RESPIRATORY LEARNING AND SOMATIC COMPLAINTS: A CONDITIONING APPROACH USING CO₂-ENRICHED AIR INHALATION

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Summary—In a differential respiratory conditioning paradigm with normal *Ss* two odors (fresh smelling niaouli and bad smelling ammonia) were used as conditioned stimuli (CS+ or CS−) and 7.4% CO₂-enriched air was used as the unconditioned stimulus (US). Three CS+ and three CS− trials were run during acquisition, followed on the next day by the same number of CS+ and CS− only trials. Respiratory frequency, minute ventilation, end-tidal fractional concentration of CO₂ and subjective complaints were measured throughout the experiment. While during acquisition all measures were affected, the conditioning effects included only respiratory frequency and subjective complaints. A selective association effect appeared in that the conditioning effects were confined to ammonia as CS+: respiratory frequency increased and more somatic complaints were presented when compared to the CS− condition. The conditioning effect on complaints was not confined to complaints of general arousal, but included respiratory complaints as well. Correlational analyses showed that increases in complaints as caused by the conditioning procedure were predicted by changes in somatic variables, but not by individual differences in Negative Affectivity.

INTRODUCTION

Respiratory learning has received little systematic research attention despite its potential implications. For example, it may help to elucidate the controversial role of hyperventilation and hypocapnia (a decreased alveolar and arterial carbon dioxide pressure, produced by hyperventilation) in panic disorder (Ley, 1991; Garssen, De Ruyter & Van Dijck, 1992; Van den Hout, Hoekstra, Arntz, Christiaanse, Ranschaert & Schouten, 1992). Some authors have advanced the hypothesis that occasional episodes of hyperventilation are learning experiences during which interoceptive cues may become conditioned stimuli (CSs) for panic and anxiety (Wolpe & Rowan, 1988; Van den Hout, 1988). Respiratory learning may also have some relevance for increased psychosomatic complaints in normals. Some attribute this phenomenon to Negative Affectivity (NA), an introspective, apprehensive, negativistic and vigilant perceptual/attentional style (Watson & Pennebaker, 1989). Others, (Wientjes & Grossman, 1994) have recently shown that decreased alveolar carbon dioxide pressure contributes significantly and independently from NA to some psychosomatic complaints in normals. It is not unlikely that occasional reductions in carbon dioxide pressure may cause both somatic responses that underlie subjective complaints and subsequently increases in NA that lower the perceptual threshold for variations in somatic responses. Obviously, understanding the dynamic relationship over time between somatic responses and subjective complaints can benefit from experiments using a well-defined learning paradigm.

The present study aimed to (1) establish respiratory learning in a Pavlovian conditioning paradigm, and (2) analyze the relationship between respiratory responses and somatic complaints during acquisition and test. Regarding the first goal, previous research has suggested the possibility of respiratory learning. In a placebo-controlled cross-over study (Van den Bergh, Vandendriessche,

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De Broeck & Van de Woestijne, 1993) we used 5.5% CO₂ inhalation to investigate effects of predictability and perceived control on somatic sensations in high and low anxious Ss. We observed important order effects (placebo vs CO₂ first) on several respiratory parameters. For example, in comparison with low anxious Ss, high anxious ones had a much higher minute ventilation to a CO₂ challenge in conditions of minimal information and control when CO₂ was given first. They seemed to continue this breathing pattern during the subsequent room air trial. This pattern was not observed when the placebo was given first or when the procedure was predictable or controllable. This suggested a (one trial) respiratory learning effect in some conditions (with the breathing equipment serving as the conditioned stimulus), that could easily be removed by providing verbal or experiential information about the procedure.

Gallego and Perruchet (1991) carried out a more controlled study. In the acquisition phase they used a hypoxic stimulus for 12 breathing cycles as an unconditioned stimulus (US) and a simultaneously delivered auditory signal as the conditioned stimulus (CS). A control group was given an explicitly unpaired sequence of CSs and USs. The results in the test phase showed a conditioned increase of the respiratory cycle duration (decrease of the respiratory frequency), but no effects on tidal volume or minute ventilation. This is rather peculiar because the main component of the unconditioned response to a hypoxic stimulus is a late increase (after some 6 to 7 breaths) in minute ventilation and in tidal volume, which co-occurs with an increase in respiratory frequency. Furthermore, because a decrease in respiratory frequency occurred also in response to the auditory stimulus alone when presented in the acquisition phase to the control group, this probably reflects an orienting effect. Therefore, the observed difference between experimental and control group in response to the auditory stimulus could be interpreted as merely a conditioned attentional response which subsequently affected respiration.

