesized to be present also in subclinically anxious and depressive groups. For example, in his review article, Grossman (1983) concludes that "…rapid, thoracic, hypocapnic breathing styles are not only an apparently normal time-limited response to a threatening situation, but can also somehow become a rather stable, built-in feature of people suffering from chronic anxiety and depression…". Several other researchers (Garssen, 1986; Stegen, 1998; Wientjes, 1993) have suggested also that hyperventilation is related to Neuroticism (N) or Negative Affectivity (NA). These are interchangeable concepts referring to the disposition to experience distress, to feel upset and to have a negative view of the self (Watson & Clark, 1984). People high in NA do not only report to experience more negative emotions, they also report more bodily symptoms (Watson & Pennebaker, 1989). Subtle and chronic hyperventilation may be an underlying cause of the latter.

Table 2D summarizes the few studies that have investigated the association of dispositional NA with resting $ETCO_2$. In line with what has been hypothesized, Stegen (1998) found that students scoring high on negative affectivity (NA) had a lower resting $ETCO_2$ than students scoring low. However, other studies found contradictory results. Wientjes and Grossman (1994) and Shershow (1973) found no association of $ETCO_2$ with, respectively, the STAI- trait and the MMPI scales. The pattern of results is complicated even further by the report of a *positive* relationship between $ETCO_2$ and the neuroticism dimension of the 'NEO Personal Inventory' (Dhokalia et al., 1998).

These inconsistencies may be due to differences between studies in respiratory measurement devices and in gender, age and inclusion criteria of the participants. Another important issue relates to the definition of a "resting" condition. Dhokalia et al. (1998) measured $ETCO_2$ while the participants were filling out the NEO personality questionnaire. It is questionable to which extent that this may be considered a resting condition. Indeed, it may potentially have induced

differential effects for high versus low neurotic participants. For example, if high neurotic participants were more committed or filled out the questionnaire more thoughtfully than low neurotic participants, this may have caused the former spending more attentional resources. As mentioned before (see 2.1.2), cognitive load may be associated with a decreased ventilation (Denot-Ledunois et al., 1998), which could have led to an increased $ETCO_2$.

Table 2D. Studies Investigating the Relationship between Resting $FETCO_2$ and Personality Traits in a Non-clinical Population

Authors	Participants	Devices	Effect
Dhokalia et al. (1998)	60 women 43 men	NI nose cannula	$ETCO_2$: positively associated with neuroticism
Stegen (1998)	428 students	I mouthpiece	$ETCO_2$: high NA (36.1 %) %) < low NA (37.1 %)
Wientjes and Grossman (1994)	83 male students	open mask	$ETCO_2$: no relationship with trait anxiety (STAI)
Shershow (1973)	33 soldiers	I mouthpiece	$PaCO_2$: no relationship with MMPI-scales

Note: NI = non-intrusive measurement; I = intrusive measurement; NA = negative affectivity

2.3. Summary

The review of critical conditions for hyperventilation responses is characterized by many inconsistent findings, which are probably due to methodological shortcomings and differences between studies. Also, few studies have been conceptualized within a broader theoretical framework. Nevertheless, a tentative conclusion may be drawn: Hyperventilation occurs when the strong action tendency underlying an emotion is not carried out. We can conclude both from research on

clinical groups and from studies manipulating emotions and stress situationally, that anxiety (as a disorder or as a state) is easily associated with hyperventilation. However, future research should investigate the occurrence of hyperventilation and other respiratory responses not only in the aversive, but also in the appetitive motivational system. With respect to the former system, the defensive cascade model of Lang et al. (1997) is very promising.

With respect to panic disorder, there is no convincing evidence that the occasionally observed lower resting values $ETCO_2$ in such patients reflect a cross-situational, trait-like feature caused by a central physiological disturbance. Indeed, an explanation in terms of an enhanced responsivity to the measurement context or anticipatory anxiety is at least equally likely. Recently, another respiratory disturbance has been described that seems to distinguish panic patients more reliably from other disorders and healthy controls. Wilhelm et al. (2001b,c,d) reviewed and investigated the within subject variability in V_T in panic patients. A highly instable V_T with the occurrence of many sighs and apneas seems to be a cross-situational, central feature of the respiratory behavior of panic patients that is not primarily related to heightened state anxiety. For example, cognitive revaluation of experimentally induced symptoms (essentially explaining that the symptoms are experienced by everyone getting the experimental induction and that they did not need to worry about them) successfully reduced the panic response, but had no effect on the respiratory irregularity (Abelson, Weg, Nesse, & Curtis, 2001). Stein, Millar, Larsen and Kryger (1995) documented an analogue respiratory irregularity in panic patients during sleep (when researchers expected anxiety not to be manifest). In sum, sighing and a highly instable V_T seem to be a more promising central feature of panic disorder than a lowered baseline $ETCO_2$. Indeed, the latter have been observed in other anxious populations as well and the reviewed evidence favors an interpretation in terms of an enhanced responsivity to the measurement context or anticipatory anxiety. However, this should be further investigated controlling properly for biological variables influencing $ETCO_2$.

Chapter 3
Aims

3.1 Psychological Triggers of Hyperventilation induced Hypocapnia

The major aim of this thesis was to study critical psychological conditions for the occurrence of hyperventilation induced hypocapnia. Both situational and dispositional factors will be studied.

3.1.1 Study 1: Hyperventilation beyond fight/flight

It was concluded from our review of $ETCO_2$ responses during emotions and stress that hyperventilation seems to occur most easily in response to an uncontrollable stressor from which physical escape is impossible. Although this corroborates a conceptualization of hyperventilation in terms of a fight/flight response, no study has ever investigated $ETCO_2$ responses within the appetitive motivational system. This was the major aim of a first study.

The relative importance of the two emotional dimensions of valence and arousal in triggering hyperventilation responses was studied. Since hyperventilation seems to result typically from a discrepancy between the metabolic "needs of the moment" and the mentally anticipated needs of future or past moments that are characterized by frustration, anxiety or fear, we thought that a mental imagery paradigm would be particularly relevant to study hyperventilation responses. In the imagery paradigm, participants are presented an emotional script and instructed to

imagine vividly that they were actually experiencing the situation depicted in the script.

3.1.2 Study 2: The role of autonomic response propositions during emotional imagery

Lang (1979) would predict that the inclusion of response information is associated with greater physiological responsivity because it facilitates the access to the emotional representation, resulting in a more vivid imagery. However, since breathing is controlled both voluntary and automatically, including response information may trigger demand effects rather easily. A second study aimed to investigate to which extent the observed $ETCO_2$ responses in the first study (3.1.1) were dependent on the inclusion of suggestions of autonomic response patterns in the emotional scripts. To this end, four emotional scripts from the first study were changed such that they did not contain any reference towards emotional autonomic responses. Effect sizes of $ETCO_2$ responses in both studies will be compared.

3.1.3 Study 3: Fear of suffocation and fear of restrictment

The first study (3.1.1) showed that $ETCO_2$ decreases were strongest during imagery of a script that depicted someone being stuck in an elevator. It was hypothesized that the suggestions of risk of suffocation and/or physical confinement in the script may constitute particularly strong triggers of hyperventilation responses. This was tested in a third imagery study, in which three fears scripts were used that differed as regards the suggested risk of suffocation and/or movement restriction. An additional aim of this study was to test whether hyperventilation responses would be more easily triggered in participants high in dispositional negative affectivity (NA) than in participants scoring low on NA.

3.1.4. Studies 4-5: resting $ETCO_2$ and negative affectivity

It was concluded from chapter two (see 2.2.3) that the findings of studies investigating the association between resting $ETCO_2$ and NA were highly inconsistent. We ran two studies in order to clarify the reported inconsistencies. In study 4, $ETCO_2$ was measured non-intrusively and its association with NA was studied. Study 5 aimed to test our interpretation given to the finding of Dhokalia et al. (1998). Indeed, these authors found a positive association between NA and $ETCO_2$, measured while participants were completing a questionnaire. In study 5, $ETCO_2$ of high and low NA participants was sampled once with a nasal cannula and once while breathing through a mouthpiece for 6 min each during rest and during completion of a personality questionnaires. In both studies, hormonal influences upon $ETCO_2$ (see 1.1.1) were properly controlled for.

3.1.5 Study 6: Anxiety and respiratory variability

Thayer and Lane's (2000) neurovisceral model of emotional (dys)regulation inspired us to study respiratory variability as a function of inter- and intraindividual differences in anxiety, rather than focusing only on mean levels of $ETCO_2$. Generally, this model predicts a reduced flexibility in psychophysiological responding during anxiety, which would be reflected in a decreased variability in several processes and parameters. Thayer and Lane (2000) illustrate this principle with the case of heart rate variability, which is clearly decreased under anxiety. Study 6 explored the within subject variability in breathing parameters during relaxation and during anxious imagery in participants scoring high and low for NA. To this end, data from study 1 and study 3 were used.

3.2 Psychological Consequences of Hyperventilation induced Hypocapnia

A second part of this thesis aimed to answer two specific questions relating to the secondary physiological changes and symptoms associated with hypocapnia.

3.2.1 Studies 7-8: Hyperventilation symptoms and negative affectivity

People high in NA report more bodily symptoms than people low in NA, without any indication of a poorer objective health (Watson & Pennebaker, 1989). Since studies 4 and 5 failed to observe habitual lower levels of resting $ETCO_2$ in high NA participants, chronic hyperventilation is not a likely cause underlying the NA – symptom-reporting relationship. However, since trait NA does not refer only to habitual individual differences in affect, but also to an enhanced reactivity to stressors, the excess of bodily symptoms in high NA people may be caused also by a higher prevalence of acute or phasic hyperventilation in response to real life stressors. This hypothesis can be tested directly using ambulatory measurements of $ETCO_2$ in real-life settings. We opted for an alternative, more indirect approach and aimed to investigate whether the association between NA and symptoms that are prototypical for hyperventilation induced hypocapnia is stronger than the association of NA with symptoms atypical for hyperventilation. Study 7 explored the associations of NA with a wide variety of individual symptoms and tried to identify symptom characteristics that are predictive for the association of a symptom with NA. Study 8 investigated to which extent the association of a symptom with NA could be predicted by the prototypicality of the symptom for hyperventilation induced hypocapnia.

3.2.2 Study 9: Hypocapnia and attentional performance

As explained in 1.3.2, hypocapnia is associated with subjective symptoms of cognitive impairment. Study 9 aimed to test whether this is mirrored in concomitant objective cognitive performance deficits. To this end, participants performed an attentional task following hypocapnic and normocapnic overbreathing. The latter served as a within control condition of the former.

Chapter 4

Hyperventilation beyond Fight/Flight: Respiratory Responses during Emotional Imagery

Van Diest, Winters, Devriese, Vercamst, Han, Van de Woestijne, & Van den Bergh (2001a). Psychophysiology, 38, 961-968.

4.1 Abstract

Hyperventilation (HV) is often considered part of a defense response, implying an unpleasant emotion (negative valence) combined with a strong action tendency (high arousal). In this study, we investigated the importance of arousal and valence as triggers for HV-responses. Forty women imagined eight different scripts varying along the arousal and valence dimension. The scripts depicted relaxation, fear, depressive, action and desire situations. After each trial, the imagery was rated for valence, arousal and vividness. $FETCO_2$, inspiratory and expiratory time, tidal volume and pulse rate were measured in a non-intrusive way. $FETCO_2$-drops and decreases in inspiratory and expiratory time occurred in all but the depressive and the relaxation scripts, suggesting that a defense conceptualization of hyperventilation is not always appropriate.

4.2 Introduction

Hyperventilation or breathing in excess of metabolic needs is associated with hypocapnia, a decreased CO_2-pressure (PCO_2) in the arterial blood (Gardner, 1996).

Alveolar PCO_2 is considered a valid approximation of arterial PCO_2 and can, in turn, be reliably estimated by measuring the end-tidal fractional CO_2-concentration ($FETCO_2$; Gardner, 1996; Pahn, et al., 1987). Both an increase in breathing frequency (number of breathing cycles per minute) and an increase in tidal volume or a combination of both may induce hyperventilation (Garssen, 1986). Ever since Cannon (1929), stress-induced hyperventilation has been viewed as the respiratory component of the fight/flight response. From this perspective, the decrease in the arterial PCO_2 can be considered a feedforward response compensating for the increased CO_2-production of the physical action implied by fighting or fleeing.

In a clinical perspective, the conceptualization of hyperventilation as a fight/flight response or, in more modern terms as a defense reaction (Turpin, 1986), has been linked to the experience of highly arousing negative emotions. Both laboratory and clinical studies showing significant PCO_2-drops in situations of stress, fear and/or pain have corroborated this (e.g., Allen et al., 1986; Alpers, Wilhelm & Roth, 2000; Beckmann, 1915; Dudley, 1969; Dudley et al., 1965; Garssen, 1980; Ley & Yelich, 1998; Suess et al., 1980).

However, in a broader psychophysiological perspective, several studies and reviews suggest that respiratory responding in general reflects the action tendency underlying an emotion. Consequently, within the two-dimensional affective space of emotions (Lang, Bradley & Cuthbert, 1990; Mehrabian & Russell, 1974) respiration covaries particularly with arousal. For example, Nyklíček, Thayer and Van Doornen (1997) found that emotions can be discriminated most successfully by the respiratory component, which was related to the arousal dimension. In their review, Boiten et al. (1994) propose three dimensions underlying respiratory responding. It is striking that none of those proposed dimensions refer to (un)pleasantness. The first dimension they distinguished is excitement, ranging from "passive withdrawal from the environment" to "active engagement". This seems to reflect arousal, namely a diffuse readiness for action and an increased perceptual sensitivity. Within the realm of respiratory hyperfunction, they define a second dimension, running from controlled activation and tenseness on the one

extreme, to excitement, unstrained activation and overt panic on the other. This dimension appears more related to activation, as conceptualized by Pribram (1981). The third dimension described by Boiten et al. (1994) reflects the metabolic appropriateness of the breathing, extending from normoventilation to hyperventilation.

Unfortunately, most studies investigating respiratory changes during emotions other than anxiety did not administer PCO_2-measures. An exception to this is the study by Dudley (1969). This author found PCO_2-drops under hypnosis during imagined anxiety and anger but not during depression, suggesting that arousal may explain more variance in PCO_2-drops than valence. In another paper, Dudley and Pitts-Poarch (1980, p.133) stated that "The correlation of respiratory hyperfunction and associated affect with action-oriented behavior indicates the preparation to escape, alleviate, or remove a stressful stimulus or engage in pleasurable pursuits". In the same way as Boiten et al. (1994), this author sees emotionally induced respiratory changes as exclusively determined by the action tendency underlying the emotion. In that case, hyperventilation responses should also show up during pleasant emotions. Some older studies suggest indeed that hyperventilation is a common response during coitus, although these studies do not report PCO_2 measurements either (Bartlett, 1956; Masters & Johnson, 1966).

To our knowledge, the present study is the first to investigate variations in PCO_2 within the two-dimensional affective space. To this end, healthy women imagined themselves as active participants in eight situations varying along the dimensions of arousal (high, low) and valence (negative, positive). Script-driven imagery is considered a valid tool to elicit emotions both in psychophysiological studies (Lang, 1979; Lang, Levin, Miller, & Kozak 1983) and in PET studies on the neuroanatomy of emotions (Davidson & Irwin, 1999; Dougherty et al, 1999; Lane, Reiman, Ahern, Schwartz, & Davidson, 1997). Following Lang's bio-informational theory (Lang, 1979) emotional imagery elicits physiological activity in the response channels affected by the actual emotional context. Therefore, imagery is particularly suited for the study of physiological concomitants of emotions. Also in respiratory

physiology, mental imagery has extensively been used in studies on the role of feedforward control mechanisms of higher nerve centers in exercise hyperpnea (Gallego, Denot-Ledunois, Vardon & Perruchet, 1996).

In line with a general psychophysiological perspective, we hypothesized that PCO_2-drops would mainly reflect the response requirements of a situation, that is, would occur during imagery of both pleasant and unpleasant high arousal scripts (hypothesis 1). However, in line with a clinical perspective, respiratory behavior may additionally be affected by specific "defense" conditions (hypothesis 2). Therefore, we will test whether fear scripts trigger stronger responses than another equally high arousing, pleasant script.

4.3 Method

4.3.1 Participants

Forty healthy women[2], all undergraduate psychology students aged 17-19 years, participated in return for course credit. Due to a technical failure, pulse rate data were unreliable for two participants.

4.3.2 Materials

Scripts

Following Lang (1979), the quality of emotional imagery is enhanced when, in addition to stimulus and meaning information, also response information is included

[2] Because men and women differ as regards volume parameters (Dhokalia et al., 1998; Han, Stegen, De Valck, Clément, & Van de Woestijne, 1996; Han et al., 1997b), adding men would have added more error variance to the design without balancing the numbers. The latter was not possible for practical reasons. In addition, we had no a priori reasons to expect differences among men and women as regards the main research questions.

in the imagery script (Lang et al., 1980; 1983). However, because of both automatic and voluntary influences upon breathing (Gallego et al., 1996), no phrasings directly referring to respiratory behavior were included in order to avoid specific demand effects.

Eight different imagery scripts were presented to each participant: three relaxation (positive valence, low arousal), two fear (negative valence, high arousal), one depressive (negative valence, low arousal), one action (neutral valence, high arousal) and one "desire" script (positive valence, high arousal). It took between 50-60 s to read the script to the participant. Table 4A contains some phrases from each script, with emphasis on illustrating references to respiration included in the scripts. The scripts were selected based on the results of a pilot study in which another group of participants had rated them on arousal and valence.

Apparatus and physiological recordings

The participants sat in a comfortable chair in a room adjacent to the equipment room. A video camera in the participant's room allowed the experimenter to monitor the participant's movements. Imagery scripts were presented via a Sony MDR-CD270 headphone plugged into the headphone jacket of a PC. A Novametrix Tidal Wave Sp handheld capnograph/oximeter measured pulse rate (range: 30-250 bpm; accuracy: 1% of full scale). Its memory retained mean values over 8 s, which were extracted by the Novacom software via a RS232 serial port communication. The oximeter's finger sensor was attached to the participant's left forefinger.

$FETCO_2$ was measured using a nasal CO_2-sampling cannula connected to a non-dispersive infrared CO_2-monitor with a resolution of 1 mmHg and an accuracy of +/- 2 mmHg (Capnograph, Poet RC, Criticare, USA). Ventilation was measured using a respiratory inductive plethysmograph (Respitrace Corporation Model 150, New York). The coils of the Respitrace were stuck to the skin, one around the rib cage under the axilla and the other on the abdomen above the pelvis. The calibration procedure consisted of a five minute period of breathing during which respiration

was measured simultaneously by means of a pneumotachograph (Fleisch No 2, Switzerland) and the Respitrace.

Table 4A. Some typical Phrasings describing each Script

D	You should be getting up, but you don't want to start the day. … What is the use of it all? … tired and heavy. … empty inside and listless.
F1	You're feeling warm, and your chest is starting to feel a bit tight. … There is not enough air in the elevator. … All you can think of is "I want to get out".
F2	… you see the huge pile of textbooks on the bookshelf. You haven't as yet made a serious go at this stuff, and exams will start soon. … You break into a sweat and your heart is pounding and your chest is feeling tight …
Des	…at the airport to pick up your boyfriend. He went abroad to study a year ago, … You feel your face blushing. … Your chest and throat feel tight.
R1	You are sitting in the back seat of a car. …It is a calm, quiet and misty day. …little traffic … Lampposts pass by at a regular pace.
R2	…an apartment overlooking the sea. … Sunbeams come in through the window, giving your body a warm comfortable glow. … The sea is calm.
R3	A Sunday afternoon at home… reading a book. The living room is cozy. … you look out of the window. Outside, it is a sunny autumn day.
A	… running competition. …your legs are moving faster and faster, your arms swinging in the same rhythm…. you break into a sweat; your system craves oxygen.

Note: D = depressive script; F1 = fear 1 (elevator) script; F2 = fear 2 (exam) script; Des = desire script; R3 = third relaxation script; R1 = first relaxation script; R2 = second relaxation script; A = action script

Both the Respitrace and the pneumotachograph signals were sampled at 20 Hz. A multiple linear regression was performed over the calibration period, yielding the regression coefficients to be used for the reconstruction of the volume out of the Respitrace signals (Strömberg et al., 1993). The multiple linear regression approach produces accurate volume data when R^2 > 85% (Han, 1995; Han et al., 1997a). We excluded the data of only one participant because of not meeting this criterion. A Labmaster Card and a PC processed the Respitrace signals and the $FETCO_2$-signals with a sampling rate of 20 Hz. The $FETCO_2$-signal and the reconstructed volume were plotted as a function of time and visually inspected for technical abnormalities and movement artifacts. Specific software extracted breathing pauses and irregularities and determined the following parameters for each breath: inspiratory and expiratory time in s, inspiratory and expiratory volume in ml and $FETCO_2$ in %. Only inspiratory volume was used as a measure of tidal volume. Breathing frequency was calculated off-line out of inspiratory and expiratory time.

4.3.3 Procedure

Students were invited to participate in an experiment announced to investigate physiological changes during imagery. Upon arrival, the experimenter told that there were eight different imagery trials, each consisting of the same consecutive phases. These were explained as Baseline : When the light was dimmed, participants were to close their eyes and one minute of relaxing music was presented through the headphone (a fragment of Sarabande, Goldberg Suite, E. Grieg). Participants were instructed simply to listen to the music and relax. Script : during the following minute the script was presented and participants were asked to start the imagery as soon as they heard the text. Silence : 90 s of silence during which they had to keep on imagining the script as vividly as possible. After 60 s, a low level short auditory signal, announced during the instructions, was given as a reminder to continue the imagery as vividly as possible. Recovery : Thereafter

followed a recovery period of 60 s with another piece of relaxing music (Gymnopédie no. 1, E. Satie). As soon as this music started, participants had to stop the imagery, to keep their eyes closed and to listen to the music. The light being turned on announced the end of an imagery trial.

Participants were told that physiological recordings would be made during imagery and the purpose of the equipment was described. It was told that the finger sensor measured pulse rate, that the nose cannula sampled the expired air to send it to an analyzer and that the two coils would be attached to their rib cage and abdomen to detect changes in posture and muscle tonus of the trunk. The latter explanation was given to avoid drawing the participant's attention to her respiration. Subsequently, the participant was invited to take a quick look in the equipment room. Back in the participants' room, they filled out an informed consent form. Next, the two coils of the Respitrace, the nose cannula and the finger sensor were attached. The participant was asked to sit down leaning on the back of the seat, to keep both feet on the floor, and to place the hands on the legs. The experimenter checked whether this position was comfortable, and it was explained that they should keep the same position during the experiment. Next, the calibration procedure was started. To this end, participants wore a noseclip and breathed through a mouthpiece that was connected to a pneumotachograph.

After the calibration phase, the importance of imagining the scene as vividly as possible was emphasized. It was explained that this implied not only creating a detailed visual picture of the scene, but especially trying to feel and experience the depicted scene as if she was a real, active participant. Finally, the consecutive phases of the imagery trial were briefly repeated. All participants received the same relaxation script during the first imagery trial. Next, the experimenter went to the participant room and asked whether the participant had succeeded in imaging the scene as a real participant. Lang et al. (1980*)* demonstrated that emotional imagery may be enhanced by prior training in response orientation. To this end, post-imagery verbal reports were elicited and the experimenter reinforced all comments referring to autonomic response activity.

The participant rated her experience during imagery on the basic affective dimensions of pleasure-displeasure and arousal-calm (Lang et al., 1990; Mehrabian & Russel, 1974), using a paper-and-pencil version of the 9-point Manikin rating system of Bradley and Lang (1994). Also, the vividness of the imagery was rated on a 9 point Likert-scale ranging from very good (1) to very poor (9).

The action script was presented as the second script. When the participants had completed the ratings of this second imagery trial, the experimenter returned to the participant's room a last time and reinforced again response oriented descriptions of the imagery experience. The experimenter explained that the following six scripts would be presented according to the same scheme. The action script was always followed by the second relaxation script. The five remaining scripts were presented in a semi-randomized way, leading to five possible presentation orders. The participants were randomly allocated (eight participants per presentation order).

Following the final imagery trial, the participants filled out a Dutch translation of the Questionnaire Upon Mental Imagery (QMI) (Sheehan, 1967). In addition, the experimenter asked whether they had voluntary controlled their breathing during one or more imagery trials.

4.3.4 Data reduction and analysis

In order to avoid potential confounding by presentation order or amount of response training, data regarding the first three imagery trials (first relaxation script, action script and second relaxation script) were left out of the analyses.

The subjective ratings on valence, arousal and imagery vividness were analyzed using one-way ANOVA's (five levels of Script: depressive, fear 1, fear 2, desire, relaxation 3) and Tukey's HSD tests for post hoc comparisons. Greenhouse-Geisser corrections were applied to these and all subsequent ANOVA's including the Script factor (five levels).

In order to check for baseline differences in breathing behavior between trials, means of $FETCO_2$, inspiratory and expiratory time, breathing frequency, tidal volume and pulse rate of the last 30 s of baseline were analyzed in an ANOVA with Script (five levels) as a within subject variable. For the same parameters, change scores subtracting the last 30 s of baseline from the mean of the last 30 s of script presentation and the 90 s of silence were calculated and analyzed in ANOVA's with Script (five levels) as a within subject variable. Tukey HSD tests were used for post hoc comparisons.

4.4 Results

4.4.1 Subjective ratings

Table 4B. Means on the Subjective Ratings for each Imagery Trial (N=40)

		D	F1	F2	Des	R3	R1	R2	A
Valence	M	7.18_a	7.88_a	7.75_a	2.13_b	2.53_b	2.95	1.65	4.53
	SD	1.63	1.40	1.24	1.38	1.50	1.72	.89	1.49
Arousal	M	3.50_a	7.30_b	6.30_c	7.55_b	1.75_d	2.35	1.92	6.07
	SD	1.65	1.62	1.59	1.36	1.24	1.63	1.58	1.74
Vividness	M	4.08_{ab}	4.20_{ab}	4.45_a	3.58_{ab}	3.18_{bc}	3.28	2.83	4.43
	SD	2.22	1.84	2.01	1.85	1.74	1.57	1.55	1.91

Note: D = depressive script; F1 = fear 1 (elevator) script; F2 = fear 2 (exam) script; Des = desire script; R3 = third relaxation script; R1 = first relaxation script; R2 = second relaxation script; A = action script
R1, R2 and Action were not included in the analysis.
Lower values indicate less aroused, more positive or more vivid imagery, all on a 1–9 scale.
Means having the same subscript are not significantly different at $p < .05$ in the Tukey honestly significant difference comparison.

As shown in table 4B, the depressive and both fear scripts were rated equally on pleasantness and more negatively than the relaxation and the desire scripts (F (4, 156) = 167, $p < .01$, $\varepsilon = .84$). The latter were equally positive.

The relaxation script was less arousing than the depressive script, which in turn was less arousing than the desire and both fear scripts. The desire and the fear 1 (elevator) script were more arousing than the fear 2 (exam) script (F (4, 156) = 156, $p < .01$, $\varepsilon = .75$, see table 4B).

The participants rated their imagery of the fear 2 (exam) script as less vivid than the relaxation script (F (4, 156) = 3.43, $p < .05$, $\varepsilon = .89$, see table 4B).

4.4.2 Physiological data

Baseline

There were no baseline differences among the five imagery trials on any parameter (F (4, 156) 's were for $FETCO_2$: .60, $\varepsilon = .86$; for inspiratory time: .99, $\varepsilon = .52$; for expiratory time: 1, $\varepsilon = .70$; for breathing frequency: .58, $\varepsilon = .86$; for tidal volume: .26, $\varepsilon = .68$; for pulse rate: F (4, 148) = 1.82, $\varepsilon = .87$); see table 4C for means and SD's).

Imagery

Table 4D displays the mean change scores and SD's during imagery. Decreases in $FETCO_2$ occurred in all but the relaxation and depressive scripts (F (4, 156) = 40.19, $p < .01$, $\varepsilon = .35$, see figure 2). This effect was stronger for the fear 1 (elevator) script than for the desire script (see table 4D).

Scripts were associated with differences in breathing frequency (F (4, 156) = 27.16, $p < .01$, $\varepsilon = .54$): increases in breathing frequency were only observed in the high arousal scripts, and these effects were stronger for the fear 1 (elevator) than for the desire script (see table 4D). Expiratory time decreased in the desire and both fear scripts but not in the relaxation and the depressive scripts (F (4, 156) = 18.07, $p < .01$,

ε = .93, see table 4D). Inspiratory time showed a similar, but weaker response pattern (F (4, 156) = 11.09, p < .01, ε = .79, see table 4D). In contrast with expiratory time, the change in inspiratory time during imagery of the desire script did not differ significantly from any other change score in inspiratory time.

Scripts differed also significantly as regards tidal volume (F (4, 156) = 3.20, p < .05, ε = .77). Imagining the fear 2 script (exam) was associated with a greater decrease in tidal volume than imagining the depressive script (see table 4D).

Pulse rate increased during imagery of the high arousal scripts and decreased during imagery of the low arousal scripts (F (4, 148) = 5.30, p < .01, ε = .81). Only the increase in pulse rate during imagining the fear 2 (exam) script was significantly different from the changes during both low arousal scripts (see table 4D).

Table 4C. Mean $FETCO_2$ (in %), Ti and Te (in s), f (per minute) Vt (in ml) and Pulse rate (in bpm) during the last 30 s of Baseline.

		D	F1	F2	Des	R3	R1	R2	A
$FETCO_2$	M	4.97	4.96	4.98	4.98	4.96	4.97	4.97	5.01
	SD	.36	.34	.36	.37	.36	.33	.36	.35
Ti	M	1.48	1.45	1.44	1.46	1.52	1.57	1.52	1.50
	SD	.27	.25	.33	.28	.50	.49	.31	.34
Te	M	2.16	2.07	2.17	2.09	2.10	2.23	2.17	2.19
	SD	.53	.38	.46	.45	.51	.59	.44	.59
f	M	17.01	17.44	17.14	17.36	17.31	16.53	16.81	16.87
	SD	2.70	2.36	2.70	2.68	2.91	3.08	2.79	2.75
Vt	M	316	316	325	319	314	350	320	327
	SD	68	75	116	76	81	84	73	68
PR	M	76.08	76.39	75.52	76.47	75.26	77.64	76.13	76.57
	SD	9.10	9.57	9.23	9.17	10.05	10.40	10.02	9.92

Note: D = depressive script; F1 = fear 1 (elevator) script; F2 = fear 2 (exam) script; Des = desire script; R3 = third relaxation script; R1 = first relaxation script; R2 = second relaxation script; A = action script; Ti = inspiratory time; Te = expiratory time; f = breathing frequency; Vt = tidal volume; PR = pulse rate
R1, R2 and Action were not included in the analyses.

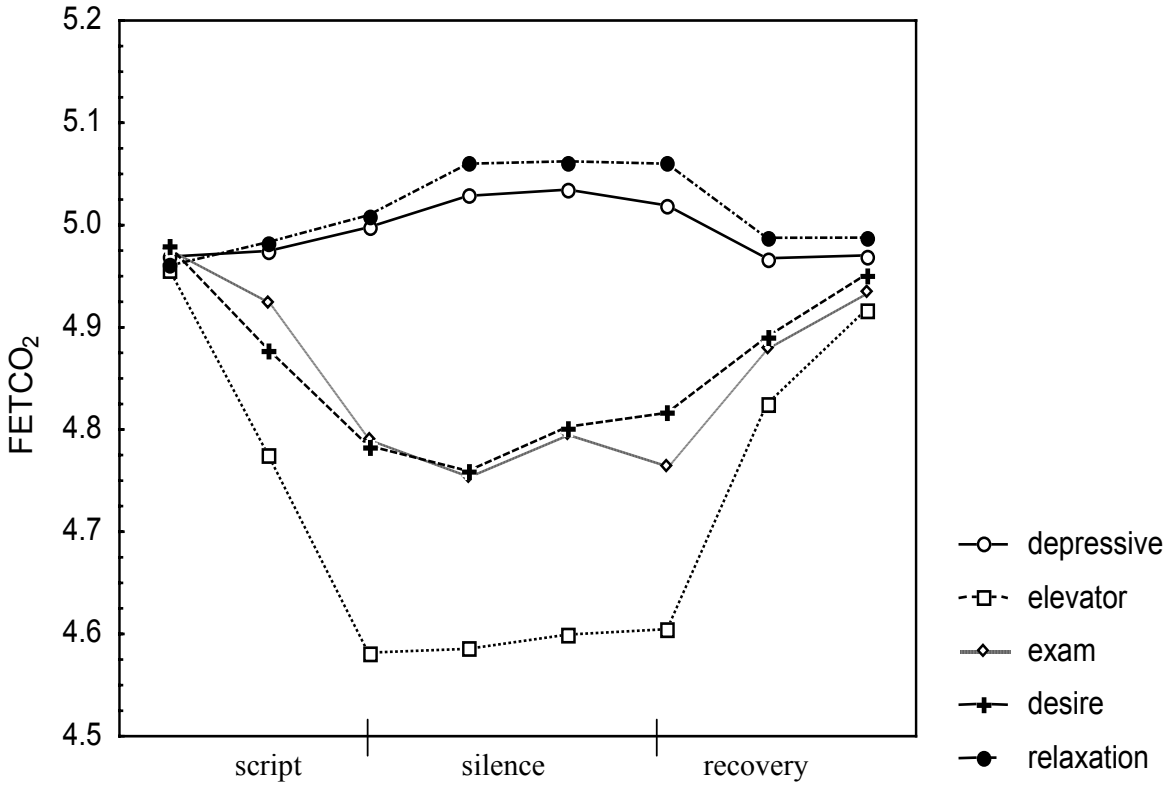


Figure 2. Mean $FETCO_2$ (per 30 s periods) for each imagery trial (last 30 s of baseline, 60 s script, 90 s silence, 60 s recovery)

QMI

A significant correlation across participants was found between the $FETCO_2$-drop in the high arousal scripts (averaged over the fear 1, fear 2 and desire scripts) and the QMI score ($\underline{r} = .33$, $\underline{p} > .05$, $\underline{N} = 40$): better imagers showed stronger $FETCO_2$-responses.

Voluntary control of breathing

No participants responded positively on the post-experimental question whether they had voluntary controlled their breathing during imagery.

Table 4D. Mean Change Scores in $FETCO_2$ (in %), Ti and Te (in s), f (per minute) Vt (in ml) and Pulse rate (in bpm) from Baseline to Imagery

		D	F1	F2	Des	R3	R1	R2	A
ΔFETCO$_2$	M	$.05_c$	$-.36_a$	$-.28_{ab}$	$-.19_b$	$.09_c$	.11	.08	-.26
	SD	.11	.40	.32	.25	.10	.12	.09	.28
ΔTi	M	$.06_b$	$-.23_a$	$-.16_a$	$-.12_{ab}$	$-.01_b$	.04	.13	-.23
	SD	.23	.36	.30	.31	.43	.36	.26	.40
ΔTe	M	$.03_a$	$-.43_b$	$-.45_b$	$-.27_b$	$.07_a$	.12	.12	-.50
	SD	.33	.55	.49	.57	.38	.30	.28	.67
Δf	M	$-.38_a$	5.69_c	3.87_{bc}	2.90_b	$-.59_a$	-.92	-1.08	4.67
	SD	2.02	6.93	4.24	4.55	2.04	1.67	1.83	5.55
ΔVt	M	$.22_a$	-32.98_{ab}	-42.78_b	-19.60_{ab}	-12.18_{ab}	-9.21	7.43	-31.44
	SD	50.95	78.66	92.59	94.48	59.58	67.24	54.83	85.07
ΔPR	M	$-.50_{ab}$	1.19_{bc}	1.42_c	$.65_{abc}$	$-.92_a$	-1.16	-1.08	2.47
	SD	3.41	3.98	3.10	2.97	3.06	3.55	2.59	3.40

Note: D = depressive script; F1 = fear 1 (elevator) script; F2 = fear 2 (exam) script; Des = desire script; R3 = third relaxation script; R1 = first relaxation script; R2 = second relaxation script; A = action script; Ti = inspiratory time; Te = expiratory time; f = breathing frequency; Vt = tidal volume; PR = pulse rate
R1, R2 and Action were not included in the analyses.
Means having the same subscript are not significantly different at $p < .05$ in the Tukey Honestly Significant Difference comparison.

4.5 Discussion

Our results clearly show that a defense reaction is not a necessary condition for hyperventilation responses: they occurred both in states of negative and positive affect. Arousal appeared to be the more important dimension in cardio-respiratory responding, which corroborates the findings of other studies using the perspective of the two-dimensional affective space (Nyklíček et al., 1997; Vanoyen-Witvliet & Vrana, 1995).

We found also evidence supporting our second hypothesis that specific "defense" conditions, defined as a combination of high arousal and negative valence, would be particularly powerful to cause hypocapnic overbreathing. In line with this hypothesis, we found a stronger decrease in $FETCO_2$ in the fear 1 (elevator) script than in the desire script (see table 4D), despite equal ratings on arousal (see table 4B). However, this may be related also to other variables in the scripts not captured by the valence and arousal dimensions. For example, situations with a particular meaning such as a risk of suffocation and/or a restriction of movement triggering a powerful action tendency to escape may be more critical for hyperventilation responses. With respect to the former, it has been shown that hypoxic stimulation in decerebrated cats triggers a full blown defense reaction, including hyperventilation (Hilton, 1982). Both risk of suffocation and restriction of movement have been emphasized in models of panic with agoraphobia (Rachman, 1997; Barlow, 1988; Bouton et al., 2001). Further research should point out to which extent both characteristics may inflate hyperventilation responses.

In all arousing scripts, significant $FETCO_2$-drops were associated with a decrease in inspiratory and expiratory time. In a study on the control of the respiratory cycle in conscious humans, Rafferty and Gardner (1996) suggested that the respiratory timing parameters are weakly controlled by the chemical drive, which allows for the non-metabolic functions of breathing (e.g., speech), whereas tidal volume would be controlled dominantly by the chemical drive. Our finding that timing parameters were more strongly affected than tidal volume by psychological, non-metabolic influences (like anticipation, emotions, mental load) is consistent with results of many other studies (Anderson et al., 1993; Denot-Ledunois et al., 1998; Mador & Tobin, 1991; Masaoka & Homma, 1999; Rigg et al., 1977; Sebej & Biro, 1978; Turner, Carroll & Courtney, 1983; Wientjes et al., 1993). In other studies of our group, it was found that breathing frequency, but not tidal volume could be conditioned to mental images (Stegen et al., 1999) or to an unpleasant odor (Van den Bergh et al., 1995).

Increases in pulse rate during imagery of the high arousal scripts are rather small when compared to the increases in heart rate reported in other imagery studies (e.g., Acosta & Vila, 1990; Carroll, Marzillier, & Merian, 1982; Lang et al., 1980; Lang et al., 1983). A first reason for this may be a longer imagery period in our study (120 s) as compared to those other studies (20-50 s). We have opted for such long imagery periods in order to increase the reliability of our respiratory measures. Secondly, the response training in our study was limited to the first two imagery trials of the experimental session, whereas the other studies used separate training sessions lasting up to one hour.

An important constraint potentially limiting the conclusions of our data is that they are collected during imagined rather than real emotional scenes. One could argue that the content of the scripts may have induced demands affecting voluntary respiratory behavior. However, no single participant reported having voluntary controlled his/her breathing at some point in time. Also, in another imagery study of our group (Van Diest et al., 2001b), we left out all suggestions towards autonomic and respiratory responses in the fear 1, fear 2, depressive and the relaxation scripts and we essentially replicated the present results: significant hyperventilation responses occurred in both unpleasant and pleasant, high arousal scripts. However, the $FETCO_2$-drops were much smaller in the study without autonomic response propositions. When comparing the current study with the study without autonomic response propositions, we found a medium effect size (.51) of response information on arousal-related changes in $FETCO_2$ during imagery of high arousal scripts. Also, the omission of autonomic response information was associated with less imagery vividness, which is in line with Lang's (1979) bio-informational theory of emotional imagery.

The argument regarding the relevance of imagined scenes for real life can also be turned the other way round. Indeed, hyperventilation responses in humans typically result from a discrepancy between feedforward influences upon breathing due to mental activity and the actual metabolic state. Such discrepancy may more likely emerge when people anticipate or imagine stressful events, because CO_2

production may be expected to be lower compared to being in the actual situation. Considering hyperventilation an inhibition failure (Fokkema, 1999*)*, the probability of such a failure may be expected to increase with the (evolutionary) increasing capacity of mental imagery. In this perspective, breathing responses triggered by imagery may actually be particularly relevant for hyperventilation as a clinical problem.

The levels of $FETCO_2$ reached during high arousing imagery mostly remained within the eucapnic range, in which both feedback (chemosensitivity) and feedforward mechanisms (e.g., anxiety/arousal related influences; Shea, 1996) remain operational (Cunningham et al., 1986). However, we believe that imagining more intensely arousing scenes during a longer period may cause hyperventilation and hypocapnia up to the level where CO_2 sensitivity decreases and/or the chemical drive to breathe disappears (Cunningham et al., 1986; Gardner, 1996). In normal cases, this typically causes apneas quickly restoring arterial PCO_2 (Van Diest et al., 2000). In clinical populations, though, the symptoms associated with low levels of PCO_2 often inflate anxiety, which may further stimulate breathing and overrule normal apneas. A spiraling, panic-like process may easily ensue.

The hyperventilation responses observed in this study should be viewed as responses reflecting the anticipatory capacity of the respiratory system that are not necessarily pathological. Indeed, our results reinforce a distinction between on the one hand hyperventilation as a common concomitant of arousal, and on the other hand the pathologies it may become involved with as a result of an interaction with other variables. For example, Salkovskis and Clark (1990) showed that bodily sensations produced by hyperventilation could be interpreted both in a positive and negative way, leading to corresponding changes in affect. Also classical conditioning has been identified as a mechanism by which hyperventilation may become involved in psychosomatic pathology (Stegen et al., 1999; Van den Bergh et al., 1997), in multiple chemical sensitivity (Van den Bergh, Devriese, Winters, Eelen, Veulemans, & Nemery, 2001) and in panic disorder (Bouton et al., 2001).

In summary, we found hyperventilation responses during imagery of pleasant and unpleasant, high arousing situations, indicating that respiratory responding during imagery varies primarly along a broad arousal continuum. In addition, aspects not captured by the two-dimensional affective space, such as a risk of suffocation or blocked action tendencies in escape situations, may increase the tendency to hyperventilate.

Chapter 5

Critical conditions for Hyperventilation Responses: The Role of Autonomic Response Propositions during Emotional Imagery

Van Diest, Proot, Van de Woestijne, Han, Devriese, Winters, & Van den Bergh (2001b). Behavior Modification, 25(4), 621-639.

5.1 Abstract

Hyperventilation is often conceived of as part of a fight/flight response, that is, triggered by situations with high arousal and negative valence. However, in a previous study using emotional imagery, we found hyperventilation responses during imagery of high arousal scenes regardless of their valence. Those imagery scripts contained suggestions of autonomic activity, which may have partly induced or enhanced the hyperventilatory responsivity. The present study (N=40) used four emotional scripts, depicting a relaxing, fearful, depressive and a pleasant situation, without suggestions of autonomic or respiratory responses. After each imagery trial, participants rated their imagery for valence, arousal and vividness. $FETCO_2$, inspiratory and expiratory time, tidal volume and pulse rate were measured in a non-intrusive way. Results showed significant $FETCO_2$-drops in the fearful and the pleasant scripts. However, this effect was much smaller compared to imagery scripts with autonomic response propositions. Participants imagining scripts without autonomic response information found it harder to imagine the scripts vividly and reported lower levels of subjective arousal. The findings are discussed as to their clinical relevance.

5.2 Introduction

The physiology of hyperventilation is relatively well understood and documented (e.g., Gardner, 1996, for an extensive review). Because hyperventilation is mostly induced by stress and is often an additional source of worry and anxiety about associated bodily symptoms, several authors have studied how hyperventilation interacts with psychological variables in a variety of pathological conditions, such as panic (with and without agoraphobia), somatization, chronic fatigue syndrome, multiple chemical sensitivity and psychosomatic complaints in the general population (Bazelmans et al., 1997; Ley, 1999; Leznoff, 1997; Papp et al., 1993; Salkovskis & Clark, 1990; Sharpe & Bass, 1992; Stegen et al., 1999; Van den Bergh et al., 1997; Wientjes & Grossman, 1994). However, very little research has tried to identify the critical triggers for hyperventilation as a stress response (Van Diest et al., 1999).

In a clinical perspective, hyperventilation as a stress response has been linked to conditions triggering fight/flight tendencies. Within a two-dimensional affective space formed by valence and arousal (Lang et al., 1990; Mehrabian & Russell, 1974), this corresponds to the experience of highly arousing, negative emotions. However, a broader psychophysiological perspective (Boiten et al., 1994; Nyklíček et al., 1997) may suggest that respiratory responding in general reflects the action tendency underlying emotions. Consequently, hyperventilation should occur during both positive and negative, highly arousing emotions.

In a previous study (Van Diest et al., 2001a), we investigated the occurrence of hyperventilation responses[3] within the two-dimensional affective space using an emotional imagery paradigm. This paradigm originates from Lang's bio-informational theory (Lang, 1979; Lang et al., 1980), in which emotional imagery is considered a process accessing an emotional representation in memory. The latter

[3] Hyperventilation was operationalized as a decrease in fractional end-tidal CO_2 ($FETCO_2$) from baseline to imagery.

can be thought of as an associative network containing three categories of information: stimulus, meaning and response information. Response information is believed to be coded in memory at a conceptual level and as a motor program. Consequently, when the emotional representation is accessed, its associated physiological responses are activated, which may produce 'efferent leakage', or low level physiological activity that is similar to the activity in real situations. In Lang's perspective, physiological responding may provide an on line measurement of the imaginal processing of an emotional representation. Moreover, the theory predicts easier access to the representation and therefore more vivid imagery when cues referring to responses are included in the image prompt. Indeed, imaginal scripts containing suggestions of autonomic responses have been found to result in a more vivid imagery and greater physiological responding (Acosta & Villa, 1990; Carroll, Marzillier, & Merian, 1982; Lang et al., 1980).

The results of our previous study followed the prediction made from the more general psychophysiological perspective on hyperventilation: hyperventilation occurred during imagery of all high arousal scenes, regardless of their valence. Based on these findings we have suggested that hyperventilation may be considered a feed-forward response compensating for the anticipated increase CO_2-production which is implied - not only in fighting or fleeing - but in action tendencies underlying both pleasant and unpleasant emotions. However, since the imagery scripts contained suggestions of autonomic and bodily responses consistent with the imagined scene, one could argue that the observed hyperventilation responses in our study primarily reflect demand effects, even though explicit suggestions involving respiratory activity had been avoided. Breathing being controlled both automatically and voluntary, this critique particularly applies to respiratory responding.

Cuthbert, Vrana & Bradley (1991) argue that physiological responding during imagery is not simply due to the instruction to imagine, since the response pattern is found to be highly dependent upon the specific emotional context and on existing memory representations, which are a function of experience and/or personal relevance. However, in our previous study, hyperventilation responses were not

confined to specific emotional contexts such as being stuck in an elevator. Instead, hyperventilation occurred in all contexts characterized by high arousal, such as the fear, the physical exercise and the pleasant-excited scripts. Furthermore, apart from responses in $FETCO_2$, also other respiratory responses showed much similarity during highly arousing imagery, independent from valence. The decreases in $FETCO_2$ in the high arousal scripts were all due to a decrease in inspiratory and expiratory time, with very little changes in tidal volume. This is in contrast with findings of Lang et al. (1980) who observed a differentiation in respiratory responding between imagining fear (increase in breathing frequency) and physical exercise (increase in tidal volume).

The present study aimed to replicate our previous finding that hyperventilatory responses would occur in relation to highly arousing imagery regardless of valence. Four scripts (depressive, fearful, pleasant, and relaxed) without any suggestion towards autonomic or respiratory responding were used. In addition, also the vividness of imagery was measured to sort out whether potential differences compared to scripts with response propositions could be explained by differences in imagery vividness or demand effects.

5.3 Method

The methods used were similar to those reported in Van Diest et al. (2001a). Therefore, only briefer description will be presented here.

5.3.1 Participants

Similar to the previous study, forty undergraduate, female psychology students (aged 17 – 20 years) participated in return for course credit.

5.3.2 Materials

Scripts

Four scripts were presented to each participant, one for each quadrant of the two-dimensional space of emotions. The scripts depicted a fearful (negative valence, high arousal), a pleasant (positive valence, high arousal), a depressive (negative valence, low arousal) and a relaxed (positive valence, low arousal) scene (see appendix I). This selection was based on the results of a prestudy in which 38 women had rated 10 different scripts for valence and arousal using a paper-and-pencil version of the 9-point Manikin rating system of Bradley & Lang (1994). Using pairwise comparisons among the 10 scripts, four scripts differing on only one of both emotional dimensions were selected for the experiment. Each scripts could be situated in one quadrant of the emotional space. The scripts depicted similar situations as the scripts used in the previous imagery study, but all the response propositions had been left out.

Apparatus and physiological recordings.

The participants sat in a comfortable chair in a room adjacent to the equipment room. Imagery scripts were presented through headphones plugged into the headphone jacket of a PC.

Fractional end-tidal CO_2-concentration ($FETCO_2$) was measured using a nasal sampling cannula connected to a capnograph (Poet RC, Criticare, USA). Ventilation was measured non intrusively with respiratory inductive plethysmography (Respitrace Corporation Model 150, New York); the coils were stuck to the skin, one around the rib cage under the axilla and the other on the abdomen above the pelvis. The calibration procedure consisted of a 5-minute period of breathing during which respiration was measured simultaneously by means of a pneumotachograph (Fleisch No 2, Switzerland) and the Respitrace. A multiple linear regression yielded the regression coefficients to be used for the reconstruction of the volume. This

calibration procedure was considered reliable and data were retained only when R^2 > 85%.

After reconstruction of the volume, the volume and $FETCO_2$-signals were plotted as a function of time and visually inspected for technical abnormalities and movement artifacts. Specific software extracted breathing pauses and irregularities and determined the following parameters for each breath: inspiratory (Ti) and expiratory time (Te) in s, inspiratory (Vi) and expiratory volume (Ve) in ml and $FETCO_2$ in %. Only inspiratory volume was used as a measure of tidal volume, V_T.

5.3.3 Procedure

Students were invited to participate in an experiment announced to investigate physiological changes during imagery. The experimenter told that there were 4 imagery trials, each consisting of the same consecutive phases. These were explained as Baseline (60 s): Participants were to close their eyes and to listen to relaxing music. Script (60 s): Participants were asked to start the imagery as soon as they heard the text. Silence (90 s): During this period, participants they had to keep on imagining the script as vividly as possible. After 60 s, a low level short auditory signal, announced during the instructions, was given as a reminder to continue the imagery as vividly as possible. Recovery (60 s): Another piece of relaxing music was presented; participants were instructed to stop the imagery, to keep their eyes closed and to listen to the music. The light being turned on announced the end of an imagery trial.

Participants were told that the nose cannula sampled the expired air to send it to an analyzer and that the two coils would be attached to their rib cage and abdomen to detect changes in posture and muscle tonus of the trunk. The latter explanation was given to avoid drawing the participant's attention to her respiration. Subsequently, the participant was invited to take a look in the equipment room. Back in the participants' room, they filled out an informed consent form. Next, the

two coils of the Respitrace and the nose cannula were attached. The experimenter checked whether the participant was sitting in a comfortable way and explained that she should keep the same position during the experiment.

After the calibration phase, the experimenter emphasized the importance of imagining the scene as vividly as possible. It was explained that this implied not only creating a detailed visual picture of the scene, but also trying to experience the depicted scene as if one were a real, active participant.

After the first imagery trial, the experimenter reinforced all response oriented descriptions of the imagery experience[4] and instructed the participant to rate her experience during imagery on the basic affective dimensions of pleasure-displeasure and arousal-calm, using the paper-and-pencil version of the 9-point Manikin rating system (Bradley & Lang, 1994). Also, the vividness of the imagery was rated on a 9-point Likert-scale ranging from very good (1) to very poor (9).

Following the second imagery trial, the experimenter reinforced again response-related descriptions of the imagery experience and explained that the other two scripts would be presented according to the same scheme. In order to avoid carry-over effects, high arousal scripts were always alternated with low arousal scripts, leading to 8 different presentation orders. Five participants were randomly allocated to each presentation order.

At the end of the experiment, the participants filled out a Dutch translation of the Questionnaire Upon Mental Imagery (QMI) (Sheehan, 1967) and the experimenter asked whether they had voluntary controlled their breathing during one or more imagery trials.

[4] Lang et al. (1980*)* demonstrated that prior training in response orientation may enhance emotional imagery.

5.3.4 Data reduction and analysis

Subjective Ratings

The subjective ratings on valence, arousal and imagery vividness were analyzed using the multivariate approach for repeated measures and Tukey's HSD tests for post hoc comparisons.

Respiratory Measures

In order to get a general impression Ti, Te, V_T and $FETCO_2$ were analyzed separately using the multivariate approach for repeated measures Three periods of interest were defined for the respiratory data. The imagining1 period consisted of the last 30 s of the script and the first 30 s of the silence period; the imagining2 period consisted of the last 60 s of the silence period; the recovery period consisted of the 60 s of relaxing music period following imagery. Change scores subtracting the last 30 s of the baseline from the imagining1, imagining2 and recovery periods were used in a Script (depressive/fear/relaxation/pleasant) x Period (imagining1/imagining2/recovery) design.

To test in a more specific way the relative contributions of valence and arousal in respiratory responses, change scores in $FETCO_2$, Ti, Te and V_T (mean change score over imagining1 and imagining 2) were predicted in a Multiple Regression Analysis, using the subjective ratings on arousal, valence and the valence x arousal interaction term as predictors.

For explorative reasons[5], both the subjective ratings and the $FETCO_2$ responses of the present study were compared with those from the previous study. Ratings were analyzed in a Study (with/without response information) x Script (depressive/fear/relaxation/pleasant) design, analyses of the $FETCO_2$ responses had an extra variable Period (imagining1/imagining2).

[5] Although participants in the previous study with response information imagined each 8 scripts, we compared the four scripts of the present study with the four corresponding scripts from the former study.

In order to shed light on the change in effect size due to the omission of response information in the imagery scripts, the effect sizes of the R^2's of both experiments (with and without response information) were calculated following Cohen's (1992) guidelines[6]. Furthermore, specific effect sizes contrasting both experiments were calculated[7]. These reflected the effect size of the use of response information on responses in $FETCO_2$ during high or low aroused imagery.

5.4 Results

5.4.1 Subjective ratings

General Manova

As shown in table 5A, the relaxation script was rated lower in arousal than all other scripts. The depressive script was less arousing than the pleasant and the fear scripts, the latter two being rated equally high on arousal. The relaxation script and the pleasant script were rated equally and more positive than the depressive script. The fear script was rated more negatively than all other scripts. The participants

[6] The formula proposed by Cohen to calculate the effect size of R^2 is: $f^2 = R^2/(1 - R^2)$.

[7] The effect size of response information was calculated separately for the high and the low arousal scripts, using the index for independent means proposed by Cohen (1992).

For the high arousal scripts (fear, pleasant):

$$t_{\text{high arousal}} = (m_{f1p1} - m_{f2p2})/\sigma_{fp}$$

For the low arousal script (depressive, relaxation):

$$t_{\text{low arousal}} = (m_{d1r1} - m_{d2r2})/\sigma_{dr}$$

with ES = effect size
m = mean change in $FETCO_2$
f = fearful imagery
p = pleasant imagery
d = depressive imagery
r = relaxing imagery
1 = first study, with response information
2 = second study, without response information

rated their imagery of the depressive script as less vivid than the relaxation script. The other scripts did not significantly differ in vividness.

Table 5A. Mean Ratings for Valence, Arousal and Vividness (N = 40)

	D	R	F	P	Rao R (3,37)
Arousal					
M	6.82_a	8.15_b	4.38_c	3.90_c	115.98**
SD	1.59	1.14	1.63	1.89	
Valence					
M	6.63_a	1.85_b	7.56_c	2.18_b	185.69**
SD	1.75	1.10	1.20	1.30	
Vividness					
M	3.85_a	2.61_b	3.51_{ab}	3.28_{ab}	3.81*
SD	2.12	1.42	1.65	1.63	

Note: D = depressive; R = relaxation; F = fear; P = pleasant.
Lower values indicate more aroused, more positive or more vivid imagery.
Means having the same subscript are not significantly different at $p < .05$ in the Tukey HSD comparison
* $p < .05$; ** $p < .01$

Comparison between both studies

Nor the main effect of Study, nor the Study x Script interaction effect were significant for the valence ratings, but they were for the arousal ratings (main effect of Study, $F(1, 77) = 3.43$, $p < .01$; Study x Script interaction, Rao $R(3, 75) = 3.05$, $p < .05$). The pleasant script was rated higher in arousal in the study with response information than in the study without response information, $F(1, 77) = 15.35$, $p < .01$. The simple main effect was only marginally significant for the fear script, $F(1, 77) = 3.57$, $p < .06$, and not significant for the relaxation and the depressive script ($F(1, 77)$'s were, respectively, .07 and .77).

Participants in the study without response information found it more difficult to imagine the scripts vividly than the participants who imagined scripts with response information (main effect of study: F (1, 78) = 5.39, p < .05). The Study x Script interaction was not significant, Rao R(3, 76) = .64, n.s.

5.4.2 Physiological data

General manova

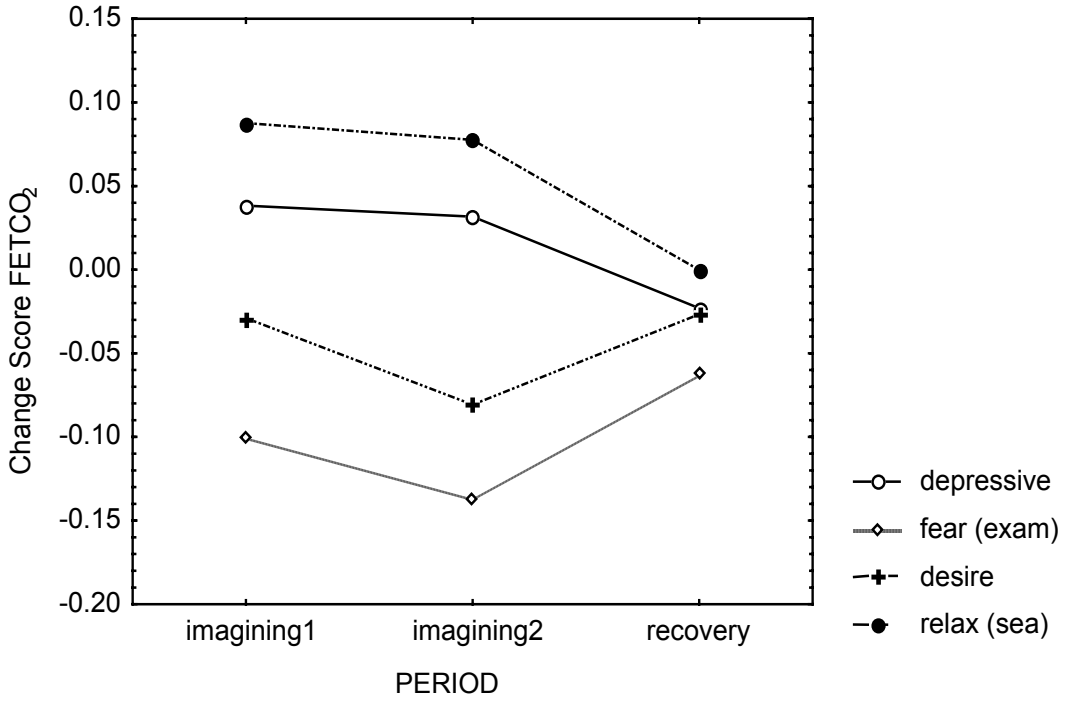


Figure 3. Mean changes in $FETCO_2$ from baseline to imagining1, imagining2 and recovery

As displayed in figure 3 and table 5B, $FETCO_2$ decreased during imagery of the high arousal scripts, increased during imagery of the low arousal scripts and returned to baseline during recovery (Script x Period interaction: Rao R (6, 33) =

5.58, $\underline{p} < .01$). Decreases in $FETCO_2$ were mainly due to decreases in Ti and Te during imagery of the high arousal scripts, with concomitant minor decreases in V_T

Table 5B. Means and SD's of the Change Scores in $FETCO_2$ (%), Ti, Te (s) and V_T (ml)

Parameter	D		R		F		P		Rao $\underline{R}$
	$\underline{M}$	$\underline{SD}$	$\underline{M}$	$\underline{SD}$	$\underline{M}$	$\underline{SD}$	$\underline{M}$	$\underline{SD}$	(6, 228)
$\Delta FETCO_2$									
I1	.04	.09	.09	.12	-.10	.18	-.03	.22	
I2	.03	.11	.08	.13	-.14	.23	-.08	.23	5.58**
Re	-.02	.10	-.00	.14	-.06	.12	-.03	.20	
ΔTi									
I1	.02	.17	.17	.32	-.16	.45	-.15	.37	
I2	.05	.29	.24	.60	-.26	.64	-.19	.47	4.70**
Re	-.04	.31	.07	.50	-.11	.59	-.09	.46	
ΔTe									
I1	.03	.42	.32	.81	-.27	.54	-.18	.64	
I2	.05	.43	.24	.64	-.34	.66	-.21	.68	9.60**
Re	-.06	.48	.03	.65	-.13	.49	-.07	.48	
ΔV_T									
I1	-15	81	13	65	6	95	-10	117	
I2	4	81	25	80	-12	93	-12	98	2.50*
Re	-4	90	19	73	-4	101	-17	88	

Note: I1 = imagining1; I2 = imagining2; Re = recovery; D = depressive; R = relaxation; F = fear; P = pleasant
* $\underline{p} < .05$; ** $\underline{p} < .01$

Comparison between both studies.

A marginally significant Study x Script interaction was found (Rao R(3, 75) = 2.66, p = .055). Subsequent simple main analyses showed that $FETCO_2$ decreases during pleasant imagery were stronger in the study with compared to the one without response information (F(1, 77) = 6.48, p < .05, means were respectively -.19 % (.27) and -.05 % (.22). The simple main tests for the relaxation, depressive and fear script were not significant (F(1, 77)'s were respectively .01, .47 and 2.47).

A significant Study x Period interaction (F(1, 77) = 8.45, p < .01) revealed a differential effect of Period in both studies. Whereas the responsivity in $FETCO_2$ tended to be strongest during imagining1 in the study with response information (F(1, 77) = 2.60, p < .11) , it was strongest during imagining2 in the study without response information (F(1, 77) = 6.21, p < .05).

Multiple regressions

Table 5C displays the multiple regression analyses. 14.7 % of the variance in $FETCO_2$ changes could be explained by the valence, arousal and the valence x arousal interaction term. Only arousal was a significant predictor for changes in $FETCO_2$, Ti, Te and V_T from baseline to imagery. The valence x arousal term did not explain significant variance in $FETCO_2$.

Effect Sizes

Effects sizes of the prediction of $FETCO_2$ changes by valence, arousal and the valence x arousal interaction term in the studies without and with response information were respectively .02 and .09. The effect sizes of the in- or exclusion of response information were .51 for the high arousal scripts and .18 for the low arousal scripts.

QMI

No significant correlation was found between the mean $FETCO_2$-drop in the high arousal scripts (fear, pleasant) and the QMI score ($\underline{r}$ = .07, n.s.).

Table 5C. Multiple Regressions: R^2 's and Changes in $FETCO_2$, Ti, Te, V_T predicted by Valence (V), Arousal (A) and Valence x Arousal (VA)

Predicted	Predictor	B	SE B	β	R^2
$\Delta FETCO_2$	V	.004	.011	.070	
	A	-.020	.010	-.258*	14.7
	VA	-.002	.002	-.203	
ΔTi	V	-.033	.027	-.21	
	A	-.074	.024	-.39*	10.8
	VA	-.005	.005	.20	
ΔTe	V	-.016	.037	-.074	
	A	-.079	.034	-.300*	10
	VA	.000	.007	.009	
ΔV_T	V	-7.58	5.48	-.250	
	A	-10.58	5.01	-.284*	3.4
	VA	1.42	1.06	.301	

Note: *$\underline{p}$ < .05

5.5 Discussion

We replicated our previous finding of an association between highly arousing imagery and the occurrence of hyperventilation responses, regardless of the valence of the imagined scene. Although the effect was smaller in this study, the omission of response information in the imagery script yielded fundamentally the same pattern of respiratory responding in the two-dimensional space of emotions.

Similarly to our findings from the study with response information, $FETCO_2$ decreases in the high arousal scripts were mainly due to decreases in Ti and Te, with concomitant minor decreases in V_T. These findings suggest that demand effects as the reason for hyperventilatory responses observed in our imagery paradigm are very unlikely. In addition, although a few participants reported moments of awareness of their breathing pattern changing during imagery, no single participant reported to have voluntary controlled or manipulated her breathing.

The variance in $FETCO_2$ explained by the entire model including valence, arousal and the valence x arousal interaction term was rather small in both studies. 14.7 % of the variance was explained in the study without response information, as opposed to 29 % in the study with response information. The specific effect size of response information on arousal-related changes in $FETCO_2$ was medium for the high arousal scripts (.51) and small (.18) for the low arousal scripts (Cohen, 1992). This may imply that response information in the image prompt is far less effective in inducing changes in respiratory behavior in low arousing as opposed to highly arousing imagery.

Taking Lang's perspective, the inclusion of response information is associated with greater physiological responsivity because it facilitates the access to the emotional representation, resulting in a more vivid imagery. Indeed, participants were overall better able to imagine the scripts vividly when response information was included. Also, for the pleasant imagery, the use of response information led to an increased level of subjective arousal and was associated with greater physiological responsivity. For the fearful imagery, these effects were only marginally significant. This may be related to the association between negative mood and an enhanced internal attentional focus (Sedikides, 1992). Cuthbert et al. (1991) argue that an internal attentional focus is the critical feature in physiological responding during imagery. The same authors argue that it is this process of "turning inward" that underlies the effect of response information and response training on physiological responding. Since the fearful imagery may have induced

an enhanced internal attentional focus by itself, the use of response information might have been redundant in this respect.

In contrast with our study using response information, there was no correlation between the QMI-score and the mean $FETCO_2$-drop in the high arousal scripts (fear, pleasant). This may imply that interindividual differences in imagery ability are particularly related to the extent to which response prompts can trigger efferent activity. This is line with Cuthbert et al. (1991), saying that the activation of the response component in a memory representation distinguishes imagery from other modes of cognitive processing.

An important question is the validity of the present findings in an imagery paradigm for hyperventilation as a stress response in real life. At a fundamental theoretical level, both imagery and hyperventilation may be two sides of the extremely developed human capacity to anticipate. Following Cuthbert et al. (1991), imagery enhances survival, because it enables an organism to try out new behaviors off line, to rehearse new behaviors and to foresee possible outcomes. In our view, also hyperventilation may be conceived as the result of an anticipatory process, emerging from the discrepancy between feed-forward influences upon breathing and the actual metabolic state of the organism. Such a discrepancy may be more likely to occur when imagining rather than actually being in stressing events, because CO_2 production can be expected to be lower in imagery compared to being in the actual situation. By definition, action tendencies underlying emotions are not fully executed when anticipating or imagining.

The replication of our finding that hyperventilation can be triggered as a concomitant of highly arousing imagery, independent of valence, urges the question why in reality its occurrence appears to be far more prominent in contexts characterized by negative valence. A first answer to this question may be that this mainly reflects a reporting bias. In a study of Clark and Hemley (1982), voluntary hyperventilation led to both pleasant and unpleasant recalls in normal subjects. Some participants recalled similar experiences during sex or being high on drugs, whereas others recalled particularly negative experiences such as fainting. It is evident that

medical doctors or psychologists are consulted only when hyperventilation is occurring in an unpleasant context. A second, more theoretical explanation may be that hyperventilation is prone to become associated with unpleasant cues. In another study of our group, it was found that breathing frequency could be conditioned to unpleasant but not to pleasant mental images (Stegen et al., 1999) or odors (Van den Bergh et al., 1995; Van den Bergh, Winters, Devriese & Van Diest, 2002). Also situations with a specific unpleasant meaning, such as a risk of suffocation, may be more likely associated with hyperventilation, because of "belongingness" between the situation and the response. This characteristic has been emphasized previously in models of panic with agoraphobia (Barlow, 1988; Bouton et al., 2001).

In summary, it can be concluded that hyperventilation is triggered by high-aroused imagery with and without response information. Including response information, however, result in stronger effects that can be explained by increased vividness of the imagery rather than by experimental demand effects.

Chapter 6

Suffocation Risk and Movement Restriction as Triggers for Hyperventilation

Van Diest, Vos, Devriese, Wellens, Van de Woestijne, & Van den Bergh (submitted,a).

6.1 Abstract

Respiratory reactivity in response to risk of suffocation and movement restriction was studied in persons scoring high or low on Negative Affectivity (NA). Fractional end-tidal CO_2-concentration ($FETCO_2$), breathing frequency and tidal volume were measured in high (n=24) and low (n=24) NA women imagining each three fear, one tension, one depressive and three relaxation scripts. The fear scripts were equal on pleasantness and arousal, but differed as regards the inclusion of suggested risk of suffocation and movement restriction. Decreases in $FETCO_2$ occurred in all fear scripts. In the fear script suggesting suffocation, high NA women showed a stronger reduction in $FETCO_2$ compared to low NA women, but this effect was unrelated to suffocation fear ratings. Fear of restriction was associated with an overall lower $FETCO_2$, but not with enhanced reactivity to imagined movement restriction. This is likely due to the respiratory measurement system causing actual movement restriction.

6.2 Introduction

Hyperventilation is a breathing pattern that exceeds metabolic requirements (Gardner, 1996): more CO_2 is being expired than produced by the body, leading to a decreased CO_2-pressure in the blood, and to a lower fractional end-tidal CO_2 concentration ($FETCO_2$). In previous studies (Van Diest et al. 2001a,b), we found hyperventilation responses (defined as decreases in $FETCO_2$) during imagery of both pleasant and unpleasant, high arousal emotional situations, but not when imagining low arousal scenes. These findings clearly point to arousal as the more important dimension in triggering hyperventilation responses. However, while both the pleasant and unpleasant high arousal imagery scripts were equally rated on arousal, the latter was associated with a stronger decrease in $FETCO_2$ (Van Diest et al., 2001a). Three explanations may account for this. First, specific "defense conditions", defined as a combination of high arousal and negative valence, may be more powerful in triggering hyperventilation responses (the so-called interaction hypothesis, see Van Diest et al., 2001a). Second, although the emotional dimension of dominance is generally believed to explain little variance in psychophysiological responding, the higher responsivity in the fear script may be related to this dimension. A third explanation refers to risk of suffocation and physical confinement (or movement restriction) as particular triggers for hyperventilation. Indeed, both physical restriction and risk of suffocation were suggested in the unpleasant, highly arousing imagery script that was associated with the strongest responses, depicting someone stuck in an elevator (Van Diest et al., 2001a). Several models of panic and agoraphobia disorders - in which hyperventilation is highly prevalent - have emphasized the role of Fear of Suffocation (FS) and/or Fear of Restriction (FR; Barlow, 1988; Bouton et al., 2001; Harris, Robinson, & Menzies, 1999; Ley, 1989; Rachman, 1997; Rachman & Taylor, 1993). This paper aimed to explore the critical value of FS and FR in triggering hyperventilation responses in non-clinical participants.

Physical restriction refers to the inability to escape from a (potential) threat and is believed to be intrinsically aversive, even in the absence of any detectable threat (Rachman, 1997, p 171). Since respiration is related to the response requirements underlying an emotion (Boiten et al., 1994; Dudley & Pitts-Poarch, 1980; Nyklíček et al., 1997; Van Diest et al., 2001a,b), hyperventilation may ensue very easily whenever an external threat triggering strong escape tendencies has to be met while one is physically restricted. Physical escape from an internal threat, e.g., a rapid heartbeat, is by definition impossible, which may partially explain why hyperventilation is very common among panic patients.

Fear of suffocation is a common fear in normal populations (Kirkpatrick, 1984), with young women showing the highest incidence (17 %; Rachman, 1997). Because of the obvious survival value of a satisfactory air supply, several authors have suggested a biological basis for FS. For example, biologically inspired theories on panic typically assume the existence of a primitive, central alarm mechanism functioning in relation to impending asphyxia (Klein, 1993; 1994). In line with this, hypoxic stimulation in decerebrated cats has been found to automatically trigger a defense reaction, including hyperventilation (Hilton, 1982).

Several other studies document a tight relationship between anxiety and somatic sensations referring to suffocation in humans. For example, dyspnea, a subjective experience of breathing discomfort, is common in anxiety, depressive and somatization disorders (Friedman, 1947; Sharpe & Bass, 1992; Wood, 1941) and patients with medically unexplained dyspnea report typically more anxiety (Han et al., 2000). Breath-holding time, inducing dyspneic sensations, is negatively associated with anxiety (Asmundson & Stein, 1994; Van der Does, 1996). In a PET study on humans, Liotti et al. (2001) found that the experience of breathlessness was associated with an increased activity in limbic and paralimbic brain regions, which are also involved in primal emotions engendered by pain and hunger.

Rachman (1997), adopting a more cognitive approach, sees fear of suffocation as a possibly "prepared" fear that is highly conditionable, a supposition that is in line with several observations. Indeed, suffocation fear can be acquired in

humans following a single conditioning trial and seems to be resistant to extinction (Campbell, Sanderson, & Laverty, 1964). Also, a study from our group showed that both dyspneic sensations and respiratory behavior could be easily conditioned to claustrophobic, but not to neutral/positive mental images (Stegen et al., 1999). If FS is a prepared fear, it can be expected that conditioned or "false alarm" responses would particularly resemble the unconditioned or the "true alarm" ones (Barlow, 1988; Bouton et al., 2001; Cook, Hodes, & Lang, 1986). Therefore, situations referring to risk of suffocation should trigger an increased ventilation more easily than other fearful situations.

In the present study, $FETCO_2$ and respiration were measured in 48 women during imagery of eight different scripts. Three fear scripts differed as regards the inclusion of suggestions pertaining to risk of suffocation and/or physical restriction. Four low arousal scripts were included as well: one depressive and three relaxation scripts. A tensed-anxiety script was additionally used to explore respiratory behavior under a more attentive, less action-oriented defensive set (Lang et al., 1997). Another explorative aim was to investigate whether people with hyperventilation symptoms in daily life and with a high level of negative affectivity (NA; Watson & Clark, 1984) would be more reactive to fearful imagery.