In this study we attempted to establish conditioning of respiratory behavior in a differential conditioning paradigm, using two odors as CSs and air enriched with 7.4% CO₂ as a US. It is empirically established that differences exist in the associability of specific CS-US combinations, although its theoretical basis is poorly understood (Mackintosh, 1983). The present experiment intended to take benefit of this phenomenon in two ways. First, odors can easily be mixed with the inhaled US-gas, rendering CS and US more intertwined (in a spatial way) than an auditory CS and a gas as US (Gallego & Perruchet, 1991). This may facilitate conditioning. Second, because we used a positively and a negatively evaluated odor (see materials), affective matching between odor CSs and the negative affective experience of breathing the CO₂-enriched air US could be arranged or not. Hamm, Vaitl and Lang (1989) showed that similarity in primary affective response organization between CS and US may be important to facilitate conditioning. Alternatively, differences in pre-existing associations may also be involved. Indeed, the odor producing substances (ammonia and niaouli) used in this experiment are probably not entirely new to human Ss. Ammonia, when inhaled in larger concentration than in this study, may indeed adversely affect respiration, which may have been experienced earlier (i.e. animal stables, cleaning products). Niaouli is a volatile oil containing eucalyptol, which is known as an additive to some ointments that may have been used to facilitate breathing during nasal congestion. So, on a number of grounds conditioning effects are expected to be stronger in the "bad odor CS+" than in the "good odor CS+" condition.

Regarding the second goal, we investigated the co-occurrence of conditioned respiratory behavior and conditioned subjective somatic complaints. If a conditioning effect appeared with respect to subjective complaints, it could be caused by different processes. CS-evoked increased respiration of room air may induce hypocapnia and subsequent somatic complaints. If no hypocapnia is present but increased complaints are observed in the test phase, they are due to other processes. For example, the CS+ may have increased an introspective, apprehensive, negativistic and vigilant perceptual/attentional focus to their bodies which may lower the perceptual threshold for somatic sensations. In this case, Negative Affectivity (NA) should predict the increase in complaints. Alternatively, the CS may evoke specific somatic responses. In the latter case, these somatic responses should be the more prominent predictors. Correlational analyses of NA, specific somatic response and psychosomatic complaints should shed light on this problem.

METHOD

Subjects

Twenty-eight healthy Ss (age between 18 and 24, 14 males, 14 females) from the psychology student population volunteered to participate in the experiment.

Materials

Apparatus. The CO₂-mixture consisted of 7.4% CO₂, 21% O₂ and 71.6% N₂, the placebo mixture was breathing air of 21% O₂ and 79% N₂. Both gases were contained in standard gas cylinders. After decompression, the gases were fed into a bag-in-box circuit (Donald & Christie, 1949) through vinyl tubes. The circuit consisted of a thin neoprene balloon, suspended in an air-tight tank. The CO₂-mixture was led into the bag, air was sent into the tank. A Y-valve could be switched to feed either the breathing air or the CO₂-mixture into a wide tube ending at a double one-way valve and a mask, enclosing mouth and nose. The S kept it slightly pressed on the face.

Room air from a separate cylinder was led through one of two aerosol devices (at a rate of 1–1.5 l/min) to take up an odor and was then fed into the wide tube, upstream from the double one-way valve and close to the mask. The smelling substances were either niaouli (a mixture of volatile oils, containing 65% eucalyptus oil) or a diluted solution of ammonia (0.085%).* The concentration of ammonia was high enough to produce a rather pungent odor, but too low to have any noticeable effects on the breathing pattern itself (see further). For niaouli no detailed dose level effect studies on breathing behavior are available. Pilot research has shown that continuous odors habituate quickly but that among the set of odors of different affective quality (good and bad odors), ammonia and niaouli produced maximal continuous discriminability.

A valve ensured complete separation of inspired and expired air: inspired gas was from the bag-box circuit, expired air was collected into a meteorological balloon to avoid the odors filling the room. During quiet breathing maximal pressures at the mouth were about 2.5 and 3.2 cm H₂O during inspiration and expiration respectively. An infrared CO₂-monitor (Capnograph, Mark II, Godart) was connected close to the mouthpiece, monitoring the CO₂-pressure continuously during inspiration and expiration. The output was sent to a multichannel polygraph, from which breathing frequency was calculated. The bag-in-box system was hooked up to a water-filled spirometer (Volutest, Mijnhardt), registering inspiratory volumes, which were transmitted via a potentiometer to the polygraph. During the S's breathing, air or the CO₂-mixture was added continuously to the circuit to keep the spirometer at a constant volume. The ECG was measured using three electrodes attached to the upper right and left chest and the left leg. The ECG signal was registered by the polygraph, from which heart rate was calculated.