6.3 Method

Methods were similar to Van Diest et al. (2001a). Therefore, a shortened description will be presented in this paper.

6.3.1 Participants

Forty-eight women, all undergraduate students (17-19 years old), participated in return for course credit. They were selected on the basis of their scores on Negative Affectivity measures (see Procedure).

6.3.2 Materials

Scripts

Eight scripts were presented to the participants (see appendix II). Three fear scripts (elevator, tree, exam) were unpleasant and highly action-oriented. The elevator script contained both elements of risk of suffocation and movement restriction. The latter suggestion was also present in the tree script, but this script did not evoke risk of suffocation. Neither suggestion was present in the exam script. A quiz script aimed to trigger an unpleasant, tense affect that was less action-oriented than the fear scripts. The depressive script was unpleasant and low in arousal, whereas the three relaxation (car, sea, living) scripts were neutral-positive and low in arousal. All scripts, with the exception of the tree and the quiz script have been used in a previous study (Van Diest et al., 2001a). Since the inclusion of response information enhances the quality of the imagery (Lang, 1979; Van Diest et al., 2001b), all scripts contained suggestions of autonomic responses. In order to avoid voluntary control of breathing, only suggestions referring indirectly to breathing responses were used (see appendix II).

Apparatus and physiological recordings

Participants were seated in a comfortable chair. Imagery scripts were presented via headphones plugged into the headphone jacket of a PC.

Fractional end-tidal CO_2-concentration ($FETCO_2$) was measured using a nasal CO_2-sampling cannula connected to a non-dispersive infrared CO_2-monitor with a resolution of 1 mmHg and an accuracy of +/- 2 mmHg (Capnograph, Poet RC, Criticare, USA). Ventilation was measured using a respiratory inductive plethysmograph (Respitrace Corporation Model 150, New York). The coils of the Respitrace were stuck to the skin, one around the rib cage under the axilla and the other on the abdomen above the pelvis. The calibration procedure consisted of a 5-minute period of breathing during which respiration was measured simultaneously by means of a pneumotachograph (Fleisch No 2, Switzerland) and the Respitrace.

Dedicated software extracted breathing pauses and irregularities and determined the following parameters for each breath: inspiratory (Ti) and expiratory time (Te) in s, inspiratory (Vi) and expiratory volume (Ve) in ml and $FETCO_2$ in %. Only inspiratory volume was used as a measure of tidal volume, V_T.

Subjective measures

In a collective group session preceding the experiment, 439 undergraduates (351 women) had completed the trait version of the Positive and Negative Affect Schedules (PANAS; Watson, Clark, & Tellegen, 1988), the Zelfbeoordelingsvragenlijst (ZBV; Van der Ploeg, 1980) and the Checklist for Psychosomatic Symptoms (CPS; Wientjes & Grossman, 1994). The ZBV is the validated Dutch version of the STAI-T (Spielberger, Gorsuch, & Lushene, 1970). Both the STAI-T and PANAS are considered good measures of Negative Affectivity (Watson & Clark, 1984), a dispositional tendency to experience psychosomatic distress (Watson & Pennebaker, 1989). The Checklist for Psychosomatic Symptoms consists of 35 hyperventilation related symptoms belonging to one of the following subsets: paresthesia, cerebral, cardiac, gastro-intestinal, respiratory, anxiety or unclassified symptoms. Four sensations that are rarely associated with hyperventilation, called "dummy symptoms" were added to this list: nasal congestion, joint pain, lower back pain and aching eyes. Participants had to rate the extent to which they had experienced each symptom during the past year (never, rarely, regularly, often, very often).

During the experiment, participants rated the images evoked by the scripts on the basic affective dimensions of pleasantness (or valence), arousal and dominance (Lang et al., 1990; Mehrebian & Russel, 1974), using the paper-and-pencil version of the 9-point Manikin rating system (Bradley & Lang, 1994). Vividness of imagery was assessed by means of 9-point Likert-scales, ranging from very (1) to not vivid (9). At the end of the experiment, each participant completed the Questionnaire Upon Mental Imagery (QMI; Sheehan, 1967).

Fear of suffocation (FS) and Fear of Restriction (FR) were assessed using a translation of Rachman and Taylor's (1993) suffocation and restriction scales. Each scale consists of six items with high loading on only one of both factors. Participants were asked to indicate the degree to which they would feel anxious in each of the situations. Responses were made on a five-point scale, ranging from "not anxious" to "extremely anxious".

6.3.3 Procedure

Forty-eight participants were selected from the pool that had completed the NA questionnaires and the CPS (see subjective measures). The aim was to create two groups that were highly distinct with respect to dispositional NA and the occurrence of hyperventilation symptoms in daily life. The low NA group (24 women) consisted of students whose scores were in the lower quartile of the STAI-T and under the median of the NA-scale of the PANAS and the CPS. The scores of the other group (high NA participants, 24 women) were situated in the upper quartile of the STAI-T and above the median of the NA-scale of the PANAS and the CPS. The selected students were invited to participate in an experiment allegedly investigating physiological changes during imagery. Upon arrival, the experimenter told that there were 8 imagery trials, each consisting of the same consecutive phases. These were explained as Baseline: When the light in the participant's room was dimmed, participants were to close their eyes and one minute of relaxing music was presented through the headphones (a fragment of Sarabande, Goldberg Suite, E. Grieg). Participants were instructed simply to listen to the music. Script: during the following minute the script was presented and participants were asked to start the imagery as soon as they heard the text. Silence : The listening period was followed by 90 s of silence during which they had to keep on imagining the script as vividly as possible. After 60 s, a low level short auditory signal, announced during the instructions, was given as a reminder to continue the imagery as vividly as possible.

Recovery: Thereafter followed a recovery period of 60 s with another piece of relaxing music (Gymnopédie no. 1, E. Satie). As soon as this music started, participants had to stop the imagery, to keep their eyes closed and to listen to the music. The light being turned on announced the end of an imagery trial.

Participants were told that physiological recordings would be made during the imagery and the purpose of the equipment was described. It was told that the nose cannula sampled the expired air to send it to an analyzer and that the two coils would be attached to their rib cage and abdomen to detect changes in posture and muscle tonus of the trunk. The latter explanation was given to avoid drawing the participant's attention to her respiration. After an informed consent was obtained, the coils of the Respitrace and the nose cannula were attached. The participant was asked to sit down in a comfortable way and explained that the same position should be kept during the entire experiment. Next, the calibration procedure was started. To this end, participants wore a nose clip and breathed for 5 minutes through a mouthpiece that was connected to a pneumotachograph.

After the calibration phase, the importance of imagining the scene as vividly as possible was emphasized. It was explained that this implied not only creating a detailed visual picture of the scene, but also trying to feel and experience the depicted scene as if one were a real, active participant. Finally, the consecutive phases of the imagery trial were briefly repeated and the first imagery trial was started. After this trial, the experimenter approached the participant and asked whether she succeeded in imaging herself as a real actor in the scene. Lang et al. (1980*)* have demonstrated that prior training in response orientation may enhance emotional imagery. To this end, post-imagery verbal reports were elicited and the experimenter reinforced all response-oriented descriptions of the imagery experience. Next, the participant was asked to fill out the pleasantness, arousal, dominance and vividness ratings. Response training was applied a second time after the second imagery trial. Afterwards, the experimenter explained that the other six remaining scripts would be presented according to the same scheme without any further intervention of the experimenter.

The presentation order of the scripts was semi-randomized. The car script was always presented as the first script. The remaining low arousal scripts (sea, living, depressive) were randomized across the third, fifth, and seventh positions, yielding 6 possible orders for low arousal scripts. The fear and tension scripts were always presented on the second, fourth, sixth and eight position in a fixed sequence (elevator – quiz – tree – exam). However, the script with which this sequence started was alternated, yielding four possible orders of fear and anxiety scripts. One low and one high NA participant were randomly allocated to each of the 24 presentation orders that resulted from combining the six possible orders of the low arousal scripts with the four orders of high arousal scripts.

Following the last imagery trial, the participants filled out the QMI (Sheehan, 1967). Finally, the experimenter asked whether they had voluntary controlled their breathing during one or more imagery trials and whether they avoid elevators in real life because they feel anxious or uncomfortable in them. Answers to the latter question were coded as 0 (“never”), 1 (“sometimes”) or 2 (“always”).

The scores on the FR- and FS-scales were obtained after the experiment. All 48 participants were invited by mail to complete the FS and FR scales. Forty-three participants returned a completed questionnaire to the experimenter.

6.3.4 Data reduction and analysis

In order to avoid potential confounding by presentation order or amount of response training, data regarding the first imagery trial (first relaxation script) were left out of the analyses.

A first set of analyses included the other seven scripts and aimed to verify whether the effects from previous studies (Van Diest et al., 2001a,b) were replicated. The subjective ratings on valence, arousal and imagery vividness were analyzed using two-way ANOVA’s (NA: high/low; Script: depressive, exam, elevator, tree, sea, living, quiz). Greenhouse-Geisser corrections were applied to

these and all subsequent ANOVA's including the Script factor (7 levels); unadjusted degrees of freedom, adjusted p's and ε's will be reported in the result section. In order to check for baseline differences in breathing behavior, means of $FETCO_2$, breathing frequency (f) and tidal volume (V_T) during baseline were analyzed in an ANOVA with NA (2 levels) as a between subject and Script (7 levels) as a within subject variable. For the same parameters, difference scores subtracting the baseline from the imagery period were calculated and analyzed in a similar design. The first 30 s of script presentation were not included in the imagery period. Only significant effects will be reported. All post hoc comparisons following up significant main effects of Script were further tested using Tukey HSD tests. NA x Script interactions were followed up using analyses on simple main levels.

A second set of analyses was run in order to test whether risk of suffocation and movement restriction are particularly easily associated with hyperventilation responses. To this end, the subjective and physiological data regarding the three fear scripts in which these content variations were manipulated (exam, elevator, tree) were analyzed in 2 (NA) x 3 (Script) designs.

In a third, explorative set of analyses, correlations between FS, FR and the CPS on the one hand, and baseline respiratory measures and respiratory change scores during imagery of the fear scripts on the other hand, were calculated.

6.4 Results

6.4.1 Subjective ratings

As shown in table 6A, the depressive, exam, elevator and tree scripts were rated equally on valence and more negatively than the sea, living room and quiz scripts ($F(6, 276) = 293$, $p < .001$, $\varepsilon = .80$). The latter script was rated more negatively than

both relaxation (sea, living) scripts, but more positively than the depressive, tree, elevator and exam scripts. High NA participants tended to evaluate the scripts more negatively than low NA participants (main effect of NA, $\underline{F}$ (1, 46) = 3.36, $\underline{p}$ < .07). Exploring the marginally significant NA x Script interaction ($\underline{F}$ (6, 276) = 1.88, $\underline{p}$ < .10, ε = .80) further, it appeared that high NA participants rated the unpleasant scripts more negatively (depressive, exam, elevator, tree, quiz; $\underline{F}$ (1, 46) = 5.58 $\underline{p}$ < .025), but not the pleasant ones (sea, living room; $\underline{F}$ (1, 46) = .78, n.s.).

Table 6A. Means on the Subjective Ratings for each Imagery Trial (N=48)

		D	Ex	El	Tree	Sea	Liv	Q
Valence	M	7.35_{a}	7.46_{a}	7.83_{a}	7.67_{a}	1.65_{c}	1.63_{c}	5.85_{b}
	SD	1.39	1.34	1.19	1.26	.98	1.12	1.62
Arousal	M	7.33_{b}	3.92_{c}	3.60_{c}	4.06_{c}	8.60_{a}	8.56_{a}	4.35_{c}
	SD	1.62	1.54	1.71	1.60	.96	1.05	1.91
Dominance	M	4.50_{c}	3.63_{bc}	2.50_{a}	2.92_{ab}	7.71_{d}	7.90_{d}	4.35_{c}
	SD	2.53	2.00	1.54	1.83	1.76	1.79	2.01
Vividness	M	3.46_{bc}	3.27_{ab}	3.33_{abc}	3.19_{ab}	2.48_{a}	2.48_{a}	4.23_{c}
	SD	2.12	1.67	1.86	1.57	1.43	1.77	1.84

Note: D = depressive script; Ex = exam script; El = elevator script; Tree = tree script; Sea = sea script; Liv = living room script; Q = quiz script
Lower values indicate more aroused, more pleasant, less dominant and more vivid imagery, all on a 1–9 scale.
Means having the same subscript are not significantly different at $\underline{p}$ < .05 in the Tukey honestly significant difference comparison.

The depressive script was more arousing than both relaxation scripts but far less arousing than the three fear scripts (exam, elevator and tree), $\underline{F}$ (6, 276) = 146, $\underline{p}$ < .001, ε = .80.

A main effect of Script ($\underline{F}$ (6, 276) = 71 , $\underline{p}$ < .001, ε = .63, see table 6A), a marginally significant main effect of NA ($\underline{F}$ (1, 46) = 3.29, $\underline{p}$ < .08) and a NA x Script

interaction effect (F (6, 276) = 3.26, $p < .05$, $\varepsilon = .63$) emerged on the dominance ratings. The latter interaction showed that the high NA group felt less dominant in the unpleasant scripts (depressive, exam, elevator, tree, quiz) than the low NA group, F (1, 46) = 6.31, $p < .025$, but no difference among both NA groups appeared for the pleasant (sea, living room) scripts (F (1, 46) = 1.35, n.s.).

Participants rated the vividness of their imagery of both relaxation scripts better than that of the quiz and the depressive scripts, while there was no difference among the latter two. The elevator script did not differ from any other script as regards vividness, while the vividness ratings of the exam and the tree scripts were higher than those of the quiz script, F (6, 276) = 7.10 , $p < .001$, $\varepsilon = .89$.

6.4.2 Respiratory responses

Baseline

There were no baseline differences among the seven imagery trials for $FETCO_2$, breathing frequency or tidal volume (see table 6B for means and SD's), nor were there any significant effects involving NA.

Imagery

Table 6B displays the mean change scores in $FETCO_2$, breathing frequency and tidal volume and SD's during imagery (see also figure 4). Decreases in $FETCO_2$ occurred in the three fear scripts (exam, elevator, tree, main effect of Script, F (6, 276) = 19.75, $p < .001$, $\varepsilon = .43$). The minor changes in $FETCO_2$ in the quiz, the depressive and both relaxation scripts did not differ among each other. The decrease in $FETCO_2$ in the exam script was not different from the quiz script (see table 6B).

Table 6B. Baseline values of $FETCO_2$ (in %), breathing frequency (per minute) and tidal volume (in ml) and Respective Change Scores (Δ) from Baseline to Imagery

		D	Ex	El	Tree	Sea	Liv	Q
$FETCO_2$	M	5.11	5.10	5.13	5.11	5.09	5.10	5.08
	SD	.49	.46	.47	.47	.46	.46	.50
f	M	15.81	15.71	15.54	15.69	15.29	15.70	15.66
	SD	2.85	2.68	2.86	3.01	2.70	2.74	2.76
V_T	M	341	338	354	344	356	350	350
	SD	82	73	95	71	83	85	96
$\Delta FETCO_2$	M	$.05_c$	$-.14_{ab}$	$-.27_a$	$-.23_a$	$.10_c$	$.09_c$	$-.03_{bc}$
	SD	.15	.27	.45	.41	.19	.11	.28
Δf	M	$.32_{ab}$	2.24_{bcd}	3.87_d	3.45_{cd}	$-.12_a$	$-.24_a$	1.76_{abc}
	SD	2.61	4.24	6.60	5.58	2.39	1.86	3.71
ΔV_T	M	-6.58	5.21	-11.78	-1.01	-10.61	-6.20	-14.69
	SD	64.01	72.63	92.59	80.98	57.36	52.89	75.90

Note: D = depressive script; Ex = exam script; El = elevator script; Tree = tree script; Sea = sea script; Liv = living room script; Q = quiz script; $FETCO_2$ = fractional end-tidal CO_2-concentration; f = breathing frequency; V_T = tidal volume
Means having the same subscript are not significantly different at $p < .05$ in the Tukey honestly significant difference comparison.

The scripts also elicited differences in breathing frequency (main effect of Script, F (6, 276) = 11.14, $p < .001$, ε = .36, see table 6B). The three fear scripts were associated with equally strong increases in breathing frequency, which were significantly higher than the breathing frequency during both relaxation scripts. The increases in breathing frequency in the elevator and the tree scripts were significantly higher than in the depressive script (see table 6B).

No significant responses in tidal volume during imagery emerged.

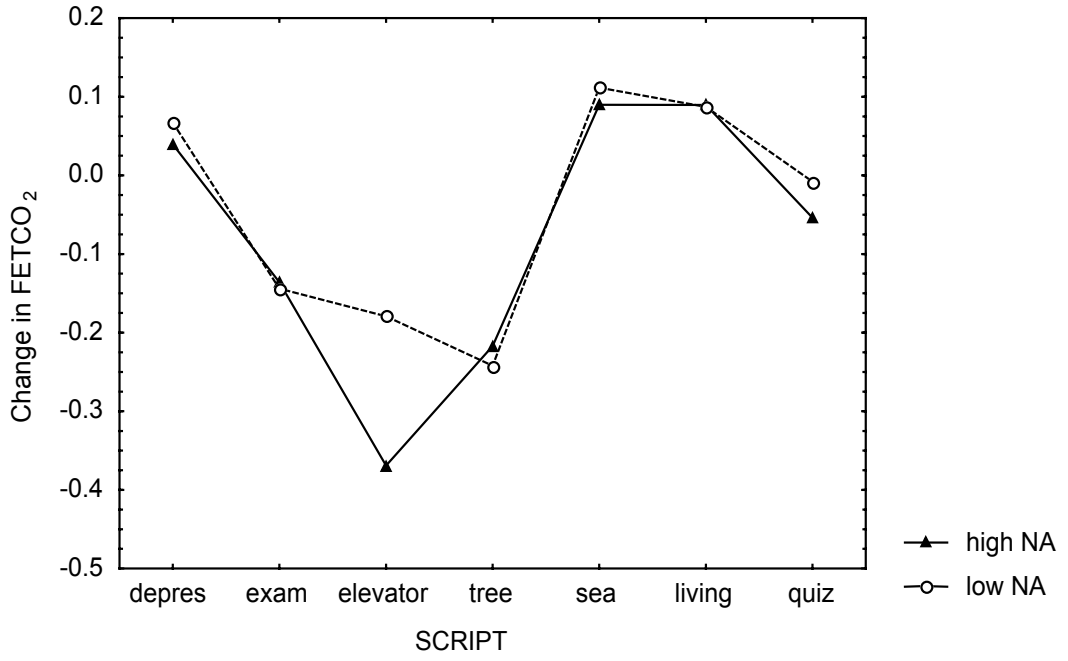


Figure 4. Change in $FETCO_2$ from baseline to imagery for high (n=24) and low (n=24) participants

6.4.3 Risk of suffocation versus movement restriction.

Subjective ratings

When only the exam, elevator and tree scripts were included in a 2 (NA) x 3 (Script) design, no significant effects for valence, arousal, or vividness were found. The exam script was rated higher in dominance than the tree and elevator scripts (main effect of Script, $\underline{F}$ (2, 92) = 10.54, $\underline{p} < .001$, $\varepsilon = .89$). The latter two did not differ from each other.

Respiratory responses

Both a main effect of Script ($\underline{F}$ (2, 92) = 5.23, $\underline{p} < .05$, $\varepsilon = .87$) and a NA x Script ($\underline{F}$ (2, 92) = 3.99, $\underline{p} < .05$, $\varepsilon = .87$) interaction was found for changes in $FETCO_2$ from baseline to imagery. Following up this interaction (see figure 4) at simple main

levels showed that in the high NA group, the decrease in $FETCO_2$ was stronger for the elevator script than for the tree and exam script (F (1, 46) respectively 8.72 and 10.99, p's < .01), which was not observed in the low NA group (F (1, 46) .25 and .23, respectively). The exam and tree scripts did not differ in either group (high NA: F (1, 46) = 2.11; low NA: F (1, 46) = 3.09).

The same pattern of results was observed for breathing frequency (main effect of Script: F (2, 92) = 4.45, p < .05, ε = .85; NA x Script interaction: F (2, 92) = 3.13, p < .057, ε = .87). Simple main analyses revealed that the increase in breathing frequency was stronger for the elevator script than for the exam script in high NA, but not in low NA participants (F (1, 46) respectively 10.24 and .024). The elevator script triggered no stronger increase in breathing frequency than the tree script (for high NA: F (1, 46) = 2.42; for low NA: F (1, 46) = .12). The tree script did not differ from the exam script in either group (for high NA: F (1, 46) = 7.11; for low NA: F (1, 46) = .54).

No significant effects on tidal volume responses during imagery were found.

6.4.4 Correlational analyses

Participants scoring high on FR had lower absolute baseline levels of $FETCO_2$ (r = -.34, p < .05) and tended to have a higher baseline tidal volume (r = .29, p = .06; see table 6C). FS was not related to respiratory measures during baseline (see table 6C).

With the exception of a negative correlation between FR and the change in tidal volume from baseline to imagery in the exam script (r = -.40, p < .01), change scores from baseline to imagery in $FETCO_2$, tidal volume and breathing frequency during imagery of the elevator, tree or exam script were not related to FR, nor to FS (see table 6C).

A stronger decrease in $FETCO_2$ during imagery of the elevator script was associated with more respiratory (r = -.32, p < .05) and paresthesia (r = -.34, p <

.05) symptoms in daily life, but not to the other symptom groups of the CPS (anxiety, cardiac, gastro-intestinal, cerebral and unclassified symptoms).

Table 6C. Correlations between Changes in $FETCO_2$, f and V_T from Baseline to Imagery and Fear of Restriction (N = 43) and Fear of Suffocation (N = 43) for the Elevator, the Tree and the exam Script

	Fear of Suffocation			Fear of Restriction		
	El	Tree	Ex	El	Tree	Ex
$\Delta FETCO_2$	-.20	-.19	-.16	-.04	-.10	.00
Δf	.08	.01	.19	.09	.16	-.01
ΔV_T	-.13	-.17	-.40**	.13	.08	-.28

Note: $FETCO_2$ = fractional end-tidal CO_2-concentration; f = breathing frequency; V_T = tidal volume; El = elevator script; Tree = tree script; Ex = exam script
** $p < .01$

6.5 Discussion

Suffocation

Specific comparisons between fear scripts showed that, compared to the low NA group, the reduction in $FETCO_2$ was more pronounced in high NA participants during imagery of the elevator script depicting a fearful situation in which both risk of suffocation and movement restriction were present. Such an effect of NA was not observed when only movement restriction was suggested (tree script), nor when neither of both claustrophobic components were included in a fearful script (exam script). This pattern of results suggests that situational risk of suffocation is a particularly strong trigger for hyperventilation in high NA people only. Several mechanisms may underlie this finding.

A first explanation in terms of a higher trait-like fear of suffocation in high NA participants as compared to low NA participants is unlikely: both NA groups

had similar scores on the FS-scale ($\underline{F}(1,41) = .22$, n.s). A second related explanation may be that, compared to the low NA group, a larger proportion of high NA participants may have been truly phobic of elevators, giving rise to stronger tendency to hyperventilate. However, our data do not confirm this interpretation either. Respiratory responses were rather modest in the 8 participants answering positively on the post-experimental question regarding avoidance behavior for elevators. Furthermore, analyses excluding these claustrophobic participants did not yield another pattern of results[8]. Thirdly, the enhanced respiratory responsiveness of high NA participants in the elevator script was not related to a stronger fear experience, nor to a more vivid imagery in that group: the observed pattern of $FETCO_2$ and breathing frequency responses in high versus low NA participants during fearful imagery was not mirrored in any of the subjective ratings on valence, arousal, dominance or vividness.

It is clear that our major finding, an enhanced respiratory responsivity to suggested situational risk of suffocation in high NA participants, it one for which we fail to offer a simple explanation. A speculative explanation may relate to a more sensitive suffocation alarm system in high NA as compared to low NA participants, in analogy to the hypothesized oversensitive suffocation alarm threshold in panic disorder patients (Klein, 1993). However, such a suffocation alarm system remains to be identified and a recent study on panic patients concluded that, if a false suffocation alarm exists, its triggering has nothing to do with respiratory chemoreflexes, as Klein (1993) originally proposed (Katzman, Struzik, Vijay, Coonerty-Femiano, Mahamed, & Duffin, 2002). We argue that before offering any further speculations, future research should try to replicate our finding using additional non-respiratory physiological (e.g., cardiovascular) measurements. The latter are important to determine to which extent the enhanced

[8] On the post-experimental question regarding avoidance behavior for elevators, 3 low NA and 2 high NA participants answered with "sometimes" and 3 high NA (but no low NA) participants with "always".

responsivity of high NA participants to situational risk of suffocation is specific for the respiratory system.

$FETCO_2$ decreases during imagery of the elevator script were specifically related to the report of typical hyperventilation (respiratory and paresthesia) symptoms in daily life. This suggests that a high $FETCO_2$ responsivity during imagery in the laboratory may be a valid predictor of responsivity in real life.

Trait-like fear of suffocation (FS), however, was unrelated to the tendency to hyperventilate during imagery of the fearful script in which suffocation was suggested (see table 6C). This may be important in the light of findings suggesting FS to be a valid predictor of anxious responding to CO_2 challenges (McNally & Eke, 1996; Shipherd, Beck, & Ohtake, 2001). Indeed, whereas FS is unrelated to an enhanced susceptibility for the triggering hyperventilation responses, it does drive anxious responding to hyperventilation-like symptoms. This suggests that interpretative, cognitive-controlled processes, rather than individual respiratory response stereotypes, may underlie FS.

Restriction

The reduction in $FETCO_2$ during imagery of the tree script, which depicted a fearful situation in which physical confinement, but not risk of suffocation was present, did not differ from the decrease in $FETCO_2$ during imagery of fear script in which neither claustrophobic component was present. This was observed for both NA groups.

Trait-like fear of restriction (FR) was not associated with an enhanced respiratory reactivity to imagined restriction. However, people with a higher FR had a consistently lower $FETCO_2$ during the entire experiment. A likely explanation for this may be the actual movement restriction in the experimental context. Indeed, several cables connecting participant's torso to the physiological recording systems and the experimenter's instructions not to move or change position (see procedure) may have triggered fear and an increased respiration in participants with FR.

More generally, these findings indicate that the actual physical restriction constituted by the measurements may have triggered fear of restriction more powerfully than imagining the tree script.

Fearful versus tensed affects

We replicated the findings of previous studies, in which we observed a decreased $FETCO_2$ and an increased breathing frequency during imagery of fearful scripts, but not during imagery of low arousal (depressive and relaxation) scripts (Van Diest et al., 2001a,b). A quiz script that aimed to trigger a less action-oriented, rather tensed-attentive defensive set of responses was exploratorily introduced. Although it was rated equally high on arousal as the fear scripts (see table 6A), it triggered generally weaker hyperventilation responses. More specifically, $FETCO_2$ reductions during imagery of the quiz script were significantly less than during imagery of the elevator and the tree script (see table 6B). $FETCO_2$ responses during imagery of the exam and the quiz script did not differ significantly. This pattern of results was exactly mirrored in the subjective ratings on dominance (see table 6A), suggesting a potentially important role for this often neglected emotional dimension in the differentiation between attentive and more action-oriented defensive response sets.

Negative affectivity

An additional aim of the present study was to explore whether high trait NA participants who reported many hyperventilation symptoms in daily life, would be more susceptible to hyperventilate in the laboratory than a low trait NA group with low levels of such symptoms. As noted above, this was only the case during imagery of a fear script that included suggestions towards risk of suffocation. No NA-differences were apparent in the other scripts.

However, in accordance with reports of stronger susceptibility in highly neurotic people for unpleasant mood inductions (e.g., Larsen & Ketelaar, 1991), high NA participants rated their feelings more negatively than low NA participants did when imagining unpleasant, but not when imagining neutral-pleasant scripts.

For dominance, a similar pattern was observed: compared with low NA, high NA participants felt less dominant during imagery of unpleasant scripts only. As already outlined above, these patterns of NA differences in the subjective appreciation of the imagery experience were not mirrored in respiratory responses.

Summary

Our findings further corroborate the general idea that respiratory responses, and $FETCO_2$ in particular, reflect the response requirements underlying an emotion (Boiten et al., 1994; Dudley & Pitts-Poarch, 1980; Nyklíček et al., 1997; Van Diest et al. 2001a). Although high NA participants do not report to be more fearful about situations with a possible risk of suffocation than low NA participants, the former respond with stronger increases in respiration and concomitant decreases in $FETCO_2$ to imagined risk of suffocation than the latter. No such NA-related enhancement of respiratory responsivity was present when imagining other fearful scripts.

Furthermore, our pattern of results suggests that the emotional dimension of dominance may be critical in the prediction of $FETCO_2$ decreases during imagery of unpleasant, highly arousing emotional scripts. Further research should replicate and extend these findings.

Chapter 7

Resting End-Tidal CO_2 and Negative Affectivity

Van Diest, Vuerstaek, Corne, De Peuter, Devriese, Van de Woestijne, & Van den Bergh (in press). Psychosomatic Medicine.

7.1 Abstract

Dhokalia et al. (1998) found a positive correlation between a trait measure of Negative Affectivity (NA, Neuroticism) and resting end-tidal fractional concentration of CO_2 ($FETCO_2$) in a non-clinical sample. This contrasts sharply with studies reporting a negative association of $FETCO_2$ with state measures of NA and with studies reporting no or a negative relationship between $FETCO_2$ and trait NA. In two studies we aimed to clarify this paradox. In the first study, 110 participants (83 women) completed the PANAS and a Checklist for Psychosomatic Symptoms in daily life. $FETCO_2$ was measured non-invasively during 5 min via a nose cannula connected to a capnograph. In the second study, $FETCO_2$ of high (n=20, 10 men) and low (n=20, 10 men) NA participants was sampled once with a nasal cannula and once while breathing through a mouthpiece for 6 min each during (a) rest, (b) completion of the NEO-PI-R questionnaire, and (c) completion of a verbal knowledge test. The first study found no association between trait NA and resting $FETCO_2$ after partialling out the effects of gender, menstrual phase and use of oral contraceptives. The second study showed that $FETCO_2$ rose significantly in the high NA group only when the particpants filled out the questionnaires, regardless of its type.

Overall, no association between dispositional NA and cross-situational $FETCO_2$ was observed. Apparently inconsistent findings may be due to improper control for hormonal status and mental load during testing.

7.2 Introduction

Hyperventilation or breathing in excess of metabolic needs leads to hypocapnia (a lowered alveolar and arterial PCO_2, which is associated with secondary physiological changes and a wide variety of symptoms in different bodily systems (Gardner, 1996). Hypocapnia is typically associated with anxiety states (Grossman, 1983): many studies report a lower baseline $FETCO_2$ in panic patients (Abelson et al., 1996; Bass et al., 1989; Gorman et al., 1986; 1988; Han et al., 2000; Hegel & Ferguson, 1997; Lee et al., 1993; Papp et al., 1997; Rapee et al., 1986; Wilhelm et al., 2001c) and decreases in $FETCO_2$ have been observed in non-clinical samples in response to stress and anxiety (Allen et al., 1986; Dudley, 1969; Dudley et al., 1965; Garssen, 1980; Ley & Yelich, 1998; Suess et al., 1980). However, less clarity exists on a possible association of $FETCO_2$ with trait measures of anxiety[9] in non-clinical samples. In contrast with the negative association of $FETCO_2$ with state measures of anxiety, Dhokalia et al. (1998) found a positive relationship between $FETCO_2$ and the Neuroticism dimension of the revised 'NEO Personal Inventory' (NEO-PI-R). However, other studies found no association of $FETCO_2$ with trait anxiety (Wientjes & Grossman), nor with any of the MMPI scales (Shershow, 1973). Stegen (1998) found a negative relationship of $FETCO_2$ with trait Negative Affectivity (NA), pooling data from 6 experiments in which $FETCO_2$ of high (n = 196) and low NA (n = 231) participants had been measured during a first baseline room air breathing trial of two minutes (Stegen et al., 1999; 1998; Stegen, Van Diest, Van de Woestijne, & Van den Bergh, 2000; 2001; Van den Bergh, Stegen, Van de Woestijne, 1998; Van den Bergh et al.,

[9] Negative Affectivity, trait Anxiety and Neuroticism can be used interchangeably (Watson & Clark, 1984).

1999). Results indicated that high NA participants had a slightly, but significantly lower $FETCO_2$ than low NA participants (means were, respectively, 5.062% and 5.213%).

The existence and direction of an association between $FETCO_2$ and trait NA is clinically important for a number of topics in the field of psychosomatic medicine. First, a high resting $FETCO_2$ has been found to be related to hypertension in women (Anderson, 2001), suggesting that psychosocial interventions may be helpful in its treatment. Second, an association of trait NA with $FETCO_2$ may help to clarify the hypothesized role of hyperventilation in quite a number of pathological conditions, such as panic disorder, somatization, chronic fatigue syndrome, chronic muscle pain and multiple chemical sensitivity (Bazelmans et al., 1997; Leznoff, 1997; Papp et al., 1993; Sharpe & Bass, 1992; Van den Bergh et al., 1997; Wilhelm et al., 2001b). Third, chronically reduced PCO_2 levels in the blood of high trait NA persons could partly explain the association between NA and symptom reports in non-clinical samples (Costa & McCrae, 1987; Feldman, Cohen, Doyle, Skoner, & Gwalthney, 1998; Larsen, 1992; Mora, Robitaille, Leventhal, Swigar, & Leventhal, 2002; Vassend, 1989; Watson & Pennebaker, 1989).

Several explanations may account for the inconsistencies between the studies on resting $FETCO_2$ and trait NA. First, the studied samples vary greatly in inclusion criteria, age and gender. For example, the participants in the study of Stegen (1998) were selected from the upper and lower quartiles of the NA distribution, which was not the case in other studies. Only men participated in the studies of Wientjes and Grossman (1994) and Shershow (1973), whereas other studies included both genders. Although gender was no significant predictor in the study of Dhokalia et al. (1998), other studies report a significantly higher $FETCO_2$ in men than in women (Han et al., 1997a; Kastrup, Thomas, Harmann, & Schabet, 1997). The absence of a gender effect in the study of Dhokalia et al. (1998) might be explained by yet another relevant, interacting variable: age. Convergent evidence shows that $FETCO_2$ decreases with age in men (Anderson, Parsons, & Scuteri, 1999; Frasetto & Sebastian, 1996), whereas the picture is less clear for women. For example,

Anderson et al. (1999) found a higher $PETCO_2$ in older women than in older men, but no association of $PETCO_2$ with age in women. Other authors report that in association with the menopause, $FETCO_2$ of women increases and approximates values observed in similarly aged men (Tatsumi et al., 1995). Extensive research by Han et al. (2000) has revealed complex interactions between trait NA, age and gender in the prediction of $FETCO_2$. We argue that whenever a wide age-ranged sample is studied, such interaction terms should be introduced in the model predicting $FETCO_2$.

Second, a methodological flaw in studies including female participants is the lack of control for hormonal influences on $FETCO_2$. Higher progesterone levels are associated with a lower $FETCO_2$ (England & Fahri, 1976; Takano, 1984). Progesterone levels are typically increased during the luteal phase of the menstrual cycle, during pregnancy, and also when using oral contraceptives.

Third, another important difference between the reported studies concerns the invasiveness of the measurement devices. In the Stegen (1998) studies, participants wore a nose clip and breathed via a mouthpiece connected to a pneumotachograph. This technique measures respiration accurately (Ritz et al., 2002), but affects spontaneous breathing quite strongly (Askanazi et al., 1980; Gilbert et al., 1972), particularly in anxious participants (Han et al., 2000). Mouthpiece breathing may constitute a respiratory challenge rather than a resting condition, which may raise ventilation and, consequently, reduce $FETCO_2$ levels more in high than in low NA persons.

The establishment of a true resting condition is problematic also in the study of Dhokalia et al. (1998). In this study, $FETCO_2$ was measured while the participants were filling out a Neuroticism questionnaire, which may have affected breathing behavior differently in high versus low NA participants, either through influences on emotional or on attentional processes. Indeed, cognitive load is associated with a decreased ventilation (Denot-Ledunois et al., 1998), which could have led to an increased $FETCO_2$.

The present investigation contains two studies that aimed to clarify the inconsistent findings reported above. In the first study ('study 4'), we assessed trait NA in 110 students and measured $FETCO_2$ for 5 minutes via a non-invasive nose cannula, controlling for progesterone related fluctuations in $FETCO_2$ in women. The other study ('study 5'; N= 40, balanced for gender and trait NA) investigated the influence on $FETCO_2$ of (1) the mental load associated with completing questionnaires (rest, filling out the NEO-PI-R, and completing a verbal knowledge test), and (2) the invasiveness of the used measurement device (nasal cannula or a mouthpiece).

7.3 Study 4

7.3.1 Method

Participants

One hundred ten undergraduates (83 women) volunteered to participate in return for course credit. Their age ranged from 17-20 years.