Subjective measures. Subjective complaints were measured using a list of 16 complaints that have been shown sensitive to CO₂ inhalation (see Table 1 in the Results section). The questionnaire was composed based on the Nijmegen Questionnaire for Hyperventilation Syndrome (Van Dixhoorn & Van Duivenvoorden, 1985) and on reports using CO₂ inhalation (Sanderson, Rapee & Barlow, 1989; Van den Bergh *et al.*, 1993). For each of these complaints, a five point graded answer, reflecting intensity, could be given to the question "did you feel any of these complaints". The categories were: not at all, slightly, medium, strong and very strong (respectively coded as 1, 2, 3, 4, and 5). The total complaint score was the sum of these scores and was treated as a continuous variable. For further in-depth analyses of the complaints, five subsets of complaints were formed and analysed separately: (1) general arousal, (2) respiration, (3) cardiac/warmth, (4) tingling sensations, and (5) unclassified (see Table 1). These subsets were formed in accordance with Wientjes and Grossman (1994).

Also the Zelfbeoordelingsvragenlijst (Van der Ploeg, Defares & Spielberger, 1980) was administered, which is the Dutch adapted version of the State-Trait Anxiety Inventory (STAI) (Spielberger, Gorsuch & Luchene, 1970). The STAI is generally considered a good measure of NA (Watson &

*On a two minute period approximately 80 mg and 40 mg of the ammonia solution and niaouli respectively were dispersed. For a ventilation of 10 l/min, the corresponding inhaled quantities are 1.7 mg/m³/min for ammonia, 2 mg/m³/min for niaouli. Because the smell-room air mixture was additionally fed into the system, the 7.4 CO₂-concentration has been slightly diluted, but this was so in a similar way for all the Ss.

Pennebaker, 1989). Both part ZBV-DY1 and ZBV-DY2 (respectively the State and Trait part) were administered on Day 1, only ZBV-DY1 was filled out on Day 2.

Procedure

Ss were informed (1) that the experiment sought to test respiratory behavior while breathing different innocuous gases; (2) that minor complaints such as a little dizziness, headache, shortness of breath could temporarily appear with some of these gases, but they would disappear quickly after the experimental session; (3) that the experiment would run on two consecutive days; (4) that they were allowed to stop the experiment at any moment. Upon informed consent, the ZBV-questionnaires were then filled out. Thereafter, the *S* was led to the experimental equipment and told that the experiment consisted of breathing 8 times for two minutes each in the mask. Between each trial, a three minute pause allowed Ss to complete the subjective complaints questionnaire. Ss were told that three different mixtures were to be inhaled. No further details were given. They were asked to wait for the signal of the experimenter to put the mask on and off.

The *S* sat on a chair, with the bag-and-box circuit and polygraph behind him/her. The experimenter manipulated the valves and watched carefully that the *S*'s mask remained in place during breathing. After finishing the series of trials, an appointment was made for the next day to repeat the measurement procedure. The second day, only the state version of the ZBV-questionnaire was administered. In other respects, the procedure was exactly the same, with the exception that only room air was used instead of CO₂-enriched air, of which the *S*s remained unaware.

On each of the consecutive days, the first two trials were habituation trials (context exposure): the *S* breathed room air through the mask, without any odor or gas added. Then, six consecutive trials were run. On the acquisition day, three of them were CS + /US compounds and three were CS - /room air compounds. On testing day, CS + and CS - were presented in room air. Half of the *S*s had ammonia as CS + and niaouli as CS -, the other half had the reversed combination. The order of the six trials was counterbalanced across *S*s, with the restriction that no more than two consecutive trials could be of the same type. This resulted in 14 possible orders for the

Table 1. Mean scores per complaint, per set of complaints and total mean scores during acquisition (CO₂ and air) and test with ammonia or niaouli as CS +