Materials

Self-report measures. The following questionnaires (Dutch translations) were completed in a group session preceding the individual sessions:

- The PANAS or the Positive and Negative Affect scale (Watson et al., 1988) consists of 20 positive and negative affect words for which the participant had to indicate to which extent he/she feels that way in general (trait version) or now (state version).
- The ASI or the Anxiety Sensitivity Index (Reiss, Peterson, Gursky, & McNally, 1986) is a 16-item questionnaire that measures an individual's fear of the symptoms of anxiety.

- The CPS or the Checklist for Psychosomatic Symptoms consists of 35 symptoms belonging to one of the following subsets: paresthesia, cerebral, cardiac, gastro-intestinal, respiratory, anxiety or unclassified symptoms. The CPS was originally developed to assess symptoms that frequently occur in association with hyperventilation (Wientjes & Grossman, 1994). We added four sensations that are rarely associated with hyperventilation, further called "atypical symptoms" to this list: nasal congestion, joint pain, low back pain and burning eyes. Participants had to rate the extent to which they had felt each symptom during the past year (never, rarely, regularly, often, very often, coded as 1, 2, 3, 4, 5, respectively).

At the end of the individual sessions, participants completed the state version of the PANAS. Finally, women were asked to indicate the phase of their menstrual cycle and whether or not they were using oral contraceptives.

Apparatus and physiological recordings. Fractional end-tidal CO_2-concentration ($FETCO_2$) was measured using a nasal CO_2-sampling cannula connected to a non-dispersive infrared CO_2-monitor (Novametrix, model 1265, USA). Its memory retained maximum values of $FETCO_2$ over 8 s. Incomplete and irregular expirations that did not reach a reliable end-tidal plateau and would result in an overall underestimation of $FETCO_2$ were discarded. Novacom software extracted the data via a RS232 serial port communication.

Procedure

The participants sat in a comfortable chair in a room adjacent to the equipment room and were monitored by the experimenter through a video camera.

In order to avoid drawing the participants' attention to their breathing, a cover story described the aim of the study as an investigation of the relationship between body temperature and temperament. It was told that the nose cannula sampled expired air to measure its temperature "far more accurately than a standard

thermometer". The participants were asked to keep their eyes open, not to move and to relax during the measurement, which would last for 5 minutes. Following the $FETCO_2$ measurement, they completed the state version of the PANAS and the questions regarding menstrual cycle and the use of oral contraceptives (for women).

Data analyses

In a first step, we analyzed our data in a similar way as Stegen (1998): a two-way ANOVA on $FETCO_2$ was performed using a NA category (lower/upper quartiles of trait NA scores) x Gender (m/f) design.

A second step in our analyses aimed to account for the influence of menstrual cycle and the use of oral contraceptives on $FETCO_2$ in women. In order to check for these effects, a two-way ANOVA on $FETCO_2$ with Menstrual phase (follicular/luteal) and the Use of oral contraceptives (yes/no) as independent variables was performed on the female subgroup.

Subsequently, $FETCO_2$ of men was predicted in a standard multiple regression analysis with trait and state NA, trait and state Positive Affectivity (PA), and the ASI scores[10] as predictors. Menstrual phase and Use of oral contraceptives were additional predictors of $FETCO_2$ for women. Our sample size of women (N = 77 women) provided a reasonable power (.83) to detect effects of medium size of the variables of primary interest (trait NA, Menstrual phase and Use of oral contraceptives) (58). This was not the case for our sample size of men (N = 27), which had only a power of .30 to detect a medium effect of trait NA . Therefore, the results for men will be reported only for explorative reasons and should be interpreted with great caution.

In a third analysis, correlations between trait NA and PA, ASI and $FETCO_2$ with the symptom scores of the CPS were calculated in order to check whether our data replicated the negative correlation between symptom reports and $FETCO_2$

[10] PA and ASI were introduced in the model for explorative reasons. Since the PA construct refers to one's level of energy and activity, it might be related to resting $FETCO_2$.

(Wientjes & Grossman, 1994) and the positive correlation of trait NA with symptom reports. For the latter correlation, the anxiety symptoms of the CPS were discarded in the calculation of the total symptom score, because of content overlap with several NA-items.

7.3.2 Results

Table 7A displays the descriptive statistics of all variables included in subsequent analyses. Gender differences were found for $FETCO_2$, state PA, total symptom score, gastro-intestinal, cerebral and unclassified symptoms. Men scored higher on state PA and women reported more symptoms, specifically more gastro-intestinal, cerebral and unclassified symptoms than men.

No significant effect of NA (F (1, 52) = 0.08, ns), nor a NA x Gender interaction (F (1, 52) = 0.01, ns) was found upon $FETCO_2$ in the two-way ANOVA with trait NA (upper/lower quartile) and Gender (m/f) as independent variables. Men had a higher $FETCO_2$ than women (Gender main effect: F (1, 52) = 5.48, p<.05).

Women using oral contraceptives and women in the luteal phase of their menstrual cycle had a lower resting $FETCO_2$ than, respectively, women not using oral contraceptives and women who were in the follicular phase (main effects of Use of oral contraceptives, F (1, 73) = 7.67, p<.01, and of Menstrual phase, F (1, 73) = 5.98, p<.05). There was no significant interaction between both variables, F (1, 73) = .25, n.s..

The ASI has been found to be a risk factor for the occurrence of spontaneous panic attacks (Schmidt, Lerew, & Jackson, 1997), which might be reflected in a lower resting $FETCO_2$.

Table 7A. Means and SD's of $FETCO_2$, Trait and State NA, Trait and State PA, ASI, and Symptom Scores for Women (n = 83) and Men (n = 27)

	Women		Men		t(108)
	M	SD	M	SD	
$FETCO_2$	4.93	0.37	5.21	0.36	3.51*
Trait NA	24.85	7.08	22.57	7.22	-1.45
State NA	13.32	4.00	13.85	4.94	0.57
Trait PA	33.11	5.34	33.35	4.62	0.21
State PA	21.72	6.13	26.59	6.67	3.51*
ASI	41.02	7.75	37.70	8.46	-1.89
Symptom score (35)	87.70	15.86	76.74	15.55	-3.13*
Anxiety (3)	9.22	2.50	8.15	2.33	-1.96
Respiratory (4)	9.84	3.69	9.59	3.09	-0.31
Paresthesia (5)	9.33	3.54	8.04	3.03	-1.70
Gastro-intestinal (4)	10.98	2.35	8.48	2.33	-4.68*
Cerebral (3)	6.27	1.79	5.00	1.54	-3.30*
Cardiac (5)	12.36	3.23	12.15	3.22	-0.30
Unclassified (11)	29.69	5.67	25.33	5.32	-3.55*
Atypical (4)	11.25	2.65	10.15	2.58	-1.88

Note: Number of items in each symptom group is indicated between brackets
NA = negative affectivity; PA = positive affectivity; ASI = anxiety sensitivity index
* $p < .01$

Tables 7B summarizes the multiple regression analyses. R^2's were 18.6% for women and 13% for men. Trait and state NA, trait and state PA, and the ASI scores did not significantly predict resting $FETCO_2$ in women, nor in men. Only Menstrual (power = .66) and the Use of oral contraceptives (power = .75) emerged as significant predictors of $FETCO_2$ in women.

Table 7B. Multiple Regression of Trait and State NA, Trait and State PA, ASI, Menstrual Phase and Use of Oral Contraceptives on $FETCO_2$ in women (N = 77), and men (N = 27)

	Women			Men		
Predictor	B	SE B	β	B	SE B	β
Trait NA	-.00	.01	-.01	-.01	.01	-.17
State NA	-.01	-.01	-.11	-.01	.02	-.05
Trait PA	.01	.01	.11	-.00	.02	-.02
State PA	-.00	.01	-.07	.02	.01	.36
ASI	-.00	.01	-.01	.01	.01	.19
Menstrual phase	-.17	.08	-.24*	-	-	-
Use of oral contraceptives	-.22	.08	-.31**	-	-	-

Note: NA = negative affectivity; PA = positive affectivity; ASI = anxiety sensitivity index
* $p < .05$, ** $p < .01$

Table 7C displays the correlations between NA, $FETCO_2$ and the symptom scores. A low, negative correlation between $FETCO_2$ and total symptom score, and a moderate, positive correlation of trait NA and ASI with total symptom score were found. Trait NA was positively related to all subset symptom scores, except for paresthesia. Trait PA was positively related to atypical symptoms but unrelated to any other symptom score. $FETCO_2$ correlated strongest with cerebral symptoms (dizziness, blackness before the eyes, fainting) and also with unclassified symptoms: more symptoms were associated with a lower resting $FETCO_2$.

Table 7C. Correlation of trait NA and PA, ASI and $FETCO_2$ with symptom scores (N = 110)

	NA	PA	ASI	$FETCO_2$
Symptom score (32)	.46**	.01	.37**	-.21*
Anxiety symptoms (3)	.73**	-.07	.32**	-.11
Respiratory (4)	.24*	-.02	.24*	-.14
Paresthesia (5)	.16	.14	.17	-.07
Gastro-intestinal (4)	.39**	.01	.28**	-.14
Cerebral (3)	.27**	.01	.26**	-.24*
Cardiac (5)	.21*	.07	.28**	-.12
Unclassified (11)	.55**	-.10	.34**	-.21*
Atypical symptoms (4)	.20*	.26**	.05	.01

Note: Because of content overlap with NA, the anxiety symptoms were not included in the Symptom score to calculate the correlation; Number of items in each symptom group is indicated between brackets
NA = negative affectivity; PA = positive affectivity; ASI = anxiety sensitivity index.
* $p < .05$, ** $p < .01$

7.4 Study 5

7.4.1 Method

Participants

Forty-eight undergraduate psychology students (22 women; age range 17-21 years) participated in the study and were free to choose between course credit or a 5 Euro fee in return. Data of eight participants (2 women) were excluded from analyses because more than 5 recorded breaths within at least one trial did not reach an end-tidal plateau. The final dataset consisted of observations on 20 high NA (10 women) and 20 low NA (10 women) participants.

Participants were selected on the basis of their scores on 2 measures of trait NA and on the CPS (see procedure). All participants smoked less than 5 cigarettes a day and had no respiratory or other major diseases. Only women not using oral contraceptives could participate and they were all tested in the second week of their menstrual cycle (follicular phase). Participants did not eat anything or drink any sugared or caffeinated beverages 2 hours preceding the experiment. In order to minimize the influence of circadian changes on $FETCO_2$, they were all tested between 1– 4 PM.

Materials

Self-report measures. Participants completed the Positive and Negative Affect scale (PANAS, 55), a validated Dutch version (Van der Ploeg, 1980) of the trait version of the State-Trait-Anxiety-Inventory (STAI, Spielberger, Gorsuch, & Lushene, 1970) and the Checklist for Psychosomatic Symptoms in daily life (CPS, Wientjes & Grossman, 1994). The STAI is a 20-item questionnaire measuring trait anxiety and is considered a good measure of Negative Affectivity (Watson & Clark, 1984).

During the experiment, they completed the Neuroticism, Extraversion and Openness scales of the Dutch NEO-PI-R[11] (Hoekstra, Ormal, & de Fruyt, 1996) and the VAT'69 (Drenth & van Wieringen, 1969). The VAT'69 assesses knowledge of the grammatical function of words. For 40 pairs of sentences, participants indicated which word(s) in the second sentence fulfilled the same grammatical function as the word(s) underlined in the first sentence. This test served to control for the potential effect of the emotional content of the NEO-PI-R items on $FETCO_2$.

Apparatus and physiological recordings. $FETCO_2$ was measured during performance of each task. Depending on the condition, expired air was sampled

[11] Since the participants had only two time windows of 6 minutes each available for completing the NEO-PI-R, it was impossible to complete all scales. The items were rearranged in such way that all items of the Neuroticism scale were situated in the first 140 items.

close to the mouthpiece (side stream) or through a nasal cannula. In the mouthpiece condition, the setup used by Stegen (1998) was replicated: participants wore a nose-clip and had to breathe via a mouthpiece that was connected to a pneumotachograph (Fleisch No 2, Switzerland). Upstream from the latter device, a double one-way valve ensured separation of inspired and expired air.

Procedure

In a group session preceding the experiment, 439 students had completed the trait version of the PANAS, the STAI and the CPS. Participants were selected from the upper and lower quartiles of the STAI, if they scored also above, respectively below the median of the PANAS (NA-scale) and the CPS[12].

After completing an informed consent form, the experimenter explained the aim of the experiment using the same cover story as in Study One. It was added that for the sake of reliability, the measurement would take place 3 times with each of two different methods. The $FETCO_2$ of each participant was measured for 6 minutes in each of the 6 trials made up by crossing the Device variable (cannula, mouthpiece) with the Task variable (resting, completing the NEO-PI-R, completing the VAT'69). The order of these six within subject conditions was semi-randomized with the restriction that nasal sampling was always alternated with mouthpiece sampling. The participants of each of the four between groups (n = 10) were similarly distributed across these 6 different orders (2 participants of each group were assigned to the first 4 orders and 1 participant of each group to the remaining two orders). Each nasal cannula and mouthpiece trial was followed by, respectively, 120 and 240 sec of recovery, during which the sampling tubes were cleaned. The recovery following mouthpiece breathing lasted longer in order to ensure that the breathing of the participant would be fully recovered. Participants who did not

[12] The criterion regarding the level of reported hyperventilation symptoms in daily life (CPS) was added in order to maximize the chance to observe an association between NA and $FETCO_2$. Using this additional selection criterion, 23.4 % of the possible participants based on the NA-criterion only (high NA with low symptom scores and low NA with high symptom scores) were excluded from the study.

finish the first 140 items of the NEO-PI-R within the foreseen time window (2 x 6 minutes), were asked to complete the remaining part of the questionnaire after the experiment.

Data analyses and Design

Mean $FETCO_2$ [13] for each 6 min period was calculated and analyzed in a NA (low/high) x Gender (female/male) x Devices (nose cannula/mouthpiece) x Task (rest/NEO-PI-R/VAT'69) design. NA and Gender were between subject variables; Devices and Task were within subject variables. Greenhouse-Geisser corrections were used wherever the task factor was involved.

7.4.2 Results

Table 7D displays the mean scores of trait NA as measured by the PANAS, the STAI and the Neuroticism scale of the NEO-PI-R, the mean symptom scores and the mean $FETCO_2$ for high and low NA men and women.

Overall, $FETCO_2$ of high and low NA participants was not different (main effect of NA, $\underline{F}(1, 36) = .02$, n.s.). Neither were $FETCO_2$ of men and women (main effect of Gender, $\underline{F}(1, 36) = .16$, n.s.). A significant main effect of Task ($\underline{F}(2, 72) = 13.75$, $\underline{p} < .001$, $\varepsilon = .65$) interacted with NA, $\underline{F}(1, 36) = 3.97$, $\underline{p} < .001$, $\varepsilon = .65$; power = .92 (58).

[13] Because (maximally 5) breaths not reaching an end-tidal plateau were discarded, the number of observation points ranged from 40 – 45.

Table 7D. Mean $FETCO_2$, Symptom Scores and Scores of trait NA as measured by the PANAS, STAI and NEO-PI-R, for low and high NA Men and Women

	Low NA				High NA				NA-effect
	Men		Women		Men		Women		
	M	SD	M	SD	M	SD	M	SD	F(1,36)
NA (PANAS)	17.6	4.45	19.7	3.37	29.4	4.86	36.1	3.87	114.0*
PA (PANAS)	38.7	5.36	39.9	3.78	29.5	2.99	32.4	3.50	43.3*
STAI	20.1	2.77	18.5	3.37	44.3	4.22	50.7	6.85	379.9*
NEO-PI-R	117.6	16.99	124.3	12.53	151.4	15.33	165.3	24.36	44*
Total symptoms	65.9	10.21	68.1	10.27	89.1	10.52	97.4	9.33	67.6*
$FETCO_2$	4.88	.40	5.02	.35	4.96	.31	4.91	.36	.02

Note: NA = negative affectivity; PA = positive affectivity
* $p < .01$

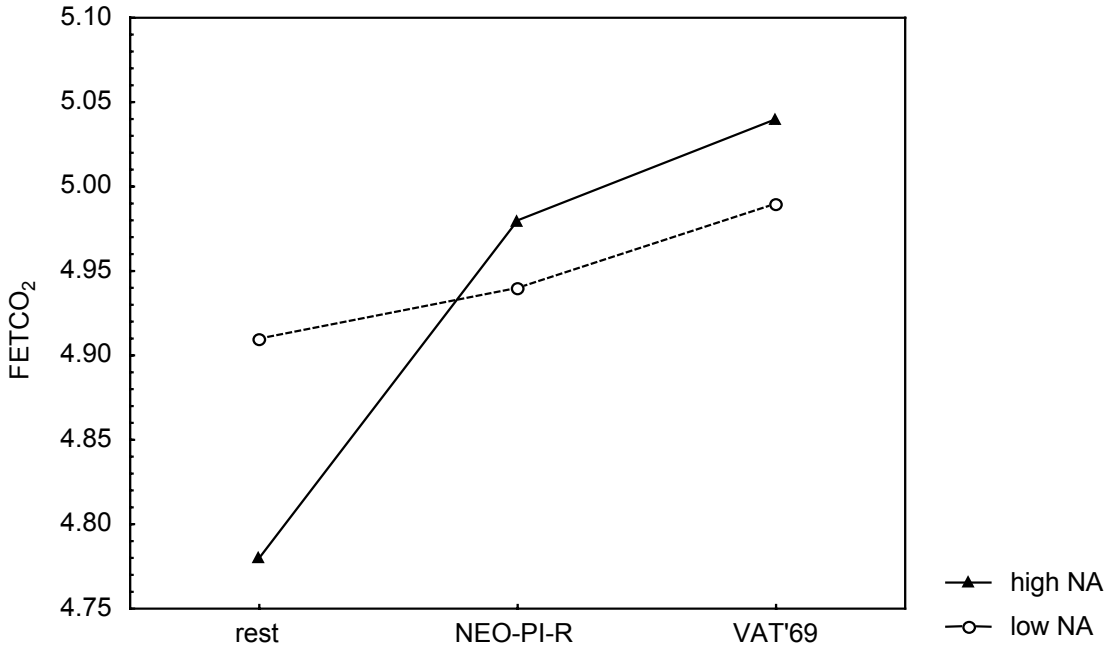


Figure 5. Mean $FETCO_2$ (in %) of high and low NA participants during rest and during completion of the NEO-PI-R and the VAT'69

As can be seen in figure 5, $FETCO_2$ of high NA participants during rest is significantly lower than during both conditions of mental load ($\underline{F}(1, 36) = 18.65$, $\underline{p} < .001$, $\varepsilon = .65$). This was not true for the low NA group ($\underline{F}(1, 36) = 1.43$, n.s., $\varepsilon = .65$). $FETCO_2$ of high and low NA participants were not different during rest, nor during completion of the NEO-PI-R or the VAT'69 (simple main $\underline{F}(1, 36)$'s were .84,.12, and .16, n.s., respectively).

$FETCO_2$ was higher in the mouthpiece than in the nasal sampling condition (main effect of Devices, $\underline{F}(1, 36) = 5.71$, $\underline{p} < .05$). A significant Devices x Task interaction ($\underline{F}(2, 72) = 3.85$, $\underline{p} < .05$, $\varepsilon = .65$; power =.70; figure 6) showed that this was the case in the VAT '69 condition ($\underline{F}(1, 36) = 21.20$, $\underline{p} < .001$), but not in the NEO-PI-R ($\underline{F}(1, 36) = 2.79$, n.s.), nor in the rest condition ($\underline{F}(1, 36) = .29$, n.s.).

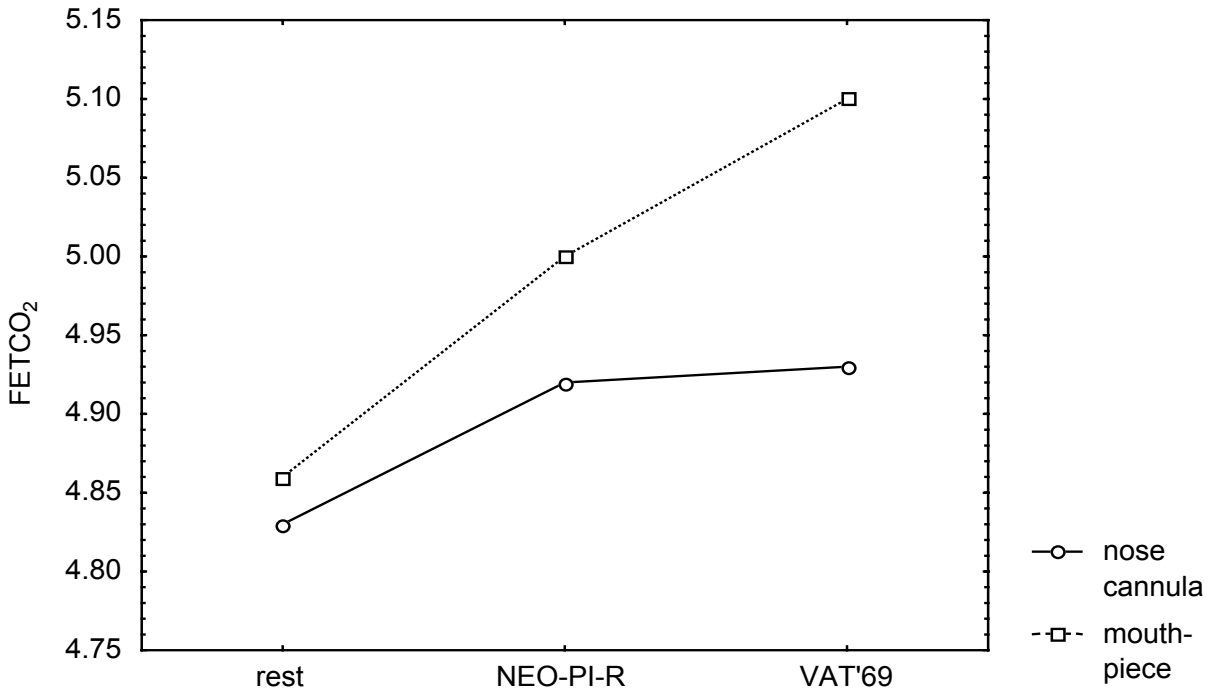


Figure 6. Mean $FETCO_2$ (in %) as measured using a nose cannula or mouthpiece during rest and during completion of the NEO-PI-R and the VAT'69

7.5 Discussion

Similarly to Wientjes & Grossman (1994) and Shershow (1973), we found no evidence for a relationship between habitual $FETCO_2$ and NA: NA was no significant predictor of $FETCO_2$ in women, and two different studies failed to detect significant differences in $FETCO_2$ between high and low NA groups. Therefore, both our hypothesis of a negative association of trait NA with resting $FETCO_2$ and the interpretation of Dhokalia et al. (1998) that a high resting $FETCO_2$ is associated with trait NA (or Neuroticism) should be rejected.

Our data, however, do confirm the findings of Dhokalia et al. (1998) in that NA is positively associated with $FETCO_2$ during filling out questionnaires, which indicates that the latter may not be considered a proper resting condition. More generally, our results strongly suggest that NA is an important modulator of situational influences upon $FETCO_2$. The increase in $FETCO_2$ in high NA participants during both the completion of the NEO-PI-R and the VAT'69 shows that not the emotional content of the personality questionnaire but rather the associated cognitive load is critical for the observed effect.

Whereas a decrease in $FETCO_2$ (or hyperventilation) is a well-known response to stress and anxiety, less attention has been paid to the opposite response, i.e. $FETCO_2$ increases. Exceptions to this are the studies of Anderson and colleagues (Anderson & Brady, 1976; Anderson, Fedorova, & Frenc, 1996), showing that an inhibited breathing pattern in animals is characteristic for states of vigilance. Fokkema (1999) provided two explanations for such an inhibited (strained) breathing pattern: it may be functional in depressing the noise associated with breathing when a predator is present and in preventing the threatened organism from hyperventilating when no physical activity is needed (yet). In humans, inhibited breathing showed up more frequently in the workplace, when people were sedentary or in social situations (Anderson et al., 1993; Haythorntwaite, 1992). Scuteri, Parsons, Chesney, & Anderson (2001) interestingly suggest that the inhibited breathing pattern may be characteristic for a typical "female"

physiological response to stress, in which sympathetically mediated "fight or flight" responses are inhibited in favor of parasympathetically mediated increases in oxytocin and reproductive hormones that support self-protective behaviors (Taylor, Klein, Lewis, Gruenewald, Gurung, & Updegraff, 2000). Another, temptative interpretation of $FETCO_2$ increases under conditions of mental load may be that, through cerebrovascular dilatation (Gotoh et al., 1965; Jibiki, Kurokawa, Matsuda, Fukushima, & Klinichi, 1992; Kastrup et al., 1997; 1998; Kennealy, McLennan, Loudon, & McLaurin, 1980), PCO_2 increases may be functional in an enhanced cognitive performance. In that case, $FETCO_2$ responses would constitute a promising measure of interest in research on test anxiety and cognitive performance.

To summarize, both increases and decreases in $FETCO_2$ may be viewed very likely as adaptive responses to stress. This is in line with studies on situational influences upon $FETCO_2$, since the occurrence of hyperventilation responses depends on the type of laboratory stressor used (Van Diest et al., 1999; 2001a). For example, $FETCO_2$ decreases in response to a cold pressor test, but not in response to a shock avoidance task (Allen et al., 1986). Since high NA participants are thought to be more reactive to stressors than low NA participants (Watson & Clark, 1984), one could expect both responses to be more frequently present in the former than in the latter. If this holds, it is not surprising that there is no habitual, cross-situational relationship between NA and $FETCO_2$ in non-clinical participants. The lower levels of resting $FETCO_2$ in panic patients (Abelson et al., 1996; Bass et al., 1989; Gorman et al., 1986; 1988; Han et al., 2000; Hegel & Ferguson, 1997; Lee et al., 1993; Papp et al., 1997; Rapee et al., 1986; Wilhelm et al., 2001c) then, suggest that such patients are more inclined to respond with decreases in $FETCO_2$ to a wide variety of stressors, whereas non-clinical participants would be better in selecting the response which is most adaptive for a particular situation. Such a reduced flexibility in selecting the most appropriate response is a key feature of anxiety pathology following Thayer and Lane's (2000) model of emotional (dys)regulation.

The negative association of trait NA with $FETCO_2$ found by Stegen (1998) remains somewhat puzzling. Since there was no interaction of Devices with NA in Study Two, Stegen's finding could not be explained by an enhanced responsiveness of high NA participants to the invasive measurement technique. Neither did we replicate the effect of Stegen (1998) when only extreme NA scorers were used for analyses (lowest/upper quartiles), similarly to his study.

In the first study, we replicated both the moderate, positive correlation between trait NA and symptom reports and the low, negative association of $FETCO_2$ with symptom reports as found by Wientjes & Grossman (1994). Except for cardiac symptoms, the correlations of symptom scores with Anxiety Sensitivity tended to be lower than with trait NA. However, whereas the correlations of trait NA with the subset symptom scores yielded a rather undifferentiated pattern, the ASI seemed to differentiate better between prototypical and atypical hyperventilation symptoms. Despite this specificity, the ASI was not significantly related to resting $FETCO_2$.

Our data clearly confirmed the influence of progesterone upon $FETCO_2$: the obtained values were lower for women using oral contraceptives and for women in the luteal phase of their menstrual cycle. Moreover, because the gender difference disappeared when testing only women not using oral contraceptives at a time of very low progesterone levels (second week of the menstrual cycle), our data suggest that there is no gender difference in $FETCO_2$ that could not be related to circulating progesterone.

In the experiment, it was found that $FETCO_2$ during mouthpiece sampling was higher than during nasal sampling, but this held only during the VAT'69 condition (see figure 6). One possible explanation for this may be that a strained breathing pattern (that is, a shortened inspiratory time with a lenghtened expiratory time, see Fokkema, 1999) may have been more prominent during the verbal ability test. In combination with the dead space of the mouthpiece and the pneumotachograph, this may have led to a more rapid and prononounced increase in $FETCO_2$.

More generally, we argue that the use of a very homogeneous sample may be an advantage when one's goal is to detect a small effect of a psychological variable on a measure that is also strongly influenced by other, biological variables. Indeed, the association between NA and $FETCO_2$ in a more heterogeneous sample would more likely be confounded with age-, sex-, and, perhaps, also disease-related influences upon $FETCO_2$.

To summarize, we found no cross-situational association between trait NA and $FETCO_2$. Whereas Dhokalia et al. (1998) suggest that their observed positive association of $FETCO_2$ with trait NA reflects a habitual state of chronic vigilance in people scoring high on NA, our data suggest that the association is induced by the situation, i.e. completing a questionnaire during the $FETCO_2$ measurement.

Chapter 8

Anxiety and Respiratory Variability

8.1 Abstract

Thayer and Lane's (2000) neurovisceral model of emotional (dys)regulation predicts a reduced flexibility in bodily systems during anxiety. This study explored the relationship of inter- and intraindividual differences in anxiety and within subject variability in breathing parameters. Using non-intrusive inductive plethysmography and a nose cannula, we measured tidal volume (V_T), inspiratory and expiratory time (Ti, Te), inspiratory drive (V_i/T_i) and fractional end-tidal CO_2 concentration ($FETCO_2$) in 98 female students during rest and fearful imagery. During rest, higher scores on trait negative affectivity (NA) were significantly associated with a reduced variability in Ti. During fearful imagery of an exam script, a significant decrease in the variability of Te and drive was observed; this was not the case during fearful imagery of an elevator script. A likely explanation for this may be that compared to the exam script, more participants left steady-state ventilation due to hyperventilation in the elevator script. Assuming that within subject SD's of volume and timing breathing parameters may considered a valid operationalization of respiratory flexibility only under steady-state conditions, our findings confirm the prediction made from Thayer and Lane's (2000) model.

8.2 Introduction

Flexibility and health have been identified with chaos in various bodily systems (heart, brain; Pool, 1989). Conversely, a loss of flexibility has been associated with sickness and it has been suggested that aging also involves a loss of variability and spectral reserve in several physiologic systems. The underlying idea is that chaos provides the system with a deterministic 'I don't know state', where new activity patterns can be generated (Skarda & Freeman, 1987).

Since an emotional response represents the *selection* of a response and the *inhibition* of other, less appropriate responses from a more or less broad behavioral repertoire (Frijda, 1999; Thayer & Lane, 2000), one could expect that emotions are associated with a diminished flexibility in responding too. For example, when confronted with a threat, an organism leaves the deterministic, chaotic 'I don't know state' and moves into a more specific psychophysiological constellation that prepares for fighting or fleeing. This view would predict a decreased variability in several psychophysiological processes associated with anxiety. Several findings corroborate this: attentional narrowing, reduced cardiac vagal tone (Friedman & Thayer, 1998) and behavioral avoidance have been found to be typically associated with anxiety and could all be viewed of as instances of decreased flexibility in responding. Although respiration has been described as chaotic behavior allowing for fast and flexible responses to sudden changes (Donaldson, 1992), there is no research linking the flexibility of respiration with psychophysiological processes such as attention and anxiety.

Yet, several observations found in literature lend - post hoc - some support to the idea that anxiety and/or attention are associated with a reduced flexibility in respiratory responding. Firstly, Boiten (1993) reports an increase in respiratory regularity during performance of mental load tasks. Secondly, following voluntary hyperventilation, anxiety patients perseverate overbreathing more and longer than normals, resulting in a delayed recovery of PCO_2 (Han et al., 1997b; Hardonk & Beumer, 1979; Wilhelm et al., 2001b). Thirdly, anxiety patients are unable to keep

their PCO_2 from decreasing when breathing via a mouthpiece (Han et al., 1997b): they increase their breathing more than metabolically required. This is not seen in normals. Both observations show that breathing of anxious patients may adapt poorly to changing demands, i.e., resume normal breathing after voluntary hyperventilation or breathing via mouthpiece.

On the other hand, reports of a highly irregular breathing pattern at rest in panic patients, characterized by many sighs and apneas (Abelson et al., 2001; Bystritsky & Shapiro, 1992; Schwartz, Goetz, Klein, Endicott, & Gorman, 1996; Stein et al., 1995; Wilhelm & Roth, 1998; Wilhelm et al., 2001c) seem at odds with our hypothesis of a reduced variability in respiration under anxiety. However, it is unclear yet whether the unstable breathing pattern in panic patients reflects unique diagnostic specificity or "normal" responses to anxiety, which may be elevated also in resting conditions in that group of patients (Wilhelm et al., 2001c).

The aim of this paper was to explore the link between respiratory variability and inter- and intraindividual differences in anxiety in a non-clinical sample. To this end, the within-subject standard deviations of several breathing parameters were assessed during relaxation and during anxious imagery in healthy, young women.

8.3 Method

In order to answer our research questions, data of two studies in which ventilation and $FETCO_2$ were measured during imagery of two fearful scripts were collapsed ('study 1': Van Diest et al., 2001a; 'study 3': Van Diest et al., submitted,a). Procedure and method were identical in both studies and have been extensively described previously (Van Diest et al., 2001a). Therefore, only a brief method section will be presented here.

8.3.1 Participants

Data were collected from 98 female undergraduates (43 from Van Diest et al., 2001a; 55 from Van Diest et al., submitted,a). Their age was 17 to 20 years and they participated in return for course credit.

8.3.2 Materials

Questionnaires

All participants completed the trait version of the Positive and Negative Affect Schedules (PANAS; Watson et al., 1988) and the Questionnaire Upon Mental Imagery (QMI; Sheehan, 1967).

Scripts

Participants imagined each 8 scripts in both studies. In order to answer our research question, we selected two fearful scripts that were applied in both studies. One script ("exam") depicted someone who is getting anxious about the upcoming exams; the other script ("elevator") depicted a panic attack of someone who is stuck in an elevator.

Apparatus and physiological recordings

A capnograph (POET, RC, Criticare) measured $FETCO_2$ (nasal sampling). Ventilation was measured non-intrusively with respiratory inductive plethysmography (Respitrace Corporation, Model 150, New York). In a calibration procedure preceding the imagery, ventilation was measured simultaneously by means of a pneumotachograph (Fleisch No. 2, Switzerland) and the Respitrace. A multiple linear regression yielded the regression coefficients needed for the reconstruction of the volume. Specific software determined following parameters

for each breath off-line: inspiratory (Ti) and expiratory (Te) time in s, inspiratory (Vi) and expiratory (Ve) volume in ml, drive (Vi/Ti) in ml/s and $FETCO_2$ in %.

8.3.3 Procedure

All participants completed the PANAS in group sessions preceding the experiments.

An imagery trial consisted of the following consecutive phases:

- Baseline (60 s): Participants were to close their eyes and listen to relaxing music
- Script (60 s): Participants were asked to start imagery as soon as they heard the text
- Silence (90 s): Participants had to continue the imagery as vividly as possible. After 60 s, a low-level, short auditory signal reminded the participant to continue imagining the scene as vividly as possible.
- Recovery (60 s): Participants were instructed to stop imagery, to keep the eyes closed and to listen to another piece of relaxing music.

Response training as described by Lang et al. (1980) was applied. After each imagery trial, the participant rated her experience during imagery on pleasantness, arousal, dominance (Bradley & Lang, 1994) and vividness. At the end of the experiment, the participants completed the QMI (Sheehan, 1967) and the experimenter checked whether or not they had voluntarily controlled their breathing during one or more imagery trials.

8.3.4 Data reduction and analyses

In order to check for differences between both studies on the scores on the PANAS and the QMI, t-tests were applied.

Within subject SD's of Ti, Te, V_T, drive and $FETCO_2$ during baseline (60 s), script (60 s) and silence (90 s) were calculated for each subject and each script.

An ANOVA with Study (one/three) as between subject variable and Script (exam/elevator) as within subject variable was run in order to check for differences between studies and scripts in the within subject SD's of Ti, Te, V_T, drive and $FETCO_2$ during baseline. Since no differences between studies and scripts were apparent on any of these baseline SD measures, the baseline data of both studies were collapsed, resulting in mean baseline within SD's across scripts for each subject.

In order to check whether trait anxiety was associated with a reduced variability in breathing parameters during rest, correlations between NA and the within subject SD's of Ti, Te, V_T, drive, and $FETCO_2$ during baseline (means across scripts) were calculated. Exploratorily, similar correlations were calculated with PA.

In order to check whether intra-individual differences in anxiety were associated with a reduction in breathing variability, within subject SD's of Ti, Te, V_T, drive and $FETCO_2$ were analyzed in ANOVA's with Study (one/three) as between subject variable and with Period (baseline, script, imagery) and Script (exam/elevator) as within subject variables. The hypothesis that anxious imagery was associated with a decrease in respiratory variability was tested more directly using planned comparisons contrasting baseline with subsequent script and imagery periods. Greenhouse-Geisser corrections were applied to all effects involving Period.

8.4 Results

Participants of both studies did not differ on the scores of the PANAS, nor on the QMI (see table 8A).

Table 8A. Mean, SD and t's of NA, PA and QMI for Study One (N = 43) and Study Three (N = 55)

	Study 1		Study 3		t(96)
	M	SD	M	SD	
NA	25.30	7.57	25.96	9.47	-.37
PA	32.87	5.10	32.27	5.80	.53
QMI	92.83	24.11	85.52	20.60	1.58

With respect to the within subject SD's of Ti, Te, V_T, drive and $FETCO_2$ during baseline, no significant main effects of Study or Script, nor Study x Script interactions were present for any parameter.

8.4.1 Trait anxiety and respiratory variability

Table 8B displays the correlations of NA and PA with the within subject SD's of Ti, Te, V_T, drive and $FETCO_2$ during baseline. All correlations were negative for NA and positive for PA, suggesting that trait NA is associated with a decreased variability in respiration during rest, and vice versa for trait PA. However, only few correlations reached statistical significance. The negative correlation of NA with the within SD of Ti was significant ($r = -.23$, $p < .05$) and marginally significant for the within SD of $FETCO_2$ ($r = -.19$, $p = .067$). The reversed pattern was found for PA: the within SD's of Ti and $FETCO_2$ correlated positively with PA (respectively $r = .21$, $p < .05$ and $r = .23$, $p < .05$). A marginally significant positive correlation between PA and the within SD of Te was observed ($r = .19$, $p = .059$).

Table 8B. Correlations between NA and PA, and the Within Subject SD's of Ti (in s), Te (in s), V_T (in ml), drive (in ml/s) and $FETCO_2$ (in %) during Baseline, N = 98

	NA	PA
Ti	-.23**	.21**
Te	-.07	.19*
V_T	-.10	.16
Drive	-.17	.15
$FETCO_2$	-.19*	.23**

Note: * $\underline{p} < .10$, ** $\underline{p} < .05$

8.4.2 Intraindividual differences in anxiety and respiratory variability

No main effects of Study, nor any interactions of Study with Period and/or Script were present for the within SD measures (see table 8C for means and SD's).

Table 8C. Mean within subject SD of Ti (in s), Te (in s), Vi (in ml), drive (in ml/s) and $FETCO_2$ (in %) during Baseline, Script and Imagery (N = 98)

	Exam						Elevator					
	Baseline		Script		Imagery		Baseline		Script		Imagery	
	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD
Ti	.31	.35	.30	.22	.33	.26	.31	.25	.31	.23	.37	.25
Te	.65	.58	.50	.32	.59	.38	.56	.42	.56	.39	.68	.45
Vt	82	80	78	69	83	59	85	88	85	81	96	96
Drive	48	29	42	22	45	23	49	39	52	28	60	38
$FETCO_2$	.15	.20	.17	.16	.22	.16	.15	.14	.25	.24	.33	.24

For Te, both a main effect of Period ($F(2, 192) = 6.32$, $p < .01$, $\varepsilon = .74$) and a Period x Script interaction ($F(2, 192) = 7.02$, $p < .01$, $\varepsilon = .74$) emerged (see figure 7). Further testing showed that the within SD of Te decreased from baseline to the script and imagery periods in the exam script, $F(1, 96) = 6.50$, $p < .05$. This was not the case when imagining the elevator script, $F(1, 96) = 1.71$, n.s..

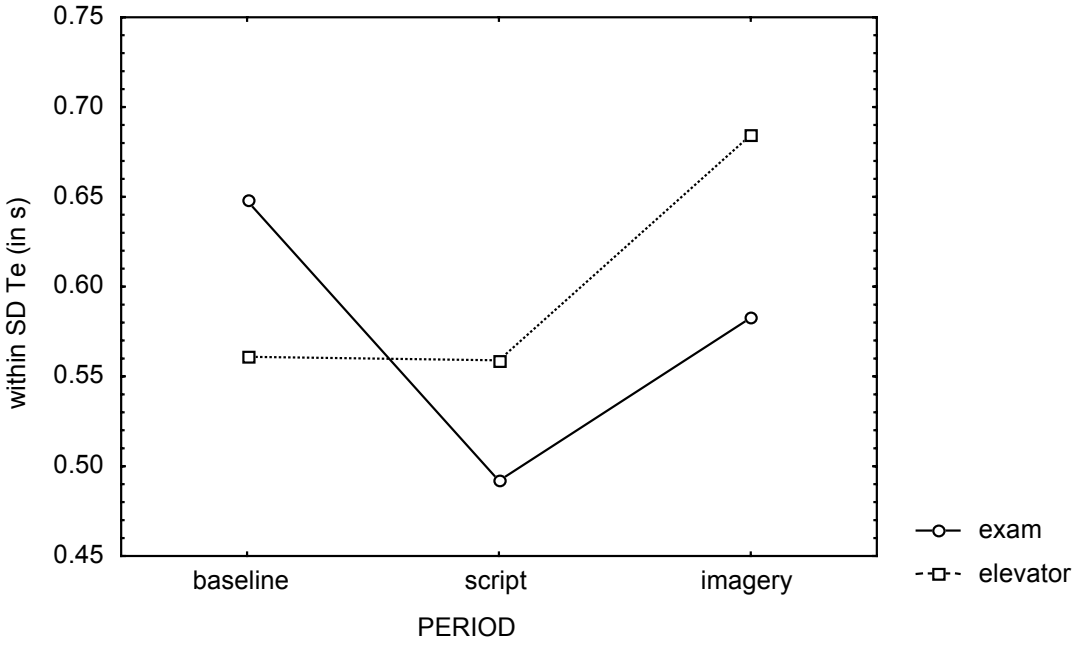


Figure 7. Within SD of Te during baseline, script and imagery

Similarly, both a main effect of Period ($F(2, 192) = 18.26$, $p < .01$, $\varepsilon = .70$) and a Period x Script interaction ($F(2, 192) = 5.95$, $p < .01$, $\varepsilon = .74$) were present for drive (see figure 8). The within SD of drive decreased from baseline to the script and imagery periods in the exam ($F(1, 96) = 3.80$, $p = .05$), but not in the elevator script ($F(1, 96) = 2.11$, n.s.).

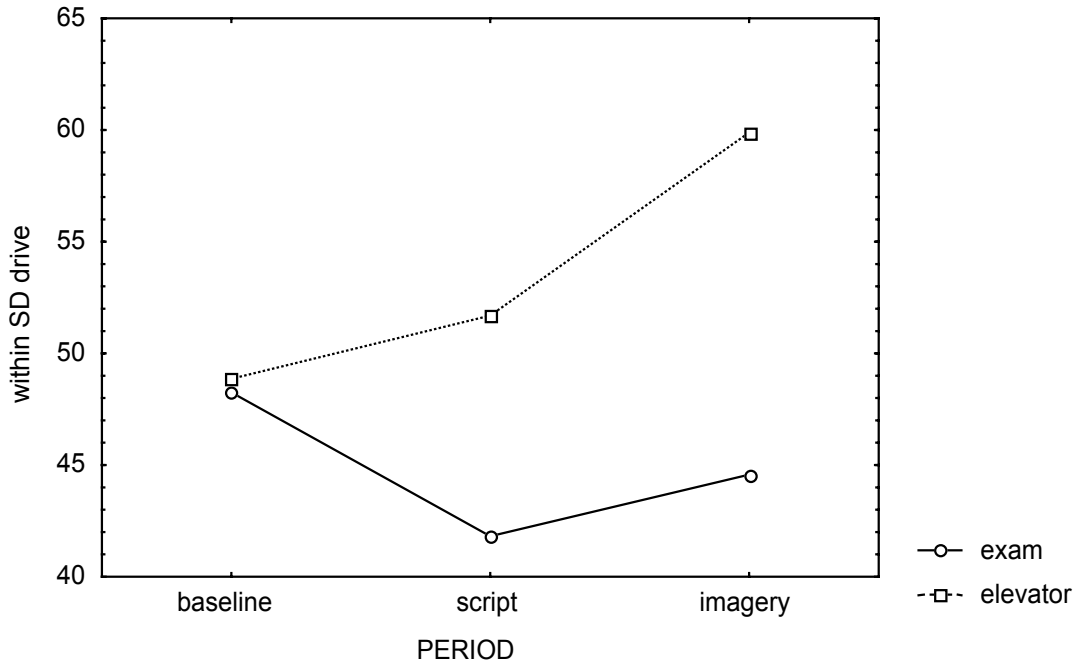


Figure 8. Within SD of drive during baseline, script and imagery

Significant main effects of Period ($\underline{F}(2, 192) = 24.03$, $\underline{p} < .01$, $\varepsilon = .70$) and Script ($\underline{F}(2, 192) = 13.28$, $\underline{p} < .01$) on $FETCO_2$, as well as Period x Script – interaction showed up ($\underline{F}(2, 192) = 10.70$, $\underline{p} < .01$, $\varepsilon = .70$, see figure 9). Compared to baseline, the within SD of $FETCO_2$ was increased during the Script and Imagery periods (exam: $\underline{F}(1, 96) = 5.07$, $\underline{p} < .05$; elevator: $\underline{F}(1, 96) = 28.36$, $\underline{p} < .001$), but less so in the exam script.

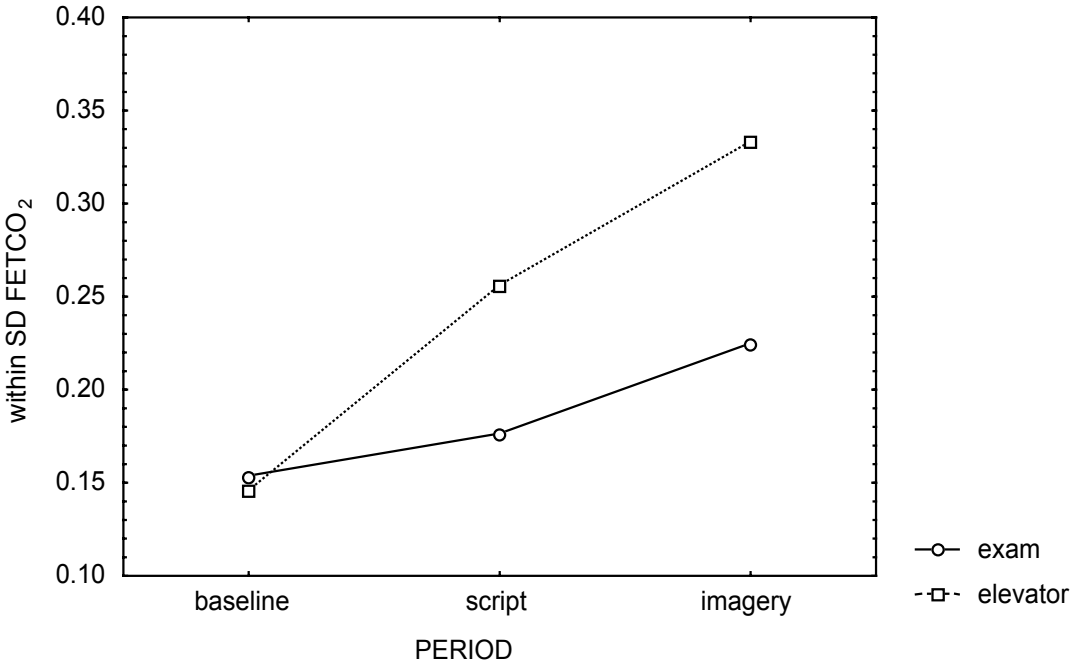


Figure 9. Within SD of $FETCO_2$ during baseline, script and imagery

8.5 Discussion

Our data clearly show that during resting ventilation, higher trait NA is associated with a reduced variability in Ti and, marginally significantly, also with a reduced variability in $FETCO_2$. The opposite is true for trait PA: higher trait PA is significantly associated with more variability in Ti and $FETCO_2$. Variability in Te tends to correlate positively with trait PA as well. Although the NA and PA are thought to reflect uncorrelated dimensions (Watson et al., 1988), they correlated -.39 in our participants, which may explain the reported opposite pattern of correlations with the within SD measures of breathing.

The mean within SD's of Ti, Te, V_T and drive during baseline are in the range that could be expected for normal resting respiration following Bruce and

Daubenspeck (1995), i.e. 10-30 % (SD/means were 18%, 24%, 23% and 21%, respectively). For $FETCO_2$, this coefficient of variation was only 3%, reflecting the tight regulation of this parameter by chemical feedback loops. Calculating correlations of NA and PA with these coefficients of variation yielded similar results as with the within subject SD's for all parameters.

The results regarding intra-individual differences in anxiety and breathing variability are more complicated. A reduced variability in Te and drive was present for the exam script, but not when imagining the elevator script. The within SD of $FETCO_2$ increased from baseline to imagery, particularly in the elevator script. This pattern of results is likely due to stronger hyperventilation responses in the elevator script as opposed to the exam script (see Van Diest et al., 2001a). Hyperventilation or a decreasing $FETCO_2$ is associated with a discontinuation of steady-state ventilation, meaning that inspiratory drive is changing over time. Evidently, such an increasing respiratory drive and a decreasing $FETCO_2$ during anxious imagery give rise to increased within SD's. However, the increased variability associated with the initializing of hyperventilation may be very different from chaotic variability. Whereas in the former, all parameters are moving in a coordinated way towards a new state characterized by an increased ventilation and a lowered $FETCO_2$, the latter refers to the uncertainty of the system growing exponentially with time. Discontinuation of steady-state ventilation, operationalized as a significant positive slope in drive, was present in 27 % of the participant during imagery of the elevator script, but only in 13% during imagery of the exam script. This may explain why the hypothesized decrease in breathing variability was present in the exam script, but not in the elevator script. In the latter, a higher proportion of participants had increased within SD's due to hyperventilation.

Our results may also shed some light on the paradoxical findings of an increased breathing irregularity in panic patients. Whereas an elevated respiratory variability during rest in normals may reflect a "healthy" power to respond to <u>any kind</u> of internal or external stimuli, it may reflect pathological readiness to respond to <u>threatening</u> stimuli in anxiety patients. The irregularity may come from an

alternation between different defensive behavior sets. For example, hyperventilation, which easily occurs during intense fear, may be alternated with more inhibitory influences upon breathing, as reflected in the occurrence of apneas and strained breathing (Fokkema, 1999). Such inhibited breathing pattern is believed to show up during anticipatory anxiety and attention (Van Diest et al., in press).

More generally, our results reveal an important constraint of using within SD's as a measure of flexibility. Indeed, within SD's may be influenced by several mechanisms of variability, distinct from chaos or flexibility in responding. Besides discontinuation of steady-state ventilation, also random variability and periodic instabilities in respiration may have influenced our measure (see Bruce & Daubenspeck, 1995, for a review on mechanisms and measures of ventilatory stability). Further research should apply more specific measures of chaos, such as the Lyapunov exponent, an index of the rate of divergence expressed in bits of information loss per s (Donaldson, 1992).

Chapter 9
Hyperventilation Symptoms and Negative Affectivity

9.1 Introduction

Negative affectivity (NA), neuroticism and trait anxiety are believed to be interchangeable concepts referring to the disposition to experience distress, to feel upset and to have a negative view of the self (Costa & McCrae, 1985; Watson & Clark, 1984). Since the NA dimension has been conceptualized as a 45° rotation of the valence and arousal dimensions (Watson & Tellegen, 1985), highly aroused and unpleasant affects can be considered as most prototypical for NA. We have found that particularly these (state) affects trigger most easily (but not exclusively) hyperventilation responses (Van Diest et al. 2001a,b; Van Diest et al., submitted,a). Therefore, the disposition to experience these affects may constitute a dispositional vulnerability factor for the occurrence of hyperventilation induced hypocapnia and its associated symptoms. Although findings from a previous study (Van Diest et al., in press) showed no evidence for an association between high levels of NA and chronic hyperventilation, NA may constitute a vulnerability factor for acute hyperventilation. Indeed, NA is thought to refer both to habitual individual differences in affect and to an enhanced reactivity to stressors (Watson & Clark, 1984). In contrast with chronic hyperventilation, a potentially higher incidence of acute hyperventilation in high NA individuals renders no straightforward prediction about PCO_2 measurements in the laboratory. However, assuming that acute hyperventilation gives rise to a set of specific hypocapnia-related symptoms, a higher incidence of acute hyperventilation in high NA individuals should lead to a

stronger relationship of NA with prototypical hyperventilation symptoms than with bodily symptoms that are less likely due to hyperventilation.

Wientjes & Grossman (1994) report a correlation of .56 between trait anxiety as measured by the Dutch version of the State-Trait Anxiety Inventory (STAI; Van der Ploeg, 1980) and the Checklist for Psychosomatic Symptoms (CPS, Wientjes & Grossman, 1994). The latter questionnaire assesses the occurrence of hyperventilation-related symptoms in daily life. At first sight, the correlation reported by Wientjes & Grossman (1994) seems to be somewhat higher than the typically found low to moderate positive correlations of trait anxiety or NA with other symptom checklists (Watson & Pennebaker, 1989). However, this may be due to the CPS including also some psychological symptoms that show obvious overlap with NA, namely "feelings of unrest or panic", "feeling anxious", "tenseness" and "fits of crying". Using data obtained from 5 consecutive cohorts of psychology freshmen in the period 1998-2003, we found a correlation of .43 (N = 1866, 1505 women) between the NA-scale of the PANAS (Watson & Tellegen, 1988) and the CPS when these four psychological symptoms were excluded in the calculation of the total symptom score on the CPS. This suggests that the CPS is not more strongly related to NA than other symptom checklists that are less specific for hyperventilation (e.g., Pennebaker, 1982; Ursin, Endresen, & Ursin, 1988). On the other hand, the symptoms of the CPS are not exclusively, nor all equally strongly related to hyperventilation. For example, although a certain relationship with hyperventilation may exist, it is very likely that symptoms such as "cold hands or feet" and "tiredness" are most often caused by mechanisms other than hyperventilation, especially in the young, non-clinical samples we have studied. Therefore, a more thoughtful approach may be to look at the differential association of NA with individual symptoms, which vary in their typicality for hyperventilation induced hypocapnia.

We thought that it would be useful to explore the variability in the correlations of NA with a wide variety of individual bodily symptoms in first step (study 7).

Indeed, only few studies have questioned to which extent symptoms differ in their relationship with NA. We argue that such an approach may reveal important processes underlying the NA – symptom relationship in general.

In a second step (study 8), we will specifically focus on the question whether symptoms that are prototypical for hyperventilation induced hypocapnia bear a stronger relationship with NA than symptoms atypical for hypocapnia.

9.2 Negative Affectivity and Subjective Health: A Closer Look into the Relationship

Van Diest, De Peuter, Eertmans, Notebaert, Victoir, & Van den Bergh (submitted,b)

9.2.1 Abstract

We studied the association between Negative Affectivity (NA) and a variety of individual symptoms. A sample (N = 720) of young, healthy students completed a 72-items symptom checklist and two trait NA measures. Psychologists (N = 52) scored each symptom on the extent to which a particular symptom (1) refers to a specific location in the body ("vagueness"), (2) is likely to be a physiological manifestation of anxiety ("anxiety"), and (3) may refer to both a physical condition and a negative emotion ("content overlap"). The correlations of individual symptoms with NA were highly variable and positively related to the vagueness dimension. The anxiety and content overlap dimensions predicted the correlations in women, but not in men. In an explorative factor analysis on the symptom checklist, two symptom factors were extracted. The first factor grouped hyperarousal symptoms typically associated with fight/flight tendencies; the second factor clustered systemic and sickness symptoms possibly stemming from a functional system promoting recuperative behavior in response to stress.

9.2.2 Introduction

People high in trait negative affectivity (NA), a disposition to experience negative mood states, tend to report retrospectively more bodily symptoms (Costa & McCrae, 1987; Watson & Pennebaker, 1989). Despite many differences between studies in questionnaires assessing NA, response formats, samples used and symptoms assessed, positive correlations have been found very systematically, ranging from .19 up to .72 (Brown & Moskowitz, 1997; Costa & McCrae, 1980, 1987; Elliot & Sheldon, 1998; Feldman et al., 1999; Gijsbers van Wijk & Kolk, 1996; Kolk, Hanewald, Schagen, & Gijsbers van Wijk, 2002; Larsen, 1992; Mora et al., 2002; Parker, Bagby, & Taylor, 1989; Smith, Pope, Rhodewalt, & Poulton, 1989; Vassend, 1989; Vassend, Watten, Myhrer, & Syvertsen, 1994; Watson & Pennebaker, 1989; Williams & Wiebe, 2000).

Although various studies point to an association of trait NA with "objective" health (e.g., Booth-Kewley & Friedman, 1987; Denollet & Van Heck, 2001; Morag, Morag, Reichenberger, Lerer, & Yirmiya, 1999), Pennebaker & Watson (1991) do not believe that objective health differences can fully account for the correlation between NA and symptom reporting. The same authors concluded that "trait NA has a general, nonspecific relationship with symptom reporting" (Pennebaker & Watson, 1991, p. 67) and proposed to broaden the concept of NA to a general "somatotopsychic distress" factor.

However, other authors found that symptom groups were differentially related to NA. For example, Diefenbach, Leventhal, Leventhal and Patrick-Miller (1996) found a cross-sectional association of depressive affect with systemic, flu-like symptoms, but not with more local, specific symptoms associated with inoculation. In contrast with depressive, respiratory and gastro-intestinal symptoms, Larsen (1992) found no significant correlation between neuroticism and aches that are mainly associated with muscle problems. Similarly, Vassend (1989) reported a weaker correlation of trait NA with musculo-skeletal symptoms than with cardiac

and fatigue symptoms. Vassend (1989) and Diefenbach et al. (1996) relate their findings to the vagueness of the symptoms: the observation and/or reporting of diffuse symptoms would be more likely to be biased by individual differences in negative affect than symptoms with a clear location in the body.

Another interpretation of the differences among symptoms in strength of their association with NA may be that the symptom groups more frequently reported by people scoring high on trait NA actually reflect physiological reactions to stress. Indeed, since high NA people are thought to experience more stress, even in the absence of any overt stressor (Watson & Clark, 1984), it almost logically follows that they would present more somatic manifestations of stress and anxiety. However, most studies investigating the relationship of NA with "objective" markers of functioning have focused on mortality rates or on serious health problems such as coronary heart diseases or cancer. Physiological stress reactions that can give rise to symptoms but do not necessarily imply an increased major health risk, have not been studied thoroughly as a possible mediating mechanism in the NA - symptom relationship[14].

Yet another process possibly contributing to the NA - symptom relationship may be a degree of overlap between words or phrases that one may use to report psychological and physical distress. For example, whereas "tooth ache" refers quite clearly to a physical condition, phrases like "fatigue" or "suffocating feeling" may refer both to psychological and physical conditions.

In the present study, we deliberately took bodily symptoms as a point of departure and focused on the association of different individual symptoms and symptom categories with measures of negative affect. The first aim was to test whether the association of an individual symptom with trait NA could be related to the extent to which that particular symptom (1) has a clear location in the body ("vagueness" dimension), (2) is likely to be a physiological consequence of anxiety

[14] Recently, we showed that hyperventilation induced hypocapnia could be ruled out as a possible candidate for a stress-related physiological disturbance underlying the association between reported symptoms and NA (Van Diest et al., in press).

("anxiety dimension"), and (3) can refer both to a physical condition and a negative emotion ("content overlap"). Because of sex differences in symptom reports (Gijsbers van Wijk & Kolk, 1997; Pennebaker, 1982), symptom perception processes (Leventhal, 1994; Pennebaker, 2000; Williams & Wiebe, 2000) and possibly also in stress physiology (Taylor et al., 2000), the associations of NA with individual symptom reports were considered separately for women and men. Students (N = 720) completed two trait NA measures and a 72-items symptom scale. Correlations of trait NA with the 72 individual symptoms were calculated and predicted by the scores of each symptom on the vagueness, anxiety, and overlap dimensions. The latter scores were obtained from 52 psychologists rating each symptom on each of the three dimensions.

A second, explorative aim of this study was to identify groups of somatic symptoms that are differentially related to different affects. To this end, the individual items of the symptom scale were factor analyzed. In subsequent multiple regression analyses, positive and negative affectivity adjectives from the PANAS (Watson et al., 1988) were used as predictors of the symptom factor scores.

9.2.3 Method

Participants

Two cohorts of psychology freshmen (first cohort: 349 women, 80 men; second cohort: 273 women, 48 men) completed two measures of trait NA and a 72-items symptom checklist. Data of 3 men and 17 women were incomplete and excluded from further analyses.

For the ratings of the symptoms on "vagueness", "anxiety" and "overlap", 175 psychologists (faculty staff) were invited to participate. From that group, 52 psychologists (18 Ph.D., 32 MA, 2 BA; 31 men) volunteered to participate (response rate of 30,3 %).

Measurements

Trait NA. Participants completed a Dutch translation of the Positive and Negative Affect Schedule (PANAS; Watson et al., 1988), and the Zelfbeoordelingsvragenlijst (ZBV; Van der Ploeg, 1980). The ZBV is the validated Dutch version of the STAI-T (Spielberger et al., 1970). Both the STAI-T and PANAS are considered good measures of NA (Watson & Clark, 1984).

Symptoms. A list of 72 somatic symptoms was constructed (see table 9A). It included 31 symptoms from the Checklist for Psychosomatic Symptoms (CPS; Wientjes & Grossman, 1994). Because these 31 items mostly refer to symptoms typically associated with hyperventilation, we added another 41 symptoms that are less likely due to hyperventilation. In order to avoid overlap with NA, psychological or anxiety symptoms such as "tensed" or "nervous" were not included. The resulting questionnaire included a broad array of respiratory, cardiac, gastro-intestinal, paresthesia, neurological, musculo-skeletal, dermatological, flu-like and cold symptoms, as well as symptoms such as lump in throat, blurred vision, shivering, ringing ears, tooth ache, irritated eyes and headache. As such, it encompassed most bodily symptoms of other regularly used symptom questionnaires (e.g., the PILL, Pennebaker, 1982; Ursin's Health Inventory, Ursin et al., 1988). Two symptoms were assessed only in women: painful breasts and menstruation pains. Participants had to rate the extent to which they had felt each symptom during the past year (never, rarely, regularly, often, very often, coded from 1 to 5).

Symptom Ratings. The psychologists rated each symptom on the following dimensions:

(1) Vagueness: To which extent does each of the enlisted symptoms refer to a specific location in the body? You may answer with "1 = very hard to locate", "2 = hard to locate", "3 = nor hard, nor easy to locate", "4 = easy to locate", "5 = very easy to locate".

(2) Anxiety as a cause: To which extent may each of the enlisted symptoms be caused by anxiety? You may answer with "1 = very unlikely", "2 = unlikely", "3 = equally likely as unlikely", "4 = likely", "5 = very likely")

(3) Overlap: To which extent can each of the enlisted somatic symptoms also express a negative emotional state? You may answer with "1 = very hardly", "2 = hardly", "3 = nor hardly, nor easily", "4 = easily", "5 = very easily".

The scores on the first dimension were reversed before analyses.

Procedure

The students completed both NA measures and the symptom checklist in collective group sessions. The psychologists were invited to participate by email and completed the ratings electronically.

Data analyses

In order to maximize reliability, a composite score for trait NA was calculated by averaging the standardized scores of the NA-scale of the PANAS and the STAI. The scores were standardized for each gender x cohort-combination separately. In order to check whether the NA – symptom reporting relationship was replicated in our data, the correlations of the trait NA score and the sum score of all symptom items[15] were calculated for women and men.

Correlations between the trait NA scores and the individual symptom scores, standardized within each gender x cohort-combination, were calculated for men and women. In a next step, these correlations were Z-transformed (Edwards, 1976) and predicted in a multiple regression analysis by the psychologists' ratings of each symptom on the three dimensions. Since the anxiety and overlap dimensions correlated highly ($r = .87$, $p < .01$), putting both predictors in the regression model

[15] Since "painful breasts" and "menstruation pains" only applied to women, the number of symptoms included in analyses on data obtained from women only differed from analyses also including men (respectively 72 and 70).

would yield unreliable regression coefficients. Therefore, two multiple regressions were run separately for men and women: a first with vagueness and anxiety, and a second with vagueness and overlap as predictors.

The underlying structure of the symptom checklist was explored using principal component analysis. Scree-plots of Eigenvalues were inspected for decisions on factors. A normalized varimax rotation was used to interpret the factor solution. In order to see which affects would be predictive for the retained symptom factors, multiple regressions were run with scores on the individual items of the PANAS as predictors for the symptom factor scores. Correlations between the items of the PANAS were calculated and checked for multicollinearity. Six items of the PANAS were discarded as predictors because they correlated more than .50 with one or more other PANAS-items.

9.2.4 Results

The correlations of trait NA with the total symptom score were .49 and .46 for women (N = 605) and men (N = 124), respectively ($p<.001$). The correlations of trait NA with each individual symptom ranged from -.02 up to .48 (see table 9A).

Table 9B summarizes the multiple regression results. The "vagueness" and "overlap" ratings explained 44% of the variance in the Fisher Z-transformed correlations in women, and 11.4% in men. In the analyses with "vagueness" and "anxiety" as predictors, R^2's were 34.2% and 11.8%, respectively. All predictors were significant in the analyses for women. For men, only "vagueness" was a significant predictor if the anxiety dimension was the other predictor in the model.

Table 9A. Correlations of Symptoms with Negative Affectivity for Women (N = 605) and Men (N = 125)

Symptom	W	M	Symptom	W	M
Loosing contact with reality	.43	.42	Upper back pain	.22	.25
Fatigue	.41	.43	Irritated eyes	.22	.07
Trouble sleeping	.41	.32	Tingling sensations in arms	.22	.13
Trouble concentrating	.40	.48	Tingling face	.21	.06
Being confused	.36	.35	Hot flushes	.21	.21
Drowsiness	.34	.40	Frequent urinating	.21	.34
Feeling separated from body	.33	.24	Stomach cramps	.19	.17
Chest feeling blown up	.32	.37	Low back pain	.19	.01
Trembling hands	.31	.46	Pain in shoulders	.19	.14
Nausea	.30	.26	Tingling fingers	.19	.19
Unable to catch enough air	.29	.32	Lump in throat	.19	.09
Tightness in chest	.29	.31	Painful breasts	.18	
Unable to breathe deeply	.28	.34	Diarrhea	.18	.05
Bloated belly or stomach	.28	.26	Being windy	.18	-.02
Feeling of nearly fainting	.28	.18	Constipation	.18	.30
Heartburn	.27	.10	Blurred vision	.18	.27
Suffocating feeling	.27	.21	Tooth ache	.17	.14
Lightheadedness	.27	.18	Pain in arms	.17	.22
Upset stomach	.26	.26	Stiffness in fingers/ arms	.17	.32
Heart palpitations	.26	.20	Blackness before eyes	.16	.13
Chest pain	.25	.27	Joint pains	.16	.15
Irregular heartbeat	.25	.18	Strong heartbeat	.16	.28
Dyspnea	.25	.31	Burning eyes	.16	.11
Buckling knees	.24	.28	Sore throat	.13	.29
Neck pain	.24	.37	Tingling feet	.13	.11
Deeper or faster breathing	.24	.18	Coughing	.12	.37
Shivering	.24	.20	Menstrual pains	.12	
Vertigo	.23	.34	Having a cold	.12	.23
Sore eyes	.23	.46	Cramps in legs or toes	.11	.09

Table 9A continued.

Symptom	W	M	Symptom	W	M
Tingling sensations in legs	.23	.05	Itchiness	.10	.28
Headache	.23	.08	Fainting	.10	.04
Dizziness	.23	.24	Dry throat	.09	.19
Numb feeling in a body part	.22	.29	Skin rash	.09	.19
Ringing ears	.22	.28	Cold hands or feet	.09	.23
Warm feeling in the head	.22	.07	Feeling warm	.02	.09
Rapid heartbeat	.22	.23	Nasal congestion	.01	.23

Note: W = women; M = men

Table 9B. Fisher Z-transformed Correlations of NA with Symptoms as Predicted by the Vagueness and Anxiety, and by the Vagueness and Overlap Dimensions for Women (N = 72) and for Men (N = 70)

	Women			Men		
Predictor	B	SE B	β	B	SE B	β
Vagueness	.04	.009	.41***	.03	.01	.29**
Anxiety	.03	.009	.33***	.01	.02	.09
Vagueness	.02	.009	.25**	.03	.02	.23*
Overlap	.05	.01	.51***	.02	.02	.17

Note: *$\underline{p}$ < .10, **$\underline{p}$ < .05, ***$\underline{p}$ < .01

Two factors that explained together 25.5% of the variance in the individual symptom reports were retained on the basis of a scree test. Table 9C displays the factor loadings of the most representative symptom items. The first factor explained 13.1 % of the variance and grouped mainly cardiorespiratory panic-like symptoms. The second factor explained 12.4% of the variance and clustered a set of "sickness" symptoms, more particularly systemic and gastro-intestinal symptoms.

The participants' factor scores on the first factor were positively related to reports of "scared", "hostile", "distressed" and "guilty" affect (R^2 = 14.6%). Factor scores on the second extracted factor were positively related to "distressed", "ashamed", "guilty" and negatively to "attentive" (R^2 = 9.8 %). Table 9D summarizes these multiple regression results.

Table 9C. Factor Loadings of the Most Representative Symptoms for Factor 1 and Factor 2

Symptom	Factor 1	Factor 2
Dyspnea	.65	-.02
Irregular heartbeat	.64	.12
Heart palpitations	.64	.12
Tightness in chest	.63	.10
Unable to catch enough air	.63	.12
Chest pain	.57	.19
Unable to breathe deeply	.56	.09
Rapid heartbeat	.56	.18
Faster/deeper breathing	.55	.11
Strong heartbeat	.55	.19
Chest feeling blown up	.55	.21
Fatigue	.20	.58
Flu-like feeling	-.04	.55
Tired eyes	.20	.54
Upset stomach	.15	.53
Dry throat	.06	.53
Nausea	.20	.49
Stomach or belly cramps	.14	.48
Bloated stomach	.25	.48
Coughing	.07	.47
Drowsiness	.21	.46
Headache	.06	.45

Table 9D. Factor Scores as Predicted by 14 Individual Affect items (N = 710)

	Factor 1			Factor 2		
Predictor	B	SE B	β	B	SE B	β
Interested	-.10	.06	-.07	.03	.06	.02
Distressed	.12	.04	.11***	.13	.05	.12***
Excited	-.09	.05	-.07	.05	.05	.04
Guilty	.07	.04	.08*	.07	.04	.08**
Scared	.19	.04	.20***	.06	.04	.06
Hostile	.11	.04	.09**	-.01	.05	-.01
Proud	.04	.04	.03	-.01	.05	-.01
Irritable	-.00	.04	-.01	.07	.04	.07
Alert	-.04	.05	-.03	-.04	.05	-.04
Ashamed	-.00	.04	-.00	.09	.04	.09**
Inspired	.06	.04	.06	-.02	.04	-.02
Determined	.05	.05	.04	.05	.05	.05
Attentive	.03	.05	.02	-.11	.06	-.08**
Nervous	.05	.04	.05	.02	.04	.02

Note. **p < .05, ***p < .01

9.2.5 Discussion

We replicated the positive, moderate correlation between NA and symptoms typically reported in other studies (e.g., Parker et al., 1989; Smith et al., 1989; Watson & Pennebaker, 1989; Williams & Wiebe, 2000). The correlations of NA with individual symptom reports were substantially lower and highly variable. Generally, fatigue and neurological symptoms correlated strongest with NA, followed by hyperventilation and panic-like symptoms (see table 9A). The pattern of correlations for men did not mirror exactly that of women. For example, 2 out of the 10 symptoms correlating strongest with NA in women (see first 10 symptoms in

table 9A), were only on the 29th ("nausea") and on the 31st position ("feeling separated from your body") in men. Also "heartburn", "tingling sensations in face", "tingling sensations in legs", "low backpain" and "being windy" were particularly related to NA in women only. Conversely, the top 10 for men contained four symptoms that were only weakly associated with NA in women: "neck pain", "stiffness in fingers or arms", "tired eyes" and "coughing" related stronger to NA in men than in women. Furthermore, "itchiness" and "nasal congestion" were particularly related to NA in men but not in women. These differential associations of NA with individual symptoms may be caused by symptoms associated with reproductive systems, but also with gender differences in stress physiology (Taylor et al., 2000), self-focused attention (Mor & Winquist, 2002; Williams & Wiebe, 2000) and/or gender role. However, it is not obvious how such gender differences may lead to the observed differential pattern of correlations in men and women. Alternatively, the differential pattern may be due to less reliable correlations for men. Indeed, our sample size of man (N = 125) was much smaller than that of women (N = 605).

The vagueness dimension was a significant predictor of the strength of association between a particular symptom and NA, both in men and in women. NA is more strongly related to the report of vague symptoms, such as fatigue, and less to symptoms with a specific location in the body (e.g., cramps in legs). Therefore, our data confirm the interpretation proposed by Vassend (1989) and Diefenbach et al. (1996) for their results. In line with evidence of an overgeneral retrieving style of self-relevant material in depressed and traumatized people (McNally, Litz, Prassas, Shin & Weathers, 1994; Williams & Scott, 1988), it may be that high NA people also encounter more difficulties retrieving specific bodily symptoms. Alternatively, vague symptoms may be more vulnerable to a mood congruent or other recall biases (Diefenbach et al., 1996). However, it may also be that physiological manifestations of stress are more apparent in general and distributed, as opposed to specific and localized somatic systems. More generally, this points to a paradox in the literature

on NA and symptom reporting: although it is often taken for granted that high NA people "overreport" or "exaggerate" their symptoms, only few research has focused on the accuracy question. Indeed, the NA – symptom reporting relationship may stem as well from a better ability of low NA people to disengage from minor, unpleasant somatic experiences. The adaptive value of such disengagement in daily life is evident.

The psychologists' symptom ratings on "anxiety as cause" correlated strongly (.87) with the ratings on the "overlap" dimension. Consequently, results were quite similar: both dimensions were significant predictors of correlations of individual symptoms with NA in women, but not in men. Several processes described in literature may account for this observed gender difference.