	Acquisition		Test				
	CO ₂	Air	Ammonia CS +	CS -	Niaouli CS +	CS -	
1. Arousal							
a. Tension	6.0	3.9	4.1	3.5	3.3	3.5	
b. Anxious feelings	5.5	3.4	3.6	3.0	3.1	3.1	
c. Feelings of panicking	5.6	3.4	3.8	3.3	3.1	3.1	
Mean	5.7	3.6***	3.9	3.2	3.2	3.2	CS + Odor × Cond***
2. Respiration							
a. Fast breathing	9.4	4.6	6.2	5.5	3.2	3.5	
b. Smothering sensations	7.5	3.5	4.9	3.8	3.0	3.0	
c. Chest tightness	6.5	3.5	4.7	3.9	3.1	3.1	
d. Feelings of choking	6.4	3.2	4.4	3.4	3.0	3.0	
Mean	7.5	3.8	5.0	4.1	3.1	3.2	CS + Odor***
3. Cardiac/warmth							
a. Pounding heart	6.4	3.8	4.2	4.0	3.0	3.1	
b. Sweating	5.6	3.9	4.3	3.7	3.5	3.7	
c. Hot flushes (head)	5.9	4.1	4.7	4.1	3.7	4.0	
Mean	5.9	3.9***	4.4	3.9	3.4	3.6	NS
4. Tingling sensations							
a. Tingling, numbness (extrem)	3.8	3.6	4.0	3.5	3.2	3.3	
b. Tingling, numbness (face)	4.5	4.1	3.8	3.7	3.5	3.6	
Mean	4.1	3.8	3.9	3.6	3.4	3.5	NS
5. Unclassified							
a. Lump in throat	4.6	3.4	3.6	3.3	3.3	3.5	
b. Headache	5.2	4.7	5.1	4.7	3.2	3.4	
c. Dizziness	6.3	4.5	5.4	4.3	3.5	3.6	
d. Cold chills	3.7	3.4	3.4	3.2	3.0	3.0	
Mean	4.9	4.1***	4.4	3.9	3.3	3.4	CS + Odor*
Total mean	30.9	20.5***	23.5	20.4	17.4	18.0	CS + Odor × Cond*

Note: **p* < 0.05; ***p* < 0.01; ****p* < 0.005.

combination CS+ (ammonia) and CS- (niaouli). Reversing the combination resulted in a total of 28 different trial orders. One *S* was run per trial order and each *S* had the same order on the two consecutive days.

Data analysis and design

Physiological parameters were collected on each trial in 4 blocks of 30 sec and included end-tidal fractional concentration of CO₂ (FCO₂), frequency per minute (*f*), tidal volume (*V_t*) and heart rate in beats per minute (bpm). Analyses were carried out on frequencies (*f*), minute ventilation ($V_E = f * V_t$) end-tidal fractional concentration of CO₂ (FCO₂) and heart rate (bpm). ANOVA's on the physiological data of the test results had a 2 × 2 × 3 × 4 design [CS + Odor (ammonia/niaouli), Conditioning (CS+/CS-), Trial (one, two or three) and Time Block (block one to four)], among which the first was a between-*S*s variable and the latter three were within-*S*s variables. ANOVAs on the acquisition data were only run on the third CS+ and CS- trial and included a Mixture variable (CO₂/air) replacing Conditioning. Analyses on subjective complaints included the Trial variable, but had no Time Block variable. Separate ANOVAs were done on the total complaint score, and on the various subscale scores. In the latter cases, the complaints were summed across three CS+ or CS- trials to avoid a skewed distribution due to a number of zero cells in the subject × complaint × trial matrix. Since heart rate data are of minor importance in this study, these results will be reported only when significant and meaningful effects are found. Greenhouse-Geisser corrections will be used when appropriate.

The relationship between NA, somatic responses and somatic complaints was analyzed using stepwise multiple regression analyses with forward inclusion of variables.

RESULTS

Context exposure

Only the first context exposure trial per day was used.

Subjective complaints. *S*s overall reported less strong complaints during the context exposure of the second day, compared to the first [$F(1,26) = 22.04$, $P < 0.001$; means were 19.5 and 17.2]. This probably reflects habituation to the measurement procedure. This interpretation is consistent with the general decrease in state anxiety from the first to the second day [38.5 to 32.5; $F(1,26) = 12.8$; $P < 0.005$].

Respiratory behavior. Breathing during context exposure on both days was affected by temporal parameters only, as could be expected. These effects comprised: (1) a significant linear and quadratic trend over time for minute ventilation (*V_E*): a general decreasing trend from the first to the fourth block, but a slight increase superimposed from the first to the second block [$F(1,26) = 7.48$; $P < 0.05$, linear; $F(1,26) = 8.89$; $P < 0.01$, quadratic]; (2) a significant linear and quadratic trend over time for FCO₂ (the inverse picture of the minute ventilation) [$F(1,26) = 14.46$; $P < 0.001$, linear; $F(1,26) = 12.72$; $P < 0.005$, quadratic]; (3) a tendency that *S*s breathed faster the second day, compared to the first (an increase from 11.9 to 13 cycles per minute) [$F(1,26) = 3.64$; $P = 0.06$]; (4) slower heart rate on the second day, compared to the first (88 bpm vs 83.7 bpm) [$F(1,26) = 7.35$; $P < 0.05$]. For both subjective complaints and respiratory effects, the procedure