Whereas men rely particularly on internal physiological cues to define their symptoms, women rely more on external cues (Pennebaker, 2000). This gender difference may be a consequence of differential socialization patterns and/or evolutionary processes and may be functional in that distress in the offspring can be empathetically assumed when external stressors are present. In as far high NA people encounter more stressors than low NA people, external stressors (e.g., time pressure, troubled relationships, life events, …) may be important cues for the perception of stress-related symptoms particularly in high NA women.

A second possible explanation relates to trait self-focused attention, which has been found to partially mediate the effects of NA on symptom reports in women, but not in men (Williams & Wiebe, 2000). Assuming that high NA is associated with an increased sympathetic activation and self-focused attention with an enhanced interoception of such activation, it may be that women scoring high on NA and on trait self-focused attention are particularly accurate in perceiving and reporting the affective and somatic experiences associated with stress.

Yet another explanation for the anxiety and overlap dimensions being significant predictors of the association of individual symptoms with NA in women, but not in men, may be found in the typically female "tend and befriend response to

stress" (Taylor et al., 2000). Compared to men, women seek and use more social support when under stress. Since a first step of this coping response necessarily implies the social sharing of the stress experience, it can be expected that high NA women are also more likely to express bodily symptoms caused by anxiety ("anxiety dimension") or bodily symptoms that may refer also to a negative emotional state ("overlap").

We argue that the use of a homogeneous, relatively healthy sample may be viewed as an advantage because the association of NA with individual symptom reports in a more heterogeneous sample would likely to be more confounded with socio-demographical and biological variables associated with disease and symptom reporting. Also, we think that taking the perspective of individual symptoms as a departure point yields new and interesting ways of thinking about the NA-symptom reporting relationship in general.

Studies using factor analysis on reports of individual symptoms have traditionally retained four to nine factors clustering symptoms belonging to different organ systems, e.g., respiratory, cardiovascular, gastro-intestinal and musculo-skeletal symptoms (Han, Stegen, Schepers, Van den Bergh & Van de Woestijne, 1998; Larsen, 1992; Ursin et al., 1988; Wientjes & Grossman, 1994). Our data yielded a similar results pattern when eight factors were retained using the criterion of Eigenvalues > 1.5. However, when only two factors were retained based on the elbow criterion, an interesting and more compelling factor structure emerged. The two extracted symptom factors could easily be interpreted as symptoms stemming from two different functional behavioral systems regulating psychic and physiological adaptations to stress (Dantzer, 1993; Maier & Watkins, 1998). The first symptom factor grouped a set of cardiorespiratory hyperarousal symptoms (see table 9C), which can be viewed as caused by enhanced sympathetic activity in the service of a rapid energy mobilization for fighting or fleeing. Multiple regression analysis provided evidence for this interpretation: reports of "scared" and "hostile" affect were strong predictors of the factor scores on this first factor. However, also

"distressed" and "guilty" affects were significant predictors, suggesting that people who report to experience frequently highly aroused negative affects and hyperarousal bodily symptoms also regularly experience lower aroused, negative affects that are less specific for fight/flight. The second symptom factor incorporated more systemic symptoms (fatigue, drowsiness, headache, flu-like feeling) and sickness symptoms (coughing, stomach cramps, flu-like feeling), which may be related to a functional system promoting recuperative behavior and defensive withdrawal reflexes. Maier & Watkins (1998) suggest that this recuperative system involves a circuitry that may be activated both by environmental stressors and infectious agents and review evidence that it is related to depressive affect. The latter was confirmed also in our data: the factor scores on the second symptom factor were positively related to reports of "distressed"[16], "ashamed", and "guilty" affect, and also negatively to one positive affectivity item ("attentive"). The latter item being a significant predictor is quite important for our interpretation in terms of depressive affect. Indeed, Clark & Watson (1991) reviewed extensive evidence that depression, but not anxiety is associated with low positive affectivity.

To summarize, we found a great diversity in the extent to which individual symptom reports are related to NA. Symptoms without a salient location in the body bear a stronger relationship to NA than more localized symptoms. Also, high NA women (but not men) tend to report particularly symptoms that are considered as probably caused by anxiety and may refer both to a somatic sensation and a negative emotional state ("overlap").

In an explorative factor analysis on a 70-items checklist, two factors emerged that could be interpreted as bodily symptoms arising from two different functional behavioral systems in response to stress: sympathetic activation in the service of a rapid mobilization of energy and a functional system promoting recuperation.

[16] "Distressed" is very hard to translate in Dutch. We translated it into the Dutch word

9.3 The Specificity of the NA - Symptom Reporting Relationship for Hyperventilation

9.3.1 Introduction

When considering the pattern of correlations of NA with a variety of bodily symptoms (see table 9A), it is obvious that hyperventilation symptoms show a relatively strong association with NA. The present study aimed to investigate whether the typicality of a symptom for hyperventilation is a significant predictor after controlling for vagueness and overlap. Since hyperventilation may be associated with a wide variety of rather unspecific symptoms (Gardner, 1996) that may be triggered by other mechanisms as well, we opted to restrict our definition of hyperventilation symptoms to symptoms that relate specifically to hypocapnia. A similar approach as in 9.2 was followed: Z-transformed correlations of individual symptoms with NA were predicted by (1) typicality for hyperventilation, (2) vagueness, and (3) overlap. The symptoms ratings on "anxiety as a cause" were not entered as predictor in the model because of its relatedness to the "overlap" dimension and possibly also to "typicality for hyperventilation".

9.3.2 Method

In a study investigating the effect of hypocapnia on attentional performance (Van Diest et al., 2000), 42 participants performed both a hypocapnic and normocapnic overbreathing trial, the latter serving as a within subject control condition of the former. Following both overbreathing trials, symptoms were assessed using an adapted state version of the CPS. Three symptoms that are unlikely associated with hyperventilation ("joint pains", "low back pain" and "burning eyes") were added to

"droevig", which, when backtranslated, lies closer to "sad", than to "distressed".

the list. Since participants were instructed to pace their breathing, the item "deeper/faster breathing" made no sense and was not assessed. The four psychological symptoms of the CPS were assessed but not used in the present analyses because of their obvious overlap with NA. Change scores of the resulting 34 symptoms on the hypocapnic minus the normocapnic overbreathing trial were calculated and served as weights of typicality for hyperventilation (hypocapnia) in further analyses. These change scores varied from -.07 to .66. Symptoms with the highest change scores were dizziness (.66), blackness before eyes, fainting, warm feeling in the head (all .34), nausea and hot flushes (both .32). Symptoms with change scores of approximately zero were: burning eyes, bloated stomach, chest pain, joint pain, shivering, stomach cramps, low back pain, drowsiness, cold hand or feet and cramps in legs or toes.

The vagueness and overlap ratings were obtained from 52 psychologists (see 9.1.3 for further details). The correlations of NA with the 34 symptoms for which typicality weights were obtained were calculated separately for women (N = 1505) and men (N = 355). Data were collected from five cohorts of psychology freshmen (1505 women, 355 men) that had completed the PANAS and the CPS in collective group sessions. Because of slight but significant effects of cohort and gender on these measures, symptom and NA scores were standardized within each of the ten cohort x gender-combinations.

9.3.3 Results

The correlations between NA and the 34 symptoms for men and women were highly similar to those reported in table 9A. Therefore, we will not report the present correlations of a subset of 34 symptoms obtained from a larger sample of participants.

Table 9E displays the correlations between all variables included in subsequent multiple regression analyses.

Table 9E. Correlations between Typicality for Hyperventilation, Vagueness, Overlap, and Association Strength with NA for men and women (N = 34 symptoms)

	Z-women	Z-man	Typicality	Vagueness
Z-women				
Z-man	.71***			
Typicality	.07	-.16		
Vagueness	.25	.08	.26	
Overlap	.70***	.48***	.26	.37**

Note. Z-women = Z-transformed correlations of trait NA with individual symptom scores (N = 34) for women; Z-man = Z-transformed correlations of trait NA with individual symptom scores (N = 34) for men **p < .05, ***p < .01

Typicality correlated .26 both with the vagueness and the overlap ratings. The latter predictors correlated .37 with each other. Table 9F summarizes the multiple regression results for women and men. The typicality of a symptom for hyperventilation was not related to its association strength with NA. The overlap dimension was the only significant predictor in the model for both genders. R^2 's were .48 % and .30 % for women and men, respectively.

Table 9F. Multiple Regression analyses: the Z-transformed Correlations of Trait NA with Individual Symptom Scores (N = 34) as Predicted by Typicality for Hyperventilation, Vagueness and Overlap for Women and Men.

	Women			Men		
Predictor	B	SE B	β	B	SE B	β
Typicality	-.04	.06	-.09	-.07	.05	-.22
Vagueness	.00	.01	.03	-.00	.01	-.09
Overlap	.05	.01	.70***	.04	.01	.58***

Note: ***p < .01

9.3.4 Discussion

The extent to which an individual symptom is typical for hyperventilation induced hypocapnia did not predict the symptom's association strength with NA. This finding is in line with our observation that the correlation of NA with the total symptom score on a hyperventilation symptom checklist (CPS, Wientjes & Grossman, 1994) was in the range of reported correlations with symptom checklists that were not specific for hyperventilation. However, our failure to observe a relationship between the association strength of a symptom with NA and its typicality for hyperventilation may also be due to the rather restricted range of symptoms (N = 34) and the restricted variability in the typicality-scores of the symptoms included in the present study. Indeed, with the exception of the three symptoms added by the present authors (burning eyes, low back pain, joint pain), all symptoms were originally selected because "they were typically reported by hyperventilation patients" (Wientjes & Grossman, 1994). This is an important constraint potentially limiting the generalizability of the present finding. We argue that this study needs to be replicated using a larger and more differentiated set of bodily symptoms that vary more in their typicality for hyperventilation.

Previous findings regarding vagueness and overlap as predictors for the association of a symptom with NA (Van Diest et al., submitted,a) were not replicated. In contrast with the previous study, vagueness was no longer a significant predictor of the association strength of a symptom with NA. Another difference between both studies relates to the overlap dimension, which was a significant predictor of the association strength in the present, but not in the former study. A possible explanation of these differences between studies may be a less reliable NA-measure in the present study. Whereas a composite score of two NA questionnaires (STAI and PANAS) was used in the first study, only one NA measure (PANAS) was available in the present study using a larger sample of five cohorts of students. In order to test this, we ran similar multiple regression analyses

on the correlations between the composite NA scores and the 34 symptoms of the CPS, obtained from the two cohorts for which both NA measures were available. This yielded exactly the same pattern of results, ruling out an explanation in terms of a less reliable NA measure for the inconsistent findings between studies.

A more likely explanation may be found in the major constraint of the present study as compared to the previous study (9.2), i.e. the lower number of symptoms included in analyses. Because the typicality weights were available for only 34 symptoms, the number of observations to calculate correlations upon was reduced with more than 50 % as compared to the former study, leading to a substantial reduction in power. Assuming a low to moderate correlation of .30 between association strength of a symptom with NA and its typicality for hyperventilation, the power to detect it with 34 observations is only .54 (one-tailed; $\alpha = .05$). A sample of 70 observations (similar to the previous study), however, would have reasonable power (.82, one-tailed).

To summarize, the present study did not replicate our previous findings regarding the overlap and vagueness dimensions, nor did it confirm our hypothesis that the association strength of a symptom with NA could be predicted by its typicality for hyperventilation induced hypocapnia. However, we believe that this study has suffered from a lack of power. Further research is needed including a larger and more variable sample of symptoms.

Chapter 10

Hyperventilation and Attention :

Effects of Hypocapnia on Performance in a Stroop Task

Van Diest, Stegen, Van de Woestijne, Schippers, & Van den Bergh (2000). Biological Psychology, 53, 233-252.

10.1 Abstract

This study aimed to investigate the effect of hypocapnia on attentional performance. Hyperventilation, producing hypocapnia, is associated with physiological changes in the brain and with subjective symptoms of dizziness, concentration problems and derealization. In this study (N=42), we examined cognitive performance on a Stroop-like task, following either 3 min of hypocapnic or normocapnic overbreathing. Both overbreathing trials were run on separate days, each preceded by a baseline trial with the same task during normal breathing. More and other symptoms were reported after hypocapnia compared to normocapnia. Also, more errors were made and progressively slower reaction times (RT's) were observed during recovery from hypocapnia. These performance deficits were only found in participants characterized by apneas. The number of symptoms did not correlate with RT's or errors. The pattern of data suggested that hypoxia, as a result of apneas during recovery from hypocapnia, caused the cognitive performance deficit.

10.2 Introduction

Stress-induced hyperventilation may cause hypocapnia or a decreased CO_2-pressure in the blood ($PaCO_2$), which is associated with a variety of secondary physiological changes and subjective symptoms. It induces respiratory alkalosis (an increase in the blood pH), which enhances the excitability of the neurons, causing symptoms of tingling hands, feet or face and muscle spasm. Hypocapnia also affects colonic tone and sensation (Bharucha et al., 1996; Ford, Camilleri, Hanson, Wiste, & Joyner, 1995), as well as cardiac activity (Gardner, 1996), causing cardiac symptoms such as pounding heart, hot flushes, irregular and rapid heartbeat. In addition, hypocapnia produces cerebral vasoconstriction, which gives rise to cerebral hypoxia (a decreased oxygen supply to the brain), which depresses cortical functions in awake state (Gardner, 1996; Gotoh et al., 1965; Jibiki et al., 1992; Bisgard & Neubauer, 1997). Hypoxia is associated with headache and with subjective cognitive symptoms of dizziness, derealization, concentration problems, disorientation and fainting.

This study aimed to determine whether the subjective cognitive symptoms are associated with actual cognitive performance deficits. The general picture produced by the research on the effects of hypocapnia on cognitive performance is rather confusing and inconsistent, which may be related to quite a number of methodological flaws that will be addressed in this study. First, most of the studies (e.g. Allen & Morris, 1962; Balke & Lillehei, 1956; Marangoni & Hurford, 1990; Rushmer, Boothby, & Hinshaw, 1941; Scow, Krasno, & Ivy, 1950; Whitehead, 1977; Whitwam, Boettner, Gilger, & Littel, 1966) lack a normocapnic overbreathing condition in which normal PCO_2-levels are maintained by adding CO_2 into the inspired air. Such a condition is, in our view, an indispensable control for possible nonhypocapnia-related effects of hyperventilation on performance. Irrespective of the presence of hypocapnia, hyperventilation produces a set of respiratory symptoms (Hornsveld & Garssen, 1996) which may affect attention and performance. In addition, normocapnic overbreathing is needed to control for the aversiveness constituted by the experimental procedure itself. In our study, each subject will perform the attentional task following both

hypocapnic and normocapnic overbreathing, the latter serving as a within subject control condition.

Second, some studies (Balke & Lillehei, 1956; Gibson, 1978; Stoddart, 1967) measured performance while participants were hyperventilating. Gallego et al. (1991) found longer reaction times (RT's) during voluntarily controlled breathing in comparison to spontaneous breathing, suggesting that voluntary control is attention consuming, which may have influenced performance in those studies measuring performance while voluntary hyperventilating. In studies that overcome this problem by measuring performance following hyperventilation, time of measurement is ranging from immediately after (Marangoni & Hurford, 1990; Rushmer et al., 1941; Scow et al., 1950) till 90 min after hyperventilating (Blenkarn, Briggs, Bell, & Sugioka, 1972), giving rise to another source of variance in the reported effects. In the present study, we opted for measuring performance during 3 min following voluntary overbreathing. In this way, hypocapnia is ensured while avoiding the attention consuming effects of voluntary controlled breathing. Also, because a partial recovery of the PCO_2 can be expected during the 3 min of task performance following overbreathing (Corfield et al., 1995), we used a continuous measurement of cognitive performance to allow a close monitoring of the effects at different levels of hypocapnia.

Third, most studies overlooked the possible attention distracting effect of experienced symptoms on performance. Only Rushmer et al. (1941) paid attention to this important issue. These authors found a negative correlation between performance on a coordination task and reported symptoms, suggesting an attention disrupting effect of experienced symptoms. Therefore, symptoms will be assessed extensively following each task performance in our study.

Fourth, some studies investigating performance after passive hyperventilation[16] under general anesthesia during surgery did not control for surgery effects (Allen & Morris, 1962; Murrin & Nagarajan, 1974; Wollman & Orkin, 1968). Furthermore, all

[16] During passive hyperventilation, artificial respiration is applied to the participant.

participants had undefined medical problems, which also may have affected performance in those studies.

Fifth, many studies had a very low number of participants (N < 10) and a wide variety of tasks has been used, ranging from perception threshold (Gellhorn & Joslyn, 1937; Whitehead, 1977) and reaction time measurement (Wollman & Orkin, 1968) over motor and coordination tasks (Balke & Lillehei, 1956; Gibson, 1978; Rushmer et al., 1941; Stoddart, 1967) to more complex tasks of intellectual performance (Gibson, 1978; Marangoni & Hurford, 1990; Murrin, & Nagarajan, 1974; Nikolov, Patchev, Kisselova, & Harleva, 1991). According to Gibson (1978) and Garssen (1986), the only consistent finding is a worsening of motor performance. Because many tasks used to assess higher functions appeal to some motor activity (pressing a button), ambiguity may arise in attributing the effects. In our study, we used a task that comprised two subtasks: an easy number-naming task was alternated with a more difficult size-counting task, the latter bearing more upon controlled processing than the former. The task was conceived such that it was highly attention consuming with minimal involvement of other cognitive processes (e.g. memory). In contrast to the attentional demands, the required motor movement to respond was identical for both alternating parts, so that a mere motor decrement could be differentiated from attentional effects which have more impact on the number-counting task.

Sixth, most studies did not take into account individual differences in apneas during recovery from hyperventilation induced hypocapnia. When PCO_2 is low at the central chemoreceptors, ventilation is depressed and apneas occur to restore PCO_2 rapidly to baseline levels (Corfield et al., 1995; Meah & Gardner, 1994). Hypocapnia consistently induces apneas during NONREM sleep and anesthesia, but during wakefulness, large interindividual variability in the occurrence of apneas exists for as yet unknown reasons (Mangin et al., 1982; Shea, 1996). However, post-hyperventilation apneas can affect performance in different ways. On the one hand, the PCO_2 of subjects showing apneas recovers more rapidly, which may cancel out quicker possibly deteriorating effects of muscle spasm, cerebral vasoconstriction and subjective symptoms on performance. On the other hand,

apneas may induce prolonged central hypoxia because the rate of delivery of oxygen may fail to keep pace with the metabolic consumption (Cummin, Telford, & Saunders, 1991; Kenneth, MacDonnell, Bowers, & Flynn, 1976; Ohi et al., 1994). For example, in the study of Chin, Ohi, Masanori, Ishimura, Wakabayashi, & Kuno (1996), a more rapid recovery of the $PaCO_2$ was significantly related to lower arterial oxygen pressure (PaO_2). For these reasons, we checked the occurrence of apneas after hypocapnic overbreathing and introduced it post hoc as a between subject variable to explore whether it affected attentional performance or not.

In summary, healthy participants performed an easy and a more difficult attentional task requiring the same motor response (RT) immediately after 3 min of overbreathing, once in a hypocapnic and once in a normocapnic condition. Both overbreathing trials were run on separate days in a counterbalanced order and were preceded each by a baseline trial in which the same task was performed during normal breathing. After each baseline and overbreathing trial, subjective symptoms were measured. Predictions were: (1) In comparison with normocapnic overbreathing, attentional performance will be poorer following hypocapnic overbreathing. (2) In comparison with normocapnic overbreathing, participants will report more typical hypocapnia-related symptoms (dizziness, tingling sensations and muscle spasm, cardiac symptoms) than following hypocapnic overbreathing. Exploratorily, we also introduced the presence/absence of apneas during recovery as an individual difference variable.

10.3 Method

10.3.1 Participants

Forty-six healthy women, all undergraduate students in psychology, volunteered to participate. One participant with asthma was excluded from the experiment. Data of 3 other participants were rejected because of technical or instructional failures, resulting

in a dataset of N=42. Participants took part in two sessions on separate days with an interval of maximum two days in order to minimize possible hormonal changes from the first to the second session. After the second day session, participants were paid 400 BEF (12 USD) for participation.

10.3.2 Materials

Subjective measures

At the start of the first session, participants completed a general health questionnaire that asked for major diseases, asthma, epilepsy, hyperventilation syndrome and panic attacks. Participants who were positive on one of these were excluded from the experiment. The other participants completed five additional questionnaires: a 39-item checklist of psychosomatic symptoms in daily life (Wientjes & Grossman, 1994) and the state - and trait version of the Positive and Negative Affect scale (PANAS) (Watson et al., 1988). At the start of the second session, participants completed only the state version of the PANAS. These questionnaires were administered for exploratory reasons. Results will only be mentioned when relevant in the present context.

After each breathing trial, a state version of the checklist for psychosomatic symptoms from Wientjes & Grossman (1994) was administered. The list was composed of symptoms belonging to one of the following subsets: paresthesia, cerebral, cardiac, gastro-intestinal, respiratory, anxiety or unclassified symptoms. Five sensations that are rarely associated with hyperventilation, called "dummy symptoms", were added to this list. Participants had to rate the extent to which they had felt each symptom during the overbreathing period (not at all, slightly, medium, much, very strong, coded as 0, 1, 2, 3, 4, respectively). Furthermore, participants completed a questionnaire asking the extent to which they had felt concentration and motor problems during the task performance (from 1: not at all, to 9: very strong).

Apparatus

Participants, wearing a nose-clip, breathed room air via a mouthpiece that was connected to a pneumotachograph (Fleisch No 2, Switzerland). Upstream from the latter device, a double one-way valve ensured separation of inspired and expired air. Expired air was sampled close to the mouthpiece. $FETCO_2$ was monitored continuously by a non-dispersive infrared CO_2-monitor with a resolution of 1 mmHg, an accuracy of +/- 2 mm Hg and a 95% response time of 125 ms (Capnograph, POET RC, Criticare, USA). The time lag between the volume- and $FETCO_2$-signal of the POET RC was 1.3 sec; the data collection software was programmed to synchronize automatically the two signals. The capnograph was calibrated each day using calibration gas containing 7.5% CO_2.

In order to maintain the end-tidal PCO_2 at baseline value during normocapnic trials, small quantities of a 35% CO_2-enriched air mixture contained in a gas cylinder were manually added at the level of the inspiratory site of the valve which was connected to a tube (85 cm long; internal diameter: 3 cm).

A Labmaster card and a PC processed the volume signals from the pneumotachograph and the PCO_2-signals of the capnograph with a sampling rate of 20 Hz. They were plotted as a function of time and visually inspected for technical abnormalities and movement artifacts. Specific software extracted pauses and breathing irregularities and determined the following parameters for each breath: inspiratory (Ti) and expiratory time (Te) in seconds, inspiratory (Vi) and expiratory volume (Ve) in ml and fractional concentration of end-tidal CO_2 ($FETCO_2$) . Irregular and shallow breaths not reaching an end-tidal alveolar plateau were rejected from analysis. Inspiratory volume was used as a measure of tidal volume, V_T.

Task

A Number-Numerosity Stroop task, originally conceptualized by Windes (1968) and adapted and computerized by Eccleston (1993) was administered to the participants. The stimuli were presented on the screen of a PC and consisted of two groups of digits, each presented within an outline rectangle (called “card”). Each card displayed

a variable number of the same digit. Both the digit on each card and the group size varied from 1 to 9, with the constraint that the digit presented never equaled the group size (see figure 10).

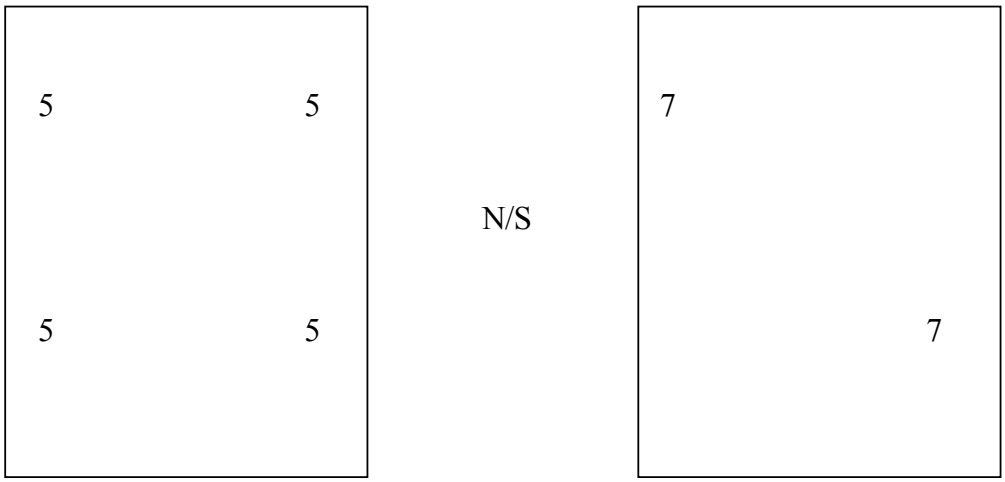


Figure 10: Task stimuli: a pair of cards presented on the computer screen. The specific task is cued by a "N" (number-naming) or an "S" (size-counting).

The task comprised two alternating parts: a number-naming and a size-counting part. Those alternating parts were cued by a letter between the two cards on the screen. A "N" indicated that the participants had to type on a computer numerical keypad the highest of the two numbers represented on each card ("7" in figure 10) (number-naming part). When a key was pressed, the next pair of cards appeared, cued by an "S". In this case, participants had to type the number that indicated the highest group size of digits ("4" in figure 1) (size-counting part). The pair of cards were presented in a random order, with the constraint that both parts of the tasks were continuously alternated during 3 minutes of the task performance. RT's and responses were recorded by the computer.

According to Eccleston (1993), this task appeals strongly on attentional resources. First, it requires overcoming the dominant stimulus ("number-naming") in the case where the highest size is to be given. The reliability of this interference effect

for the computerized version of the Number-Numerosity was confirmed by Eccleston (1993). Second, information from different sources must be compared and a decision must be made. Following Baddeley (1986), this is one of the functions of the central executive. The continuous switch between the number-naming and the size-counting part of the task is a third factor that increases the demand on attentional resources.

10.3.3 Procedure

At the start of the first day session, the participant was presented a text, explaining that the experiment aimed to elucidate the possible effects of respiration rate on attention. Next, the subjective measures were administered. Following this, the participant was asked to sign an informed consent form, reading that harmless symptoms might occur and that she was allowed to stop the experiment at any moment. Then the participant was led to the experimental equipment and the procedure was explained.

Before the first baseline trial actually began, the participant breathed through the mouthpiece for 30 s in order to adapt to the system. Then, the task was explained and the participant could practice on four pairs of cards. It was told that speed and accuracy were equally important. During the first breathing trial (baseline), participants breathed at their own pace through the mouthpiece while performing the task. After 3 min of task performance and respiratory registration, the experimenter instructed the participant to stop the task, to take out the mouthpiece and to complete the subjective symptoms checklist and the task-related questionnaire. The second trial was different in that the participant had to breathe three minutes as deeply as possible at the pace of the metronome (30 breaths per minute) before she performed the task. Depending on the randomization, the experimenter did or did not maintain unobtrusively the normocapnic level while the participant was hyperventilating[17]. The

[17] As a consequence, the experimenter was not blinded to the experimental condition. However, care was taken to avoid any systematic bias in the treatment of the participants and/or the data.

target value was set at the participant's mean $FETCO_2$ during the preceding baseline trial. After stopping the metronome, the participant was told to resume breathing at her own pace and was instructed to start the task. At this point, the experimenter kept on adding CO_2 to cancel out a slight decrement in PCO_2 due to a delayed recovery of overbreathing, also called "afterdischarge phenomenon" (see Corfield et al., 1995; Wagner & Eldridge, 1991). After the task, the participant completed the symptom checklist and the task questionnaire. The session on the second day was similar, except that hypocapnic overbreathing was replaced by normocapnic overbreathing or vice versa. At the end of the session, the participant was asked (1) in which of the two sessions she had felt most symptoms, (2) what else she had felt differently and (3) a possible reason for this difference. Finally, the participant was paid for cooperation.

10.3.4 Data analysis and design

An apnea was defined as a period of at least 4 s without ventilation. Considering a breathing frequency of 15 breaths per minute as a normal value, our definition of an apnea corresponds to skipping one total breath cycle. Apnea (absent/present) was a between factor in all ANOVA's. The Apneic subgroup consisted of participants showing at least one such apnea following hypocapnic overbreathing.

Baseline, overbreathing and recovery data were analyzed separately. No comparisons of baseline with overbreathing or recovery trials were made. For the analyses of subjective symptoms and performance data during overbreathing and/or recovery, the baseline data were used as covariates.

For both baseline trials, ANOVA's on subjective symptoms were run on the total symptom scores and on the various subsets of symptoms in an Apnea (absent/present) x Type (baseline preceding hypocapnia/normocapnia) design. For the overbreathing trials, the symptom scores of the preceding baseline were used as covariates for the symptoms scores following overbreathing. The various subsets of symptom scores

were analyzed in an Apnea (absent/present) x Type (hypocapnic/normocapnic) design each. Type was a within subject variable, Apnea was a between subject variable.

RT's exceeding +/- 3 standard deviations of the participant's mean RT for the subtask on that trial were excluded from analyses. RT's of correct answers and percent errors of baseline trials were analyzed in an Apnea (absent /present) x Type (baseline preceding hypocapnia/normocapnia) x Block (first/second/third minute) x Task (number/size) design. Only Apnea was a between subject variable. RT's and percent errors during recovery were analyzed in an Apnea (absent/present) x Type (hypocapnic/normocapnic) x Block (first/second/third minute) x Task (number/size) design. Each of the twelve within subject baseline measures (RT's or percent errors on each level of Type x Block x Task) was used as a covariate for the corresponding within subject measure following overbreathing (changing covariates).

The ratings on the task-related questionnaire were analyzed in an Apnea (absent/present) x Type (hypocapnic/normocapnic) design, using the ratings on the same questionnaire of task performance during the preceding baseline as covariates.

The following respiratory parameters were analyzed: inspiratory time (Ti), expiratory time (Te), both in seconds, frequency per minute [f = 60/(Ti + Te)], tidal volume in ml (V_T), minute ventilation in ml/min ($V'_E = f \times V_T$), end-tidal fractional CO_2-concentration ($FETCO_2$) and number of expiratory pauses (Pexp). All means were calculated over a 1 min period. The two baseline trials, overbreathing trials and recovery trials were analyzed in an Apnea (absent /present) x Type (hypocapnia/normocapnia) x Block (first/second/third minute) design. Only Apnea was a between subject variable.

Greenhouse-Geisser corrections were made in all analyses including the Block factor.

10.4 Results

10.4.1 Apneas

Nineteen of the 42 participants exhibited apneas after hypocapnic overbreathing. In this apneic subgroup, apneas occurred with a median value of 3 times (sd = 1.98; maximum value was 7 times) and the median duration was 6.35 s.

10.4.2 Baseline

Table 10A. Mean and SD's of Percent Errors and RT's in ms, f per min, V_T in ml, V'_E in l/min, and $FETCO_2$ during Baseline

		Minutes					
		1		2		3	
		M	SD	M	SD	M	SD
Errors	NN	4.00	4.78	3.57	4.17	3.61	3.15
	SC	5.91	6.29	5.17	4.61	5.76	4.55
RT	NN	1831	317	1902	407	1927	402
	SC	2202	439	2051	472	2043	470
Ti		1.49	.48	1.42	.36	1.37	.33
Te		2.28	.78	2.25	.71	2.20	.66
f		17.4	4.2	17.8	4.7	18.2	4.4
V_T		642	174	593	142	553	127
V'_E		10.6	2.19	10.09	1.98	9.63	1.86
$FETCO_2$		5.05	.32	4.98	.33	4.97	.33

Note: NN = number-naming task; SC = size-counting task

Task performance

Participants made more errors on the size-counting task than on the number-naming task (5.68 % versus 3.78 %, main effect of Task: $F(1, 40) = 11.30$, $p < .01$). Also,

RT's were slower on the size-counting task compared to the number-naming task (2097 ms versus 1889 ms, main effect of Task, $F(1,40) = 32.8$, $p < .001$). However, there was a significant Block x Task interaction ($F(1, 40) = 18.69$, $p < .01$) for RT's, showing that the difference in RT's between the tasks was strongest during the first minute (see table 10A).

Physiological parameters

Table 10A shows the mean values and the standard deviations per minute for the respiratory parameters across baseline. Across 3 min baseline measurement, Ti decreased, f increased and V_T decreased (main effects of Block, $F(2, 80)$'s were for Ti: 8.73, $p < .01$, $\varepsilon = 0.66$; for f: 5.36, $p < .001$, $\varepsilon = 0.87$; for V_T : 26.03, $p < .001$, $\varepsilon = 0.79$). As a result of these changes in volume and timing parameters, V'_E decreased during baseline trials ($F(2, 80) = 21.21$, $p < .01$, $\varepsilon = 0.64$). $FETCO_2$ decreased 0.08 % during baseline trials ($F(2, 80) = 20.81$, $p < .001$, $\varepsilon = 0.68$).

Subjective symptoms and task-related questionnaire

There were no differences in symptoms scores, nor in the ratings on the task related questionnaire between the baseline preceding hypocapnic overbreathing and the baseline preceding normocapnic overbreathing.

10.4.3 Overbreathing

Physiological responses

Figure 11 shows the course of $FETCO_2$ for baseline, overbreathing and recovery trials, indicating a successful manipulation. Three minutes of hypocapnic overbreathing led to a drop in $FETCO_2$ of about 50% (see also table 10B). This did not occur in the control condition because CO_2-enriched air was added into the inspired air (Type x Block interaction, $F(2, 78) = 229.8$, $p < .001$). There was a significant Apnea x Type interaction ($F(1, 39) = 13.2$ $p < .001$). A simple main test showed that the $FETCO_2$ of

participants showing apneas was lower during hypocapnic overbreathing than that of participants not showing apneas ($FETCO_2$ = 2.57 % versus 2.89 %), $\underline{F}(1, 39) = 6.97$, $\underline{p} < .05$. During normocapnic overbreathing, there were no differences between both groups ($\underline{F}(1, 39) = 2.02$, n.s.).

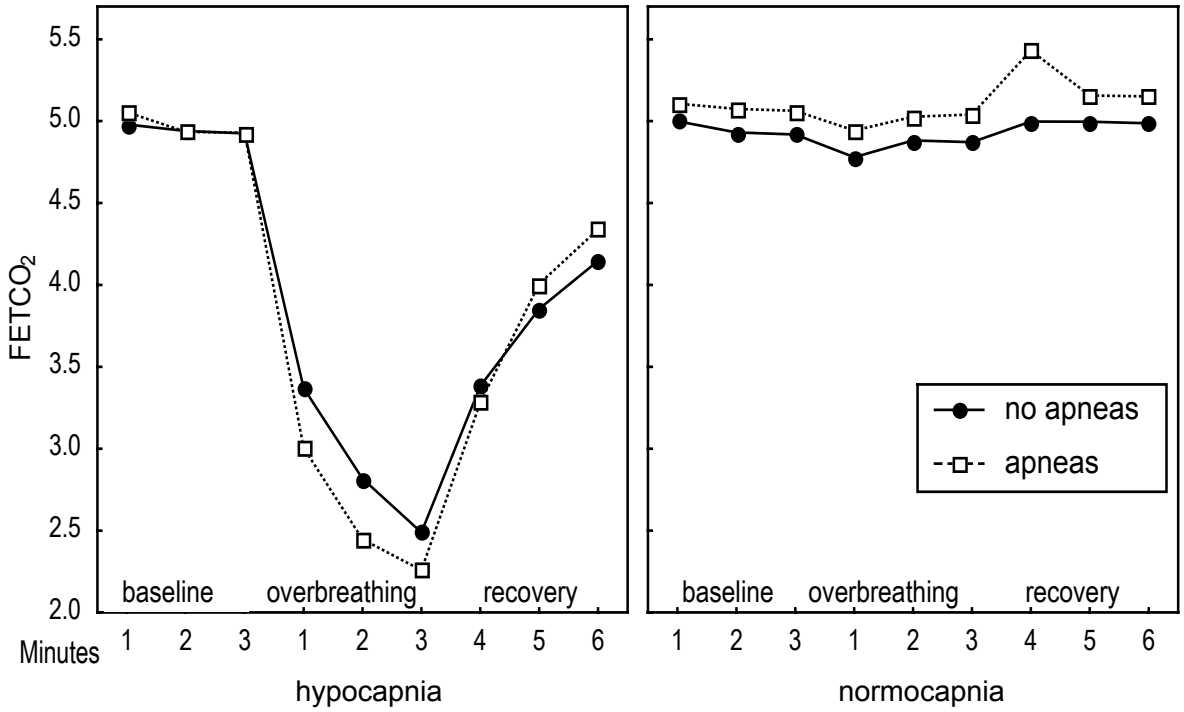


Figure 11: $FETCO_2$ during hypocapnic and normocapnic overbreathing and recovery

Subjective symptoms

Participants reported more symptoms following hypocapnic than following normocapnic overbreathing. This effect on total symptom score was due to an increase in the following subsets of symptoms: tingling hands, head or feet, gastro-intestinal symptoms, cardiac symptoms, unclassified symptoms and symptoms of dizziness.

There were no effects of Type on respiratory, anxiety-related and the subset of dummy symptoms (see table 10C). There were no differences in symptom scores between participants showing apneas or not following hypocapnic overbreathing.

Table 10B. Means and SD's of f per min, V_T in ml, V'_E in l/min and $FETCO_2$ per minute for each Group (Apnea/No Apnea) during Hypocapnic and Normocapnic Overbreathing and Recovery

			Overbreathing						Recovery					
		Minutes	1		2		3		1		2		3	
			M	SD	M	SD	M	SD	M	SD	M	SD	M	SD
Hypocapnia	A	f	30	.9	30.4	1.7	31.3	4.3	17.2	6.3	14.7	8	14.4	5.6
		V_T	1095	306	1194	346	1112	302	563	237	428	147	425	121
		V'_E	32.7	9.3	36.1	10.2	34.5	9.5	9.5	4.8	6	3.5	6	2.5
		$FETCO_2$	3.0	.34	2. 5	.3	2.3	.2	3.3	.3	4.0	.5	4.35	.55
	\A	f	29.8	.5	29.8	1.1	30.7	2.6	22.7	8.0	21.5	8.1	20.3	6.7
		V_T	1144	489	1243	370	1288	443	557	213	429	161	408	211
		V'_E	34.3	14.7	37.1	11.5	39.3	13.4	11.8	4.1	8.7	3.6	7.8	3.9
		$FETCO_2$	3.4	.6	2.8	.5	2.5	.4	3.4	.4	3.9	.5	4.2	.5
Normocapnia	A	f	29.8	.7	29.5	1.5	30	1.0	16.7	5.8	17.6	457	18.6	4.3
		V_T	996	294	1101	307	1124	312	569	175	495	121	492	131
		V'_E	29.7	9	32.6	9.6	33.8	9.4	9.6	4.4	8.6	2.5	9.0	2.8
		$FETCO_2$	4.9	.5	5.1	.4	5.0	.4	5.4	.7	5.2	.4	5.2	.3
	\A	f	30.9	2.7	30.0	.1	29.9	.2	20.6	5.7	20.8	5.5	20.1	4.9
		V_T	932	250	1081	211	1110	210	640	225	509	190	489	142
		V'_E	28.4	6.9	32.4	6.3	33.3	4.5	12.7	4.5	10.0	2.9	9.4	2.1
		$FETCO_2$	4.8	.4	4.9	.4	4.9	.4	5.0	.60	5.0	.45	5.0	.35

Note: A = apnea group; \A = group without apneas

Table 10C. Mean Symptom Scores and SD's for Hypocapnic and Normocapnic Overbreathing Trials and Corresponding F-values.

Subsets of Symptoms	Hypocapnic		Normocapnic		F(1,39)
	M	SD	M	SD	
Dizziness	2.46	2.17	1.02	1.29	35.79**
Tingling hand/head/feet	1.03	1.72	.56	1.02	4.20*
Unclassified	3.63	2.93	2.64	2.44	6.98*
Cardiac	5.66	4.68	4.44	3.58	6.36*
Gastro-intestinal	.67	1.22	.35	.69	5.46*
Anxiety	3.46	2.76	2.92	2.50	2.69
Respiratory	3.28	3.18	2.99	2.70	.55
Dummy	.25	.59	.32	.85	.23
Total symptom score	20.19	14.30	14.93	10.52	12.44**

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

10.4.4 Recovery

Task performance

Table 10D contains the performance data as a function of Apnea, Type, Block and Task. Following hypocapnic overbreathing, participants made more errors than following normocapnic overbreathing (6.69 % versus 4.18 %, main effect of Type, $F(1, 40) = 10.04$, $p < .01$). There was no significant main effect of Task , $F(1, 40) = 2.03$, n.s). Percent errors decreased over 3 minutes (from 8.51%, over 4.15% to 3.65% in the last minute, main effect of Block, $F(1, 40) = 14.8$, $p < .01$, $\varepsilon = 0.68$). The significant Apnea x Type x Block interaction ($F(2, 78) = 3.62$, $p < 0.05$, see figure 12) shows that these main effects of Type and Block are made up by a strong increase in percent errors during the first minute of recovery in participants showing apneas following hypocapnic overbreathing.

Table 10D. Mean RT's and SD's in ms and Percent Errors and SD's per minute for each Group (Apnea/No Apnea) following Hypocapnic and Normocapnic Overbreathing.

			Reaction Times						Percent Errors					
	Minutes		1		2		3		1		2		3	
			M	SD	M	SD	M	SD	M	SD	M	SD	M	SD
Hyocapnia	A	NN	1749	331	1754	141	1803	469	13.6	19.7	3.7	4.3	7.83	5.5
		SC	1929	552	2042	577	2099	731	19.0	18.0	5.4	6.5	9.7	9.8
	\A	NN	1612	400	1681	431	1737	394	4.7	5.2	3.3	5.8	0.8	2.2
		SC	1827	450	1820	503	1814	441	6.3	7.1	5.6	7.5	4.5	6.9
Normocapnia	A	NN	1680	256	1708	335	1746	397	4.8	11.2	4.2	5.5	4.2	2.2
		SC	1952	513	1843	438	1863	420	6.9	11.6	6.1	8.6	4.5	3.9
	\A	NN	1659	329	1654	331	1672	389	3.6	5.4	1.9	2.7	2.3	4.2
		SC	1941	514	1802	521	1873	558	5.0	2.7	2.8	4.9	1.9	4.0

Note: A = apnea group; \A = group without apneas; NN = number-naming task; SC = size-counting Task

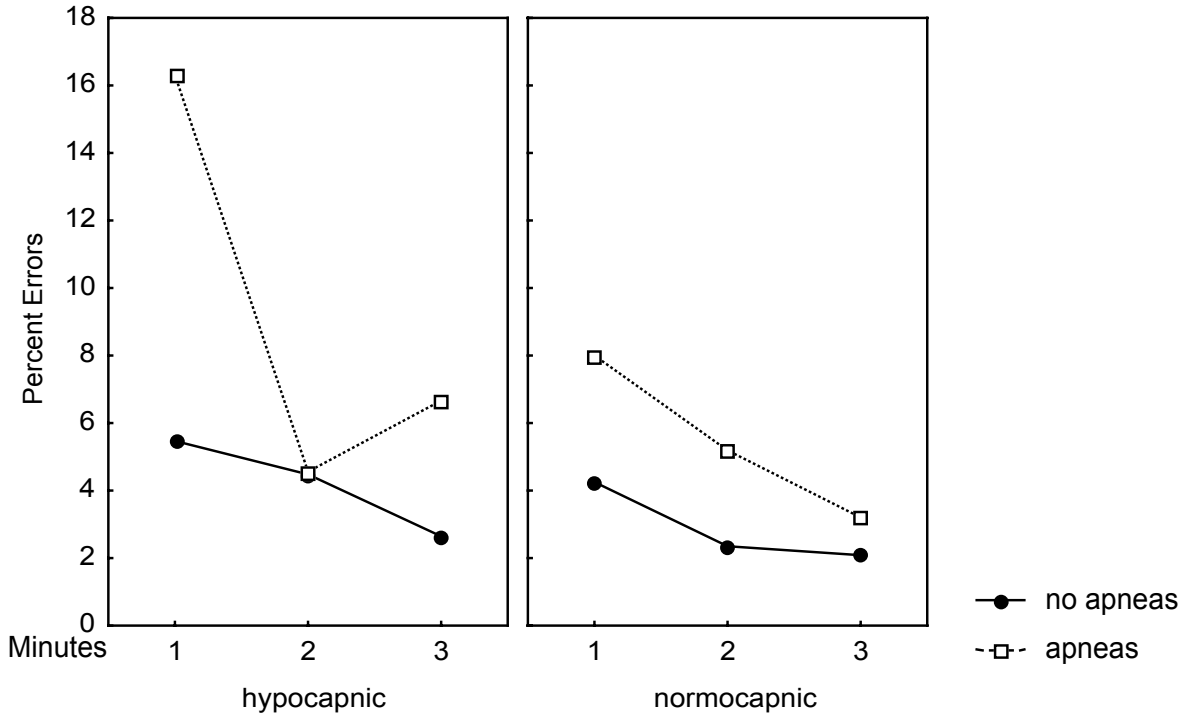


Figure 12: Percent errors for each group (apnea/no apnea) following hypocapnic and normocapnic overbreathing

There were no main effects of Apnea, Type, Block or Task for RT's. Figure 13 shows the significant Type x Block interaction ($F(2, 78) = 3.35$, $p < .05$). RT's increased progressively over three minutes of task performance following hypocapnic overbreathing. Trend analyses revealed a positive linear trend in RT's following hypocapnic overbreathing, $F(1, 39) = 5.67$, $p < .05$ that was absent following normocapnic overbreathing, $F(1,39) = 0.04$, n.s..

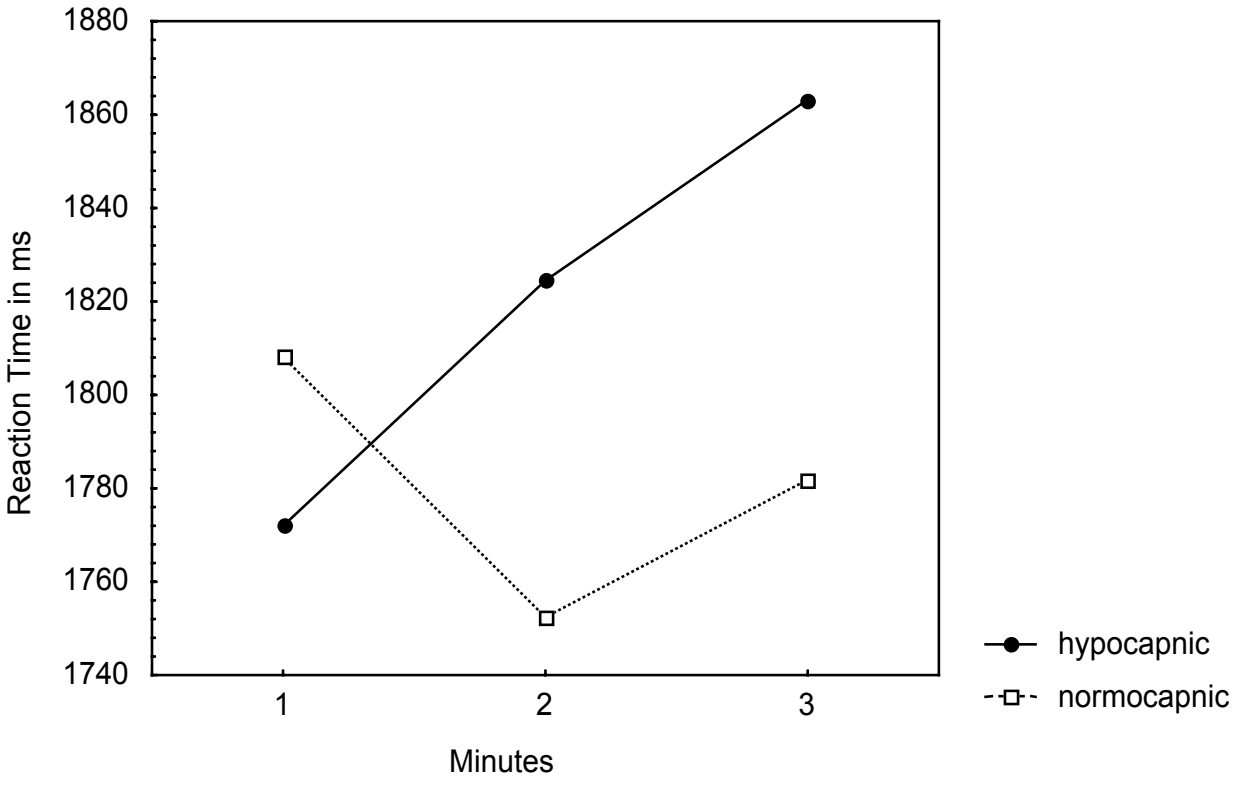


Figure 13: RT's in ms per minute following hypocapnic and normocapnic overbreathing

Figure 14 shows a significant Apneas x Type x Task interaction, $F(1, 39) = 4.19$, $p < .05$. A simple main test showed that following hypocapnic overbreathing, participants showing apneas had slower RT's on the size-counting task than participants not showing apneas ($F(1, 39) = 7.09$, $p < .05$). As to RT's on the number-

naming task following hypocapnic overbreathing, there was no difference between both groups ($F(1, 39) = .58$, n.s.). Other simple main tests comparing hypocapnic with normocapnic overbreathing on each level of Apnea and Task, showed that the only significant increase in RT's from normocapnia to hypocapnia was found on the size-counting in participants showing apneas ($F(1, 39) = 4.50$, $p < .05$).

There was no significant correlation between percent errors and symptom scores ($r = .10$, n.s) nor between RT's and symptom scores ($r = .27$, n.s.).

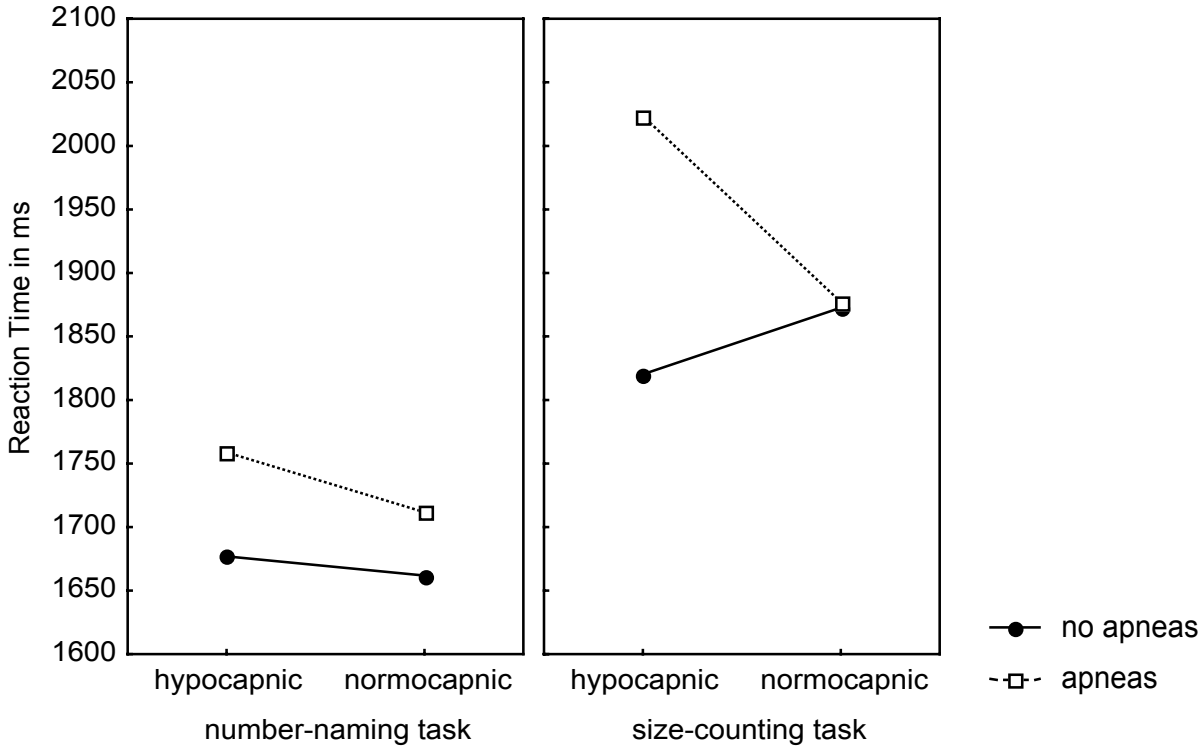


Figure 14: RT's in ms for each group (apnea/no apnea) following hypocapnic and normocapnic overbreathing

Physiological responses

As expected, $FETCO_2$ was partially restored during recovery following hypocapnic overbreathing (Type x Block interaction, $F(2, 78) = 62.85$, $p < .001$) (see figure 11 and table 10B).

V_T was lower following hypocapnic than following normocapnic overbreathing (470 ml versus 535 ml, main effect of Type, $F(1, 39) = 9.47$, $p < .01$). V_T changed over 3 minutes from 584 ml over 468 ml to 545 ml (main effect of Block, $F(2, 78) = 41.04$, $p < .01$, $\varepsilon = 0.67$).

Because we calculated f out of Te and Ti, apnea-times were added to Te, in order not to overestimate f and V'_E. Consequently, participants showing apneas had a longer Te and a lower f (main effect of Apnea, for Te: $F(1, 39) = 6.21$, $p < 0.05$; for f: $F(1, 39) = 7.47$, $p < 0.01$). Because this was not compensated for by a larger V_T ($F(1, 39) = .09$, n.s) the apnea group had a lower V'_E (main effect of Apnea, $F(1, 39) = 6.65$, $p < 0.05$) during recovery from overbreathing. Te of participants showing apneas increased strongly following hypocapnic overbreathing (Apnea x Type x Block interaction, $F(2, 78) = 4.36$, $p < 0.05$, see table 10B). The Apnea x Type x Block interaction for V'_E was not significant $F(2, 78) = 1.96$, $p < 0.15$.

Compared to recovery following normocapnic overbreathing, breathing following hypocapnic overbreathing was characterized by a stronger decrease in f and V'_E (Type x Block interaction, $F(2,78)$ were: for Te, 8.31, $p < .001$; for f, 6.59, $p < .01$; for V'_E, 6.20, $p < .01$, see table 10B).

Task-related questionnaire

A simple main test on the Apnea x Type interaction ($F(1,39) = 4.70$, $p < .05$) demonstrated that participants showing apneas following hypocapnic overbreathing experienced more difficulties with concentrating on the task following hypocapnic overbreathing than following normocapnic overbreathing (means were 6.03 versus 5.10, $F(1,39) = 4.50$, $p < .05$). This was not true for the subgroup of participants not showing such apneas (means were 5.46 versus 5.80, $F(1,39) = .78$, n.s.).

Participants reported more motor problems following hypocapnic overbreathing than following normocapnic overbreathing (means were 4.67 versus 4.06, main effect of Type: $F(1, 39) = 7.36$, $p < .01$). Also, there was a main effect of Apnea, $F(1,39) = 5.15$, $p < .05$: participants showing apneas experienced more motor problems than participants not showing apneas (means were 4.88 versus 3.87). The Apnea x Type interaction was not significant.

In the normocapnic condition, there was a positive relationship between percent errors and reported motor problems ($r = .37$, $p < .05$). This effect was only marginally significant in the hypocapnic condition ($r = .28$, $p < .07$). Also in the normocapnic condition, there was a positive correlation between RT's on the size-counting task and subjective ratings on difficulties with concentrating ($r = .31$, $p < .05$). This was not the case in the hypocapnic condition ($r = .01$, n.s.).

10.5 Discussion

In line with our prediction, cognitive performance was poorer following hypocapnic than following normocapnic overbreathing. In the hypocapnic condition, the participants made more errors and RT's increased progressively across three minutes. Importantly, performance following hypocapnic overbreathing was poorer in participants showing apneas compared to those not showing apneas. The apneic subgroup made more errors on both tasks during the first minute following hypocapnic overbreathing. Also, their RT's were longer, but this was only true for the size-counting task. All performance deficits were accounted for by the participants showing apneas. Together with the observation that the apneic subgroup reported more difficulties with concentrating, our results suggest that the increase in RT's in participants showing apneas is mainly an attention deficit. It is not clear whether the effect on errors in the first minute and elevated RT's in the second and third minute reflects a change in strategic options of the participants. Possibly, the error inflation in the first minute was rectified via a more precise but slower processing strategy. In any

case, apneic participants clearly had overall more cognitive performance problems across the entire time window.

The reported performance deficit cannot be due to attention disruption caused by experiencing more or other symptoms: the cognitive performance was unrelated to the symptom scores for that condition, nor did participants showing apneas differ in symptom scores from participants not showing apneas.

Also an explanation in terms of peripheral motor disruption cannot explain the complete pattern of results. If it was only a matter of a disrupted motor performance, both tasks should have been affected equally. The RT data were incompatible with this explanation. In addition, participants showing apneas did not report more motor problems than those without apneas, despite the measure being sensitive enough to find more motor problems in the hypocapnic compared to the normocapnic overbreathing condition. However, an explanation in terms of a peripheral motor decrement cannot be excluded for percent errors : the apneic subgroup being slightly more hypocapnic during overbreathing, might have had stronger tetany and muscle spasm.

The results with regard to symptoms are in line with our prediction. Tingling hands, head or feet, dizziness, unclassified, cardiac and gastro-intestinal symptoms are specifically elevated in the hypocapnia condition (Hornsveld & Garssen, 1996). However, overbreathing causes more and other symptoms as well, such as respiratory and anxiety-related symptoms. Nevertheless, the participants were fairly accurate in determining the most symptom provoking condition : 75 % indicated hypocapnic overbreathing, 12% did not experience any difference and 13% indicated normocapnic overbreathing. Depth of hypocapnia was unrelated to the amount and the intensity of symptoms.

Although our study was not set up to test an explanatory mechanism, the fact that attentional performance deteriorated across 3 min of recovery in the apnea-subgroup only suggests a potential role for central hypoxia. Apneas, resulting in a lower V'_E, may both help to restore PCO_2 more quickly and retard the rate of delivery of oxygen to the brain, resulting in prolonged central hypoxia. In a recent

(unpublished) parameter study of our group with the same methodology as the present one, we found that after 3 min of hypocapnic overbreathing, SaO_2 (oxygen saturation) decreased across 3 minutes from 97.8 % to 95.1 % and 92.9 % in participants showing apneas and from 97.7 % to 96.2 % and 96.1 % in participants not showing apneas. Furthermore, our findings are consistent with results from other studies. For example, in a study of McCarthy, Corban, Legg and Faris (1995), the participants were asked to make speeded judgments concerning the orientation of visual stimuli while breathing air in a hypobaric chamber, corresponding with high altitudes. At a nominal altitude of 7000 ft, giving rise to a mean SaO_2 of 96.8 %, there was a significant increase in response time. At a nominal altitude of 12000 ft (mean SaO_2 = 91.2 %), there was a decrement both in response time and accuracy. Several other studies (MacDonnell, Bowers, & Flyn, 1976; Corfield et al., 1995) report SaO_2 decreases following hyperventilation in the same range or lower as found by McCarthy et al. (1995). However, the role of central hypoxia as an explanation for the current findings is at present only a post hoc hypothesis. A direct PAO_2 measure is necessary to test it appropriately.

An alternative explanation of both the occurrence of apneas and the performance deficit in apneic participants could be a decreased wakefulness/alertness in that group. Indeed, decreased wakefulness appears to induce apneas (Mangin, 1982; Shea,1996). In that perspective, a decreased wakefulness could explain the observed association between apneas and the deteriorated cognitive performance. However, this explanation seems unlikely. First, any relationship between baseline reaction times and the occurrence of apneas during recovery was absent, excluding an explanation in terms of a pre-existing difference between both groups in wakefulness. Second, because the task was quite demanding, requiring sustained attention and continuous responding for 3 min, all participants appeared very alert and aroused during task performance.

In summary, the present study documented attentional performance deficits in young women associated with hyperventilation-produced hypocapnia, up to three minutes after hyperventilating. These deficits are not caused by attention disruptions

due to experiencing symptoms, and they cannot be explained completely by peripheral motor problems while responding. Our results suggest that central hypoxia might be a causative factor. Our findings are important for situations in which attentional performance may be critical during high stress situations. Because the effects do not correlate with the level of subjective symptoms and may continue after recovery from hypocapnia, the importance of processes related to hyperventilation may be easily overlooked.

Chapter 11
General Discussion and Conclusions

Our conclusions with respect to psychological triggers for hyperventilation will be discussed from a situational (S), a personality (P) and a situation x person (SxP) interactional perspective. In a last part, conclusions regarding our studies on consequences of hyperventilation induced hypocapnia will be dealt with.

11.1 Situational Responsivity

11.1.1 Hyperventilation beyond fight/flight

Studies 1-3 investigated $FETCO_2$ responses within the two-dimensional emotional space formed by Valence and Arousal. A first major conclusion is that hyperventilation responses are not confined to states in which an individual experiences threat or - yet broader defined - unpleasant affects. Indeed, in study 1, decreases in $FETCO_2$ occurred also during imagery of a pleasant, highly aroused emotional script. Theoretically, this corroborates the idea that respiration reflects the general action tendency underlying an emotion (Boiten et al., 1994; Dudley & Pitts-Poarch, 1980; Nyklíček et al., 1997) and extends it to responses in $ETCO_2$. In order to provide further evidence for this idea, however, future research should investigate $ETCO_2$ responses under yet a broader array of positive and negative affects (e.g., anger, euphoria, contentment). Also, the question whether hyperventilation may occur outside an emotional context should be posed. A relatively neutral, action-oriented script was used in our first study. Interestingly, this imagery script was associated with decreases in $ETCO_2$ too, suggesting that

hyperventilation responses may have nothing to do with emotions, but everything with "action"[18]. On the other hand, one may question whether it would be possible to trigger or achieve strong action tendencies without any underlying motivational direction of approach or avoidance.

A promising technique would be to apply brain imaging to clear out whether or not the same brain circuitries are involved in the triggering of hyperventilation in positive, negative or neutral contexts. Ideally, such studies may, in the long run, result in a better understanding of breathing regulation, more specifically in a deeper insight in behavioral or feedforward breathing control.

11.1.2 Timing versus volume parameters

Across the three imagery studies, changes in $FETCO_2$ from baseline to imagery were consistently accompanied by changes in respiratory timing parameters. Concomitant changes in V_T were very small and in the opposite direction from the observed changes in total ventilation, drive and $FETCO_2$. This pattern of results confirms the suggestion made by other authors (Gallego et al., 1996; Rafferty & Gardner, 1996), namely that feedforward influences upon breathing are mainly reflected in changes in the timing, and less in volume parameters.

In contrast with this, Lang et al. (1980) found that fearful imagery was associated with an increased f, whereas imagery of a physical exercise script triggered increases in V_T. This differentiation is likely due to the inclusion of very explicit suggestions regarding breathing pattern in the imagery scripts. For example, the physical exercise script used in the study of Lang et al. (1980) started with the phrasing "You breathe deeply as you run…". The fearful script included the phrasing "You breathe in short quick gasps…". It is evident that such explicit

[18] However, since the action script was presented always as the second script, this result does not allow to draw any firm conclusion: the pattern of results may have been confounded by presentation order and/or the amount of response training already given.

references to breathing pattern may have triggered voluntary controlled changes in breathing, especially when considering the effort spent to motivate the subject to imagine the scenes as vividly as possible (cf. "the response training", Lang et al., 1980).

It would be particularly interesting to compare fear and anger with respect to responses in $ETCO_2$, f and V_T. The few studies that have compared f and V_T responses during fear and anger reveal contradictory results. For example, whereas most studies conclude that both emotions are associated with similar increases in f (Feleky, 1914; Philippot, Chapelle, & Blairy, 2002; Schachter, 1957; Stemmler, Heldmann, Pauls, & Scherer, 2001), Ax (1953) observed greater increases in f for fear than for anger. Several findings (Ax, 1953; Sabatinez & Bloch, 1986; Philippot et al., 2002) point to an increase in V_T during anger, but not during fear. This is in contradiction with the results of Feleky (1914) who reported an equal increase in V_T during fear and anger.

11.1.3 The relative importance of valence, arousal and dominance

It was concluded from our review of studies investigating $ETCO_2$ changes in response to emotions or stress (see 2.1.1) that the prototypical trigger for hyperventilation seemed to be an uncontrollable threatening situation. On the basis of our additional findings, we would like to formulate another conclusion: "Hyperventilation responses occur in both pleasant and unpleasant contexts in which strong action tendencies are blocked". The "blocking" aspect should be understood in its broadest sense. It may refer to actual physical constraints as well as to the impossibility to act because the stressor is not actually present. In line with ideas formulated by Dudley and Pitts-Poarch (1980), our findings clearly indicate that the notion of action tendency is the crucial one with respect to the triggering of hyperventilation. Scripts suggesting strong action tendencies (e.g., fear and desire script) consistently triggered hyperventilation responses, whereas a quiz script

depicting a tense anticipatory situation, or other low action-oriented scripts (depressive, relaxation) did not. In this light, the question regarding the relative importance of valence, arousal and dominance in $ETCO_2$ responses should be reformulated into: How do the emotional dimensions of valence, arousal and dominance relate to action tendencies?[19]. This is a fundamental theoretical question that goes beyond the scope of this thesis. On a more practical level, studying the relative contribution of each of the three dimensions in the triggering of hyperventilation responses would require a study in which the emotional dimensions of valence, arousal and dominance are uncorrelated, which can be only obtained through a thoughtful selection of the scripts to be included in the study. Ideally, the selected scripts should be perfectly distributed over the three dimensional affective space, which would be very difficult to achieve. For example, it is difficult to imagine an extremely pleasant or unpleasant situation that is not associated with arousal. Also, one can assume that most people prefer (valence) situations they can control above situations they cannot (dominance). However, although such dependencies among the emotional dimensions do not allow for exact estimations of their relative contributions in the triggering of hyperventilation, our findings clearly suggest that particularly arousal and dominance may explain a fair amount of the variance in $ETCO_2$ responses. Indeed, irrespective of valence, $ETCO_2$ decreases occurred in all high arousal scripts. An exception to this was a non-action-oriented tense script (study 3), which was rated equally high on arousal, but higher on dominance compared to the fear scripts associated with hyperventilation responses.

[19] A simple answer to this would be to equate the intensity of the action tendency with arousal, its direction in terms of approach or avoidance with valence and the ability to actually consume it with dominance.

11.1.4 The imagery paradigm

As previously discussed, the imagery paradigm is particularly relevant for the study of hyperventilation responses, because hyperventilation is believed to be triggered easily when breathing is changing along with the metabolic needs of mentally represented future or past moments in time instead of with the actual needs (Gilbert, 1999). Action tendencies resulting from such mental representations are by definition hard to be carried out immediately (cf. "blocked"). Despite the relevance of the imagery paradigm, other paradigms should be applied in order to corroborate our major finding that hyperventilation may occur in pleasant contexts as well.

11.1.5 Variability in $ETCO_2$ responses

The mean $FETCO_2$ decreases observed in studies 1-3 differ from clinical hyperventilation in that they were much smaller and did not reach the threshold under which symptoms can be expected to occur (see 1.3.2). Figures 15 and 16 show the distributions of the mean changes in $FETCO_2$ from baseline to imagery for the elevator and exam script, respectively. Data were obtained from studies 1 and 3, in which identical versions of the elevator and the exam scripts[20] were applied (N = 88).

In line with Suess et al. (1980) who found that the degree of hyperventilation responses can vary widely across subjects, the figures show a large interindividual variability in the $FETCO_2$ responses during fearful imagery.

Shea (1997) reported an intraindividual variability in $PETCO_2$ of 1-2 mmHg (in $FETCO_2$: .14-.28 %) within a 2 h strictly defined resting period. We used this value as criterion to distinguish responders from non-responders during imagery of the elevator and exam scripts. For the elevator script, 38 out of 88 subjects (43.2%)

[20] The scripts used in study 2 differed from studies 1 and 3 in that the former contained no autonomic response information.

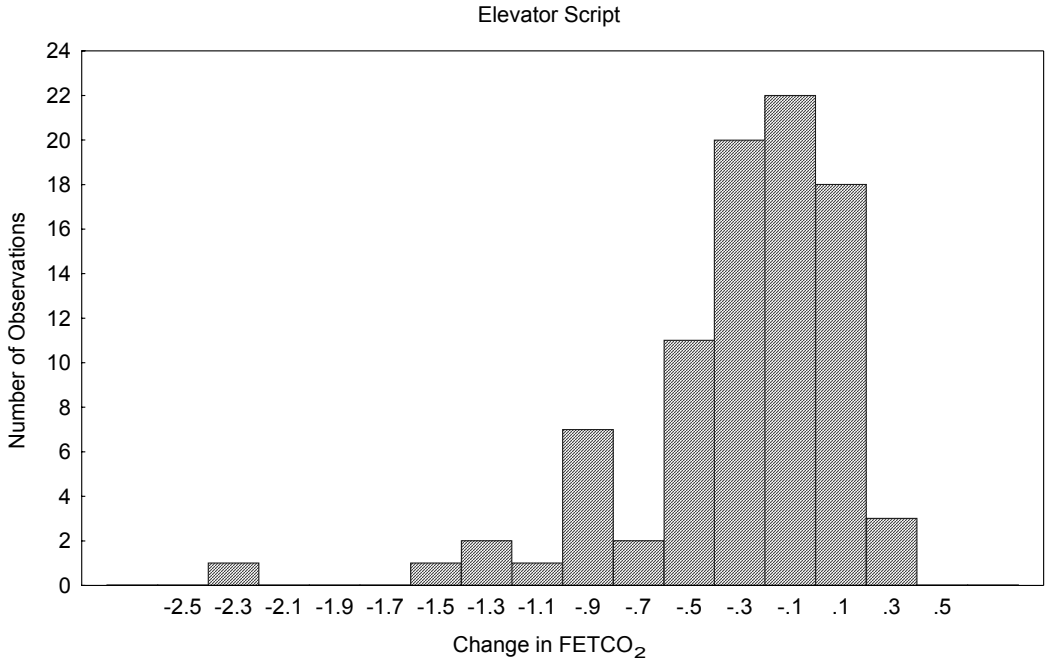


Figure 15: Distribution of the Change in $FETCO_2$ from Baseline to Imagery of the Elevator Script (studies 1 & 3; N= 88)

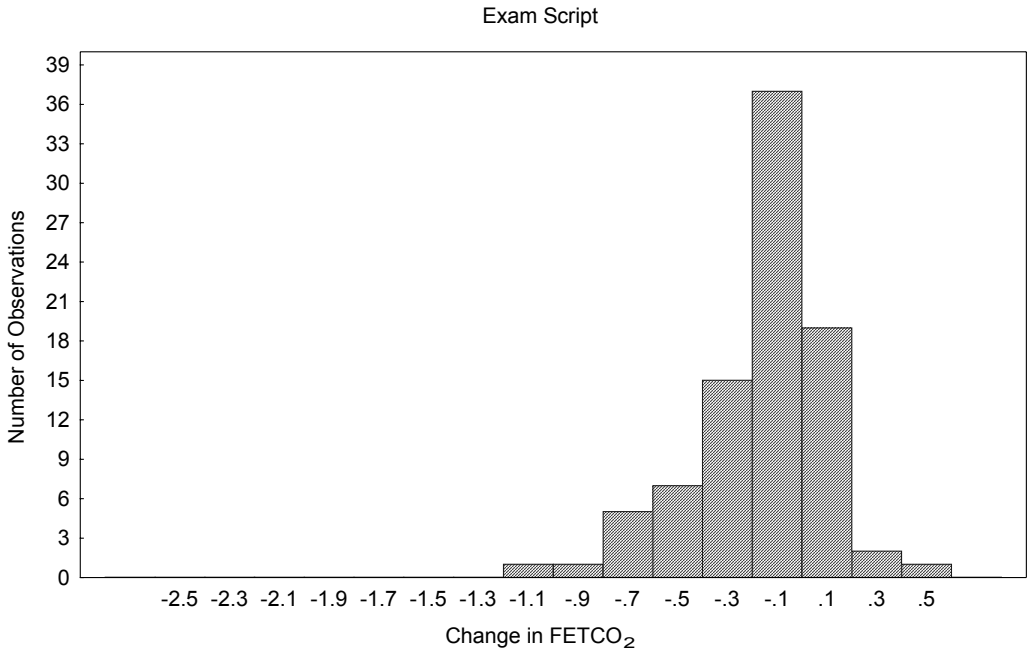


Figure 16: Distribution of the Change in $FETCO_2$ from Baseline to Imagery of the Exam Script (Studies 1 & 3; N= 88)

were classified as responders (mean change in $FETCO_2$ < -.28%), 49 (55.6%) as non-responders (mean change in $FETCO_2$ > -.28% and <.28), and 1 (1.1%) subject responded in the opposite direction (>.28%). For the exam script, these numbers were 21 (23.7%), 66 (75%) and 1 (1.1%), respectively.

The correlations (N = 88) between mean change in $FETCO_2$ and the subjective ratings on vividness, valence and dominance were not significant for neither script, meaning that interindividual differences in responsivity were not related to concomitant differences in imagery vividness, nor to interindividual differences in the subjective appreciations of the script referring to valence or dominance. More subjective arousal was related to a stronger decrease in $FETCO_2$ during imagery of the elevator script ($r = .22$, $p < .05$), which corroborates our finding that arousal is a critical dimension also on the interindividual level. However, such association was not significantly present for the exam script ($r = .14$, n.s.), which may be due to less variability in the $FETCO_2$ responses.

Responsivity in the elevator script correlated .85 with responsivity in the exam script, indicating that participants responding in the fear script were likely to respond proportionally in the exam script. This is an interesting observation, suggesting individual hyperventilation response specificity.

11.2 Dispositional Responsivity

11.2.1 Differentiating responders and non-responders

The data of the elevator and exam scripts from studies 1 and 3 were also used to explore whether responsivity in $FETCO_2$ during fearful imagery was related to trait-like variables. To this end, a cross-situational "hyperventilation reactivity" score was calculated for each subject: the mean change score in $FETCO_2$ across the elevator and exam script.

In a first step, correlations of this mean change score in $FETCO_2$ with various variables were explored. We cheched whether hyperventilation responsivity was related to baseline values of f, V_T and $FETCO_2$ (means over scripts), and to $FETCO_2$ responses during imagery of the relaxation (apartment, living room) scripts[21]. No significant correlations emerged, indicating that one's resting or relaxed breathing behavior was not related to hyperventilation responsivity during fearful imagery. We also checked whether hyperventilation responsivity during fearful imagery was related to dispositional negative (NA) and positive (PA) affectivity (PANAS, Watson et al., 1988), scores on the Questionnaire upon Mental Imagery (QMI; Sheehan, 1967), and scores on the subsets of hyperventilation symptoms in daily life[22] (CPS; Wientjes & Grossman, 1994). Only one significant correlation emerged: hyperventilation responsivity was associated with more symptoms of paresthesia in daily life ($r = -.25$, $p < .05$). Although no causal inferences could be drawn from this observation, the most evident interpretation is participants who were responsive in the laboratory tend to hyperventilate also in daily life, giving rise to the specific hypocapnia related symptoms of paresthesia.

In a third step, a descriptive discriminant analysis (Huberty, 1984) was applied in order to check whether the combined set of trait-like variables could predict hyperventilation responsivity. The criterion of -.28% as the upper limit for hyperventilation responses during fearful imagery was used to define a group of responders and non-responders.

[21] It may be that participants who tend to hyperventilate easily display a different breathing pattern during rest (baseline). It may as well be that a tendency to hyperventilate during fearful imagery is related to stronger (or weaker) $FETCO_2$ increases during imagery of the relaxation scripts. Such observations would be relevant in that hyperventilation responses observed in specific contexts may be related to a general respiratory responsivity that goes beyond hyperventilation or to characteristics of the breathing pattern in less specific contexts.

[22] Following subsets of hyperventilation symptoms were studied: respiratory, cerebral, paresthesia, cardiac, gastro-intestinal and unclassified symptoms. Dummy and anxiety symptoms were not included in these analyses. The former because they are not relevant to hyperventilation; the latter because they show too large an overlap with trait NA.

Thirty participants (34.1%) were classified as responders and 57 (65.9%) as non-responders. Thirteen trait-like variables were entered in the discriminant analysis: mean baseline values of f, V_T, and $FETCO_2$, mean $FETCO_2$ response during imagery of the relaxation scripts, QMI-score, trait NA, trait PA and the subsets of hyperventilation symptoms in daily life. Results indicated that respiratory and cerebral symptoms in daily life were the only variables that significantly discriminated responders from non-responders ($p < .05$): the former reported more respiratory and cerebral symptoms in daily life than the latter. The total model, however, did not reach significance (Wilks' $\lambda = .78$, $p < .10$), indicating that the linear discriminant function of 13 variables could not significantly discriminate responders from non-responders.

Both the correlational and the discriminant analyses found an association of hyperventilation responsivity in the laboratory with hyperventilation symptoms in daily life. No other other trait-like variables were found to predict hyperventilation responsivity. Paresthesia symptoms were significantly associated with hyperventilation responsivity in the correlational analysis, but did not emerge as a significant discriminator in the discriminant analysis. In the latter analysis, however, respiratory and cerebral symptoms were found to discriminate significantly between responders and non-responders. This pattern of results is likely due to interdependencies between different subsets of hyperventilation related symptoms. As already noted (see 6.5), $FETCO_2$ decreases during fearful imagery were specifically related to hyperventilation symptoms in daily life, and this indicate that the former are a valid measurement of responsivity in real life.

11.2.2 NA and chronic hyperventilation

It is clear from studies 4 and 5 that there is no convincing evidence for a cross-situational association of NA with $FETCO_2$. Consequently, it is unlikely that chronic hyperventilation underlies the correlation between NA and subjective symptoms. Even if a small effect would have been left undetected due to a lack of power in our studies, one should conclude that such a potentially small effect is not relevant, because it would explain less variance in $FETCO_2$ than occurring hormonal influences upon $FETCO_2$ in women.

However, we found that $FETCO_2$ of high NA people (but not low NA people) increased during the cognitive load constituted by completing questionnaires (study 5). This finding strongly suggests that NA may modulate situational influences upon $FETCO_2$.

11.3 A more Dynamical Perspective: P x S - Interactions

11.3.1 Suffocation risk and negative affectivity

In study 3 (chapter 6), it was found that high NA women showed a stronger reduction in $FETCO_2$ than low NA women during imagery of a fear script suggesting suffocation. Interestingly, this was not mirrored in a concomitant effect of NA on the scores on the fear of suffocation scale, nor on the subjective ratings on pleasantness, arousal or dominance. We could not offer a viable explanation for this effect. Speculatively one could conceive of a more sensitive suffocation alarm system in high NA subjects, or point to prior respiratory conditioning in the high, but not in the low NA group. Further research should try to replicate this finding. Also, it would be particularly interesting to extend the findings of Stegen et al. (1999). These authors found that an increase in f could be conditioned to claustrophobic, but not to neutral imagery. Future research may try to distinguish

between both claustrophobic components (suffocation and restriction) in their susceptibility for the conditioning of respiratory behavior. Also, in order to shed more light on our findings that risk of suffocation triggered particularly strong hyperventilation responses in high NA participants only, it may be helpful to study these conditioning processes in high NA and low NA participants separately.

11.3.2. Respiratory flexibility and anxiety

In study 6 (chapter 8), we studied respiratory behavior from the broader perspective of emotional regulation and did not specifically focus on the occurrence of hyperventilation responses. In line with predictions made from Thayer and Lane's (2000) model, interindividual differences in trait negative affectivity (NA) were significantly associated with a reduced variability in Ti during resting breathing. This observation corroborates the idea of a loss of flexibility in several psychophysiological and behavioral processes under anxiety (e.g., heart rate variability, hypervigilance and avoidance behavior; Thayer & Lane, 2000). However, it is in contradiction with reports of a highly irregular breathing behavior of panic patients at rest (e.g. Wilhelm et al., 2001c). This paradox may be due to an imprecise operationalization of flexibility in terms of statistical variability. Indeed, a higher standard deviation of breathing parameters may be caused by several, very distinct mechanisms (Bruce & Daubenspeck, 1995), which may have played a role in our findings regarding intraindividual differences in anxiety and breathing variability. A significant decrease in the variability of Te and drive was observed during fearful imagery of the exam script, but not during the elevator script. Our explanation offered was that more participants left steady-state ventilation due to hyperventilation in the latter (27%) as compared to former script (13%). Future research should explore the value of other possible operationalizations of rigidity/flexibility. A first option would be to study the coupling between time and volume parameters in it's function to maintain a constant PCO_2. Another

operationalization may be the extent to which breathing responds in an (un)adaptive way to changes in the internal or external environment.

11.4 Consequences of Hyperventilation induced Hypocapnia

11.4.1 Hyperventilation symptoms and negative affectivity

Many studies have documented the association between NA and subjective reports of bodily symptoms, but only few studies have tried to identify psychological mechanisms underlying this relationship. Since hyperventilation induces a wide variety of symptoms (see 1.3.2) and is easily triggered in high negative affective states (see chapters 2, 4 and 5), it may be hypothesized that hyperventilation constitutes a potential mechanism underlying the NA – symptom reporting relationship. This hypothesis was not confirmed, neither for chronic hyperventilation (studies 4-5), nor for acute hyperventilation (study 8). Study 8 found that the association strength of a symptom with NA could not be predicted by its typicality for hyperventilation induced hypocapnia. However, it may be that our study lacked the power to detect such relationship. Further research on this topic should us a larger set of symptoms that vary more in their typicality for hyperventilation induced hypocapnia.

In study 7, we did not specifically focus on hyperventilation symptoms. The aim was to identify general symptom characteristics that were predictive for the association strength of a symptom with NA. These were (1) the vagueness of the symptom, (2) the extent to which a symptom is viewed as likely to be caused by anxiety, and (3) the extent to which a symptom refers to both a physical and a psychological condition ("overlap"). The reported findings (see 9.2.4) are only a first step in the study of mechanisms underlying the NA – symptom reporting relationship. Indeed, they do not provide clear-cut answers and have even raised more questions. However, we feel that the questions raised are on a more specific

level and may guide future research on this topic. As outlined in 9.2.5, some important questions raised are:

(1) Does our finding that NA is more strongly related to the report of vague symptoms reflect a recall bias or not? Indeed, it may well be that bodily symptoms associated with stress and anxiety are more apparent in distributed somatic systems.

(2) How does self-focused attention relate to perceptual accuracy of somatic sensations? Although self-focused attention is often believed to facilitate accurate judgments of somatic aspects, Silvia and Genolla (2001) argued that there is no convincing evidence for such relationship.

(3) Do NA and gender mediate or moderate the relationship between self-focused attention and interoceptive accuracy?

11.4.2 Cognitive performance and symptoms associated with hypocapnia

Study 9 found that hypocapnia was associated with cognitive performance deficits in a subgroup of participants who showed post-hyperventilation apneas. The pattern of results favored an interpretation in terms of hypoxia resulting from such apneas, suggesting partially distinct mechanisms for the observed objective cognitive performance deficits on the one hand, and subjective neurological symptoms (dizziness, confusion, blackness before eyes) associated with hypocapnia on the other hand. Indeed, whereas the former may be a post-hyperventilation phenomenon, the latter were originally thought to result from cerebral vasoconstriction during hyperventilation (see 1.3.2). Our findings revealed a mechanism by which such neurological symptoms may continue to occur after a period of obvious overventilation and which may partially explain why clinical cases typically present such symptoms without manifest signs of an exaggerated breathing pattern.

Dutch Summary/Samenvatting

Hypocapnie door Hyperventilatie: Psychologische Oorzaken en Gevolgen

Hyperventilatie wordt meestal gezien als onderdeel van de vecht-of-vluchtrespons (e.g., Wilhelm e.a., 2001b), d.i. een algemene, diffuse sympathische activatie die het organisme toelaat adequaat te reageren op een bedreigende gebeurtenis (Cannon, 1929). Hyperventilatie veroorzaakt een snelle PCO_2-daling in het bloed ('hypocapnie') die in bedreigende situaties zou kunnen beschouwd worden als een *feedforward mechanisme* dat compenseert voor de verhoogde CO_2-productie die de fysieke actie van vechten-of-vluchten impliceert. Echter, wanneer er geen fysieke actie gesteld wordt en de verhoogde CO_2-productie uitblijft, is het optreden van deze respiratoire stressrespons dysfunctioneel.

De conceptualisatie van hyperventilatie in termen van de vecht-of-vluchtrespons heeft echter weinig voorspellings- en verklaringskracht. Er bestaat bitter weinig onderzoek over welke persoonskenmerken, situationele kenmerken en eventuele persoon x situaties - interacties als kritisch kunnen beschouwd worden voor het ontlokken van deze respons. Een eerste deel van dit proefschrift (studies 1-6) tracht een tip van de sluier op te lichten door de emotionele dimensies van valentie en arousal en het persoonskenmerk negatieve affectiviteit (NA) te toetsen op hun kritische waarde voor het ontlokken van hyperventilatieresponsen. Een tweede deel van dit proefschrift (studies 7-9) concentreert zich op enkele gevolgen van hypocapnie.

Voorafgaand aan deze studies beschrijven we de bestaande literatuur waarin gerapporteerd wordt over onderzoek dat persoons- en/of situatiekenmerken die als relevant kunnen beschouwd worden in het tot stand komen van acute of chronische

hyperventilatie in kaart brengt (gebaseerd op Van Diest e.a., 1999). Bevindingen van vier soorten studies worden hiertoe gepresenteerd en becommentarieerd: (1) studies die PCO_2-responsen onderzoeken tijdens emoties en stress in een normale populatie, (2) studies die PCO_2-responsen onder condities van cognitieve belasting onderzoeken, (3) studies die de gemiddelde PCO_2 tijdens rust van patiënten met stemmingsstoornissen vergelijken met een gezonde controlegroep, en (4) het verband tussen PCO_2 en NA in een normale populatie. Drie belangrijke conclusies die ons onderzoek verder zouden bepalen, werden uit dit literatuuroverzicht gedistilleerd. (1) Conform aan de idee van hyperventilatie als een vecht- of vluchtrespons lijken acute hyperventilatieresponsen steeds op te treden in contexten gekarakteriseerd door een negatieve valentie en een hoge activatie. De studies beperken zich echter tot zulke typische vecht- of vluchtcontexten. Er zijn geen studies die PCO_2-responsen bestuderen tijdens positieve emoties. (2) Hoewel hyperventilatie frequent voorkomt bij paniekpatiënten, lijkt deze respons geen exclusieve of specifieke relatie tot paniekstoornis te onderhouden. Niet alle paniekpatiënten vertonen hyperventilatieresponsen en hyperventilatieresponsen blijken evengoed voor te komen bij andere angststoornissen of bij een hoge mate van toestandsangst in een normale populatie. (3) Omtrent het verband tussen het persoonskenmerk NA (of neuroticisme) en hyperventilatie worden in de literatuur tegenstrijdige resultaten vermeld.

In ons onderzoek omtrent situationele invloeden op PCO_2-responsen (studies 1-3) maken we gebruik van een inbeeldingsparadigma, waarbij de proefpersoon een script te horen krijgt en gevraagd wordt zich levendig in te beelden dat hij/zij het beschrevene op dat moment in werkelijkheid meemaakt. Scriptgedreven inbeelding is een ethisch algemeen aanvaarde manier om emoties op te wekken. Het wordt tevens als een valide manipulatie beschouwd in zowel psychofysiologische studies (Lang, 1979; Lang, e.a., 1983) als in PET studies die de neuroanatomie van emoties onderzoeken (Davidson & Irwin, 1999; Dougherty et al, 1999; Lane e.a., 1997). Volgens Lang's bio-informationele theorie (Lang, 1979) ontlokt emotionele inbeelding fysiologische activiteit in de responskanalen waarin ook activiteit

ontlokt wordt in de reële, actuele emotionele situatie. Daarom is volgens Lang emotionele inbeelding uitermate geschikt om de fysiologische reacties onderliggend aan emoties te onderzoeken. Ook in de respiratoire fysiologie heeft men inbeelding gebruikt om de rol van feedforward controlemechanismen van de hogere hersencentra in inspanningshyperpnea te onderzoeken (Gallego e.a., 1996).

Hyperventilatie wordt gekenmerkt door een discrepantie tussen de reacties die het lichaam stelt op een geanticipeerde bedreiging en de momentane metabole behoeften van het lichaam. Zo gesteld kan hyperventilatie gezien worden als een typisch *menselijk* fenomeen, vanwege de bij mensen sterk ontwikkelde mentale capaciteit tot anticiperen. Mentaal vertoeven wij immers dikwijls niet zozeer "in het huidige moment", maar wel in een ander, verleden of toekomstig moment dat kan gekarakteriseerd worden door frustratie, angst of woede (Gilbert, 1999). In zulk geval vervagen ruimte en tijd gemakkelijk en stimuleert onze mentale activiteit ons lichaam om zich voor te bereiden op actie. Aangezien actie een verhoogde O_2 consumptie en CO_2 productie impliceert, is hyperventilatie een voor de hand liggende respons. Daarom menen wij dat het inbeeldingsparadima niet zomaar "een" manier is om emoties te wekken, maar dat het bijzonder relevant is voor de studie van hyperventilatieresponsen, die per definitie kunnen beschouwd worden als gevolg van een discrepantie tussen de *geanticipeerde of ingebeelde* en de *actuele* toestand. In de eerste drie studies wordt steeds dezelfde inbeeldingsprocedure gebruikt. De proefpersonen krijgen eerst gedurende één minuut relaxerende muziek te horen die ze eenvoudigweg beluisteren. Daarna wordt het inbeeldingsscript aangeboden gedurende 60 seconden, gevolgd door een stilte van 90 seconden. Zowel tijdens het script als tijdens de stilte moeten de proefpersonen zich zo levendig mogelijk de situatie inbeelden ("alsof ze het op dat moment werkelijk aan het beleven zijn"). Wanneer er weer een relaxerend muziekfragment van 60 seconden wordt aangeboden, moeten ze stoppen met de inbeelding. Tijdens de instructiefase wordt sterk benadrukt dat het niet zozeer de bedoeling is dat ze zich alles in detail visueel voorstellen, alsof ze naar een foto kijken, maar wel dat ze

trachten te voelen wat er beschreven staat, alsof ze het werkelijk meemaken op dat moment (cf. 'response training', Lang e.a., 1983).

Studie 1: *Het relatieve belang van Arousal en Valentie in het ontlokken van hyperventilatieresponsen (Van Diest e.a., 2001a)*

Indien we hyperventilatie beschouwen als een onderdeel van de vecht- of vluchtrespons, zou het enkel mogen optreden bij emoties gekenmerkt door een negatieve valentie en hoge arousal. In een eerste studie werd het relatieve belang van valentie en arousal nagegaan als ontlokkers van hyperventilatieresponsen. Veertig studentes beeldden zich acht emotionele scripts die varieerden langs beide emotionele dimensies. De scripts beschreven situaties waarin de proefpersoon depressieve, ontspannen, angstige, actievolle momenten of een moment vol van verlangen beleefden. Na elke inbeelding beoordeelden de proefpersonen hun ervaring op valentie, arousal en levendigheid. PCO_2, inspiratie- en expiratietijd, teugvolume en polsslag werden op een noninvasieve manier gemeten. Significante dalingen in PCO_2 en kortere inspiratie- en expiratietijden kwamen in alle hoge arousal scripts voor, ook in het verlangenscript dat gekenmerkt werd door een positieve valentie en hoge arousal. Deze resultaten tonen aan dat hyperventilatieresponsen niet uitsluitend voorkomen tijdens negatief valente emoties en dat een conceptualisatie van hyperventilatie in termen van een vecht- of vluchtrespons niet altijd valide is.

Studie 2: *De rol van autonome responsinformatie in het ontlokken van hyperventilatieresponsen tijdens emotionele inbeelding (Van Diest e.a., 2001b)*

In studie 1 bevatten alle gebruikte scripts suggesties van autonome responsen, evenals indirecte suggesties van respiratoire responsen. In dit tweede inbeeldingsexperiment wilden we nagaan in hoeverre de geobserveerde hyperventilatieresponsen te wijten waren aan zulke suggesties. Het depressieve, angst-, ontspannings-, en verlangenscript werden deze keer zonder suggesties van autonome responsen aangeboden aan 40 andere studentes. Procedure en metingen

waren identiek aan studie 1. Opnieuw traden er significante dalingen in PCO_2 op in alle hoge arousal scripts. De effecten waren echter kleiner dan in het experiment waar de scripts wel suggesties van autonome responsen bevatten. Het gebruik van autonome responsinformatie bleek samen te hangen met de levendigheid waarmee de proefpersonen zich de situatie konden inbeelden.

Studie 3: *De rol van "verstikkingsvrees" versus "vrees voor bewegingsrestrictie" in het ontlokken van hyperventilatieresponsen (Van Diest, Vos, Devriese, Wellens, Van de Woestijne, & Van den Bergh, submitted,a)*

Hoewel hyperventilatieresponsen niet uitsluitend optraden in het kwadrant van de twee-dimensionele ruimte van emoties dat gekenmerkt wordt door negatieve valentie en hoge arousal, bleken de hyperventilatieresponsen in sommige scripts toch gemakkelijker ontlokt te worden dan in andere. Hoewel beide scripts even hoog gescoord werden op de arousal dimensie, waren de hyperventilatieresponsen sterker wanneer de proefpersonen zich inbeeldden dat ze alleen opgesloten zaten in een lift tussen twee verdiepingen (lift script) dan tijdens het verlangen script (studie 1). Dit zou er op kunnen wijzen dat specifieke "vecht- of vlucht-" condities, gedefinieerd als een combinatie van hoge arousal en negatieve valentie, gemakkelijker hyperventilatieresponsen ontlokken dan andere hoge arousal scripts (de zogenaamde 'interactie-hypothese'). Een andere mogelijke interpretatie houdt in dat het sterke effect van het lift script te wijten is aan factoren die niet gevat worden door de valentie en arousal dimensies. Bijvoorbeeld, situaties met een specifieke betekenis zoals het risico op verstikking of de beperking van de bewegingsvrijheid, zouden zeer sterke actietendensen kunnen ontlokken, en daarom extra kwetsbaar zijn voor het optreden van hyperventilatie. Beide betekenissen blijken inderdaad bijzonder relevant te zijn in theoretische modellen over paniek en agorafobie (Barlow, 1988; Bouton e.a., 2001; Rachman, 1997), een syndroom waar hyperventilatieresponsen frequent voorkomen. In dit onderzoek wilden we beide betekenissen onafhankelijk van elkaar manipuleren en onderzoeken op hun kritische waarde voor het ontlokken van hyperventilatieresponsen. Tevens wilden we

exploratief de PCO_2-responsen onderzoeken tijdens inbeelding van een gespannen-angstig script waarin geen overte actietendensen worden geëvoceerd. Vanuit het theoretische onderscheid tussen angst en vrees (cf. Bouton e.a., 2001; Lang e.a., 1997) zouden we immers kunnen voorspellen dat hyperventilatieresponsen enkel voorkomen in scripts die een hoge actie-oriëntatie oproepen (vreesscripts). Een ander exploratief doel van studie 3 was te onderzoeken of de PCO_2-responsiviteit van hoge NA personen verschilt van lage NA personen. Achtenveertig studentes (24 hoog NA/24 laag NA) beeldden zich 8 verschillende scripts in, waaronder 3 verschillende vreesscripts met een hoge actie-oriëntatie: (1) een lift script waarin beide betekenissen aanwezig waren (risico op verstikking en beperkte bewegingsvrijheid), (2) een script waarin de proefpersoon klem komt te liggen onder een boom (beperkte bewegingsvrijheid zonder risico op verstikking) en (3) een script waarin iemand angstig anticipeert op de nakende examens. Daarnaast beeldden ze zich ook een angstig-gespannen, een depressief en drie relaxatiescripts in. Enkel de vreesscripts ontlokten hyperventilatieresponsen, maar het lift script ontlokte een sterkere PCO_2-daling bij proefpersonen die hoog scoorden op NA dan bij lage NA proefpersonen.

Studies 4-5: *PCO_2 en NA (Van Diest e.a., in press)*

In twee studies onderzochten we het verband tussen NA en PCO_2 tijdens rust in een normale populatie. Een voor de hand liggende hypothetische verklaring voor het verband tussen NA en (hyperventilatie)klachten (Stegen, 1998; Wientjes & Grossman, 1994) is immers dat hoge NA personen zouden gekenmerkt worden door een lichte mate van chronische hyperventilatie, waardoor ze geregeld hyperventilatieklachten ervaren (en rapporteren). Bij chronische hyperventilatie komt er na enkele uren via de nieren een compensatiemechanisme op gang dat erop gericht is de pH in het bloed te herstellen (Gilbert, 1999). Het resultaat hiervan is een herstelde pH, maar de PCO_2 blijft verlaagd. Deze toestand van een nieuw evenwicht met een verlaagde PCO_2 (hypocapnie) kan gemakkelijk worden onderhouden door enkele occasionele zuchten of een diepe ademhaling van tijd tot

tijd (dus zonder een zichtbare overventilatie). In zulke toestand bevindt het lichaam zich voortdurend op de grens van symptomen die te wijten zijn aan hypocapnie. Indien dit mechanisme verantwoordelijk zou zijn voor het verband tussen NA en hyperventilatieklachten, zouden hoge NA mensen moeten gekenmerkt worden door een habitueel lagere PCO_2 tijdens rust. Omtrent het verband tussen NA en PCO_2 worden er in de literatuur sterk tegenstrijdige resultaten gerapporteerd, gaande van een negatief verband (Stegen, 1998), een gebrek aan verband (Wientjes & Grossman, 1994) tot een positief verband (Dhokalia e.a., 1998). Terwijl in de eerste twee vernoemde studies de PCO_2 metingen werkelijk tijdens rust plaatsvonden, vulden de proefpersonen in de laatste studie de neuroticisme schaal van de NEO-PI in tijdens de PCO_2 meting. Een andere belangrijk verschil tussen de geciteerde studies is de wijze waarop PCO_2 werd gemeten: Stegen (1998) gebruikte een mondstuk, Wientjes & Grossman (1994) een open masker en Dhokalia e.a. (1998) een neuscanule.

Studie 4 werd opgezet om na te gaan of het negatief verband tussen NA en PCO_2, gerapporteerd door Stegen (1998), kon gerepliceerd worden wanneer we gebruik maakten van een noninvasieve meetmethode. 83 vrouwelijke en 27 mannelijke studenten vulden de NA schaal van de PANAS (Watson e.a., 1988) en de hyperventilatieklachtenlijst van Wientjes & Grossman (1994) in. Tevens werd de PCO_2 tijdens rust gedurende vijf minuten gemeten op een noninvasieve manier (via neuscanule). Er werd geen verband tussen NA en PCO_2 gevonden indien er statistisch gecontroleerd werd voor de hormonale invloeden op PCO_2 (geslacht, pilgebruik en fase in de menstruatiecyclus bij vrouwen).

In ***studie 5*** werd de PCO_2 van 20 hoge NA studenten (10 mannen) en 20 lage NA studenten (10 mannen) gemeten in zes verschillende condities gedurende telkens 6 minuten. Twee binnensubject-manipulaties werden daartoe met elkaar gekruist: (1) de proefpersonen ademden via een neuscanule (noninvasief) of via een mondstuk (invasief), (2) de PCO_2 werd gemeten tijdens rust, tijdens het invullen van de NEO-PI-R vragenlijst, en tijdens het invullen van een test voor verbale intelligentie (VAT69). Er werd geen hoofdeffect van NA gevonden, maar NA bleek

wel de PCO_2-responsiviteit te moduleren. De PCO_2 van de hoge NA groep steeg significant van rust naar de condities waar de vragenlijsten werden ingevuld; dit was niet het geval binnen de lage NA groep. Hieruit concluderen we dat het invullen van een vragenlijst de PCO_2-responsiviteit differentieel beïnvloedt voor de hoge en lage groep en dus niet zonder meer als een "rust"-conditie mag beschouwd worden. Bovendien werpt deze observatie licht op het - op het eerste gezicht - vreemde positief verband tussen NA en PCO_2 gerapporteerd door Dhokalia e.a. (1998).

We kunnen besluiten met te stellen dat er geen overtuigende evidentie is voor een stabiel, crosssituationeel verband tussen NA en PCO_2 in een normale populatie, indien er noninvasieve metingen gebruikt worden en statistisch wordt gecontroleerd voor hormonale invloeden. Wel blijkt NA een belangrijke, situatieafhankelijke, modulerende rol te spelen in de PCO_2-responsiviteit.

Studie 6: *Angst en respiratoire variabiliteit*

Thayer en Lane's (2000) denkkader aangaande emotionele (dys)regulatie inspireerde ons om de variabiliteit in verscheidene respiratoire parameters te bestuderen in functie van intra- en interindividuele verschillen in angst. Hun model voorspelt immers een verminderde flexibiliteit in psychofysiologische processen tijdens angst. Dit principe illustreren ze aan de hand van observaties van een reductie in de variabiliteit van de hartslag tijdens angst. In studie 6 exploreerden we de binnensubject-variabiliteit in verscheidene parameters tijdens ontspanning en tijdens de inbeelding van vreesscripts (N = 98). Data van studies 1 en 3 werden hiertoe gebruikt. In lijn met de verwachtingen toonden de resultaten aan dat een hoge mate van dispositionele NA in verband stond met een verminderde variabiliteit in de inspiratoire tijd tijdens relaxatie. De resultaten betreffende intra-individuele verschillen in angst en respiratoire variabiliteit waren minder eenduidig. Een verminderde variabiliteit in expiratoire tijd en inspiratoire drive werden vastgesteld tijdens de inbeelding van een vreesscript waarin iemand beseft dat

hij/zij onvoldoende voorbereid is voor de examens, maar niet tijdens inbeelding van een ander vreesscript waarin iemand opgesloten zit in een lift.

Studies 7 – 8: *Symptomen van Hyperventilatie en NA (Van Diest, De Peuter, Eertmans, Notebaert, Victoir & Van den Bergh, submitted,b)*

Studies 4-5 leverden geen evidentie op voor een verband tussen NA en chronische hyperventilatie. Echter, ook acute hyperventilatie zou een verklaring kunnen bieden voor het verband tussen NA en hyperventilatieklachten (Stegen, 1998; Wientjes & Grossman, 1994). NA verwijst naast habituele verschillen in affect immers ook naar een sterkere reactiviteit ten aanzien van acute stressoren (Watson & Clark, 1984). Wanneer het frequenter voorkomen van acute hyperventilatie bij hoge in vergelijking met lage NA personen een oorzaak zou zijn van de hoge klachtenrapportage bij hoge NA individuen, zou het verband tussen NA en klachten sterker moeten zijn voor typische hyperventilatieklachten dan voor lichamelijke klachten die niet door hyperventilatie kunnen teweeg gebracht worden.

Vooraleer deze predictie te testen, onderzochten we in studie 7 exploratief de associatie van NA met verscheidene symptomen. Hiertoe vulden 720 studenten twee NA-vragenlijsten en een 70-items tellende klachtenlijst in. Elk symptoom werd door 52 psychologen beoordeeld op de mate waarin het (1) naar een specifieke locatie in het lichaam verwijst (‘vaagheid’), (2) waarschijnlijk een fysiologische manifestatie van angst is (‘angst’), en (3) het zowel naar een fysieke als een naar een psychologische conditie kan verwijzen (‘overlap’). We vonden een grote variabiliteit in de correlaties tussen NA en individuele lichamelijke klachten. Correlaties berekend op vragenlijstgegevens van vrouwelijke studenten (n=605) konden significant voorspeld worden door ‘vaagheid’, ‘angst’ en ‘overlap’. Alleen ‘vaagheid’ was een significante voorspeller van de correlaties berekend op de gegevens van mannelijke studenten (n=125). In een exploratieve factoranalyse op de klachtenlijst werden 2 factoren getrokken. De eerste factor laadde hoog op typische symptomen van arousal en paniek. De tweede factor groepeerde

systemische en ziektesymptomen die mogelijkerwijs te maken hebben met een functioneel systeem dat recuperatief gedrag promoot in respons op stress.

In studie 8 werd de associatiesterkte tussen NA en een symptoom voorspeld door de 'typicaliteit' van het symptoom voor hyperventilatie geïnduceerde hypocapnie, 'vaagheid' en 'overlap'. In tegenstelling tot 'overlap', waren 'typicaliteit voor hyperventilatie' en 'vaagheid' geen significante predictoren. We vermoedden echter een powerprobleem in studie 8 en besloten dat verder onderzoek een groter aantal symptomen in de analyses zou moeten betrekken om betrouwbare conclusies te kunnen trekken.

Studie 9: *Hyperventilatie en aandacht: Effecten van hypocapnie op de performantie op een Stroop-taak (Van Diest, Stegen, Van de Woestijne, Schippers, & Van den Bergh, 2000)*

Hyperventilatie geïnduceerde hypocapnie gaat gepaard met tal van fysiologische veranderingen in de hersenen en subjectieve symptomen zoals duizeligheid, concentratieproblemen en derealisatie. In studie 9 (N=44) onderzochten we de performantie op een Stroop-achtige taak na drie minuten hypocapnische of normocapnische overventilatie. Beide overventilatiebeurten hadden op verschillende dagen plaats en werden voorafgegaan door een basislijn tijdens dewelke de proefpersonen dezelfde taak uitvoerden. De hypocapnische overventilatie veroorzaakte meer en andere symptomen dan de normocapnische overventilatie. Na hypocapnische overventilatie werden er meer fouten gemaakt en waren de reactietijden trager dan na normocapnische overventilatie. Deze slechtere performantie trad enkel op bij proefpersonen die gekarakteriseerd werden door het voorkomen van apneas na hypocapnische overventilatie. Het klachtenniveau correleerde niet met de performantiematen. Deze resultaten suggereren dat hypoxie, als resultaat van de apneas tijdens het herstel van hypocapnie, verantwoordelijk was voor de slechtere performantie op de aandachtstaak.

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Appendix I

Depressive Script (D)

It's a grey morning and it's though waking up. You prefer keeping your eyes shut. You should be getting up, but you don't want to start the day. The idea that you should be getting on with your daily routines makes you feel miserable. What is the use of it all? You're laying in bed, motionless, you don't feel any tendency to move. You are feeling empty inside and listless. You have a hard time thinking clearly. Moreover, you don't want to think at all. In fact, all you want is it to be night again, so you could just go to bed and feel miserable no more. You're feeling lonely. No one understands you.

Fear Script (F)

You are studying. Looking up from your desk, you see the huge pile of course texts on the bookshelf. You haven't as yet made any serious go at this stuff, and exams will start soon. You realize that time is running short. All of your best friends are far better off than you. A nervous, anxious feeling is coming over you. In fact, this is a kind of mission impossible. Failing the exams would be a disaster, this just may not happen to you. You cannot get the exams and the pile of books out of your mind anymore. Fretting like this, your concentration drops even further. You've become too nervous.

Pleasant Script (P)

You are at the airport to pick up your boyfriend. He went abroad to study a year ago, and today he is finally returning. Very soon you will see him again. You've been looking forward to this moment so many times. The impatience you're feeling

is hardly to bear. In fact, you can already discern him at a distance, or … is it someone else? Yes, it's really him, but you cannot reach him yet. He must pass ID control first. You are so excited that you can hardly stand still . You really want to take him into your arms.

Relaxation Script (R)

You are in an apartment overlooking the sea. You just came back from a walk on the beach and you are relaxing in an easy chair. You've taken off your shoes and with half an ear you are listening to the radio. It's spring. Sunbeams fall through the window. You're feeling content. You take a look out of the window and watch the sea. The sea is calm. It is high tide, but as yet the beach is large and wide. Some children are building a sand castle. A few people walking their dog stroll by. They are scattering the seagulls away from the beach.

Inspired by: Stegen et al. (1999)

Appendix II

Depression (D)

It's a grey morning and you wake up. You keep your eyes closed. You should get up, but you don't feel like starting the day. The thought you that should start the daily routines makes you miserable. What's the use of it? Your body feels tired and heavy. You feel empty inside and apathetic. Your head feels and you can't think straight. What's more, you don't want to think . Actually, you wish it were evening again, so that you could go to bed again and not feel this miserable. You feel lonely. Nobody understands you.

Exam (Ex)

You're studying. You look up from your desk and you see the huge pile of books on your bookcase. You must study them all yet and the exams will start soon. You're getting warm. You're realizing you're running out of time. You feel nervous. All your best friends are better off. You start sweating en your heart is pounding strongly and rapidly. You're anxious and nervous. You cannot get the exams and that pile of books out of your mind. All this worrying makes studying even harder. Failing your exams would be a disaster. You're heart is pounding heavily and your chest is tight.

Elevator (El)

You are alone taking an elevator. Suddenly, the elevator stops and the light turns out. You're caught in between two levels. The door remains closed. It's a little place without any ventilation. You're warm en you feel a bit tight in the chest. You want to get out as soon as possible. Anxious feelings come over. You're sweating and you feel your heart pounding strongly. There is too little air in the elevator. In

despair, you're pushing on all the buttons, but nothing happens. You're body is streaming with perspiration and your chest feels oppressed. There is there is almost no air available anymore in this little place. You pull the door with all your strength. Your heart pounds wildly and you can feel it all over your body. The only thing you can think of is: "I want to get out".

Tree

It's early in the evening and you're walking alone along a path in the forest. A strong wind is blowing. All of a sudden, there is a squall and you hear a loud, cracking noise. Before you realize what is happening, you're down and a heavy branch bands on your right leg. Your leg is ok, but you find you're stuck under the branches. You start sweating. You're really stuck and will never get out without help. This idea makes you feel panicky. Your heart is pounding strongly and your chest feels oppressed. You feel warm and tight. You want to get out, but that's impossible. Nobody really knows you're here, and it will take a long time before any one will notice you're missing. You're heart is beating like crazy. You want to escape, but you're stuck.

Car

You're sitting on the back seat of a moving car. The driver drives relaxed and is well concentrated on the road. The radio is playing softly and the passengers don't talk very much. You're staring through the window. It's a calm, misty day. There's little traffic on this long straight way in the country. The lampposts pass you by in a steady rhythm. From time to time you can see a cyclist or a pedestrian . The fog hangs above the fields and the meadows along the road. In the distance, you can see the vague contours of a forest.

Sea

You are in an apartment overlooking the sea. You're just back from a walk on the beach and you're relaxing in a seat. You took off your shoes and the radio is

playing in the background. It's springtime. The sun shines inside through the window and gives your body a comfortable warmth. Sitting back, you look out of the window watching the sea. The sea is calm. The tide is high but the beach still stretches out a good way. Some children are building a sandcastle. A few walkers with a dog are passing by. They make the sea gulls fly away from the sand.

Living room (Liv)

Sunday afternoon at home. In the most relaxing seat, you're at your ease reading a book. It's cozy inside the living room and a fragrant cup of coffee stands next to you. Sitting back, relaxed, you look out of the window. It's a sunny autumn day outside. Red and brown leaves drift slowly down from the trees. A passing car blows them up again. A little breeze takes them further away. A few walkers are passing by. You tip your coffee and put the cup on the table again. You pick up your book again.

Quiz (Q)

You're participating in a television quiz show. You've already earned a huge amount of money. In a moment, the final test will start: a series of difficult mental arithmetic questions that you should answer correctly and rapidly. If you succeed, the amount of money will be doubled. If you fail, you will lose everything. You're tense and concentrated to the full. The quiz master calls for silence. The music and hubbub fade; it is silent now. You're extremely concentrated. "Are you ready?", the quizmaster is asking, "here are the questions". You're awaiting the questions…you hardly dare to move…you are as paralyzed…

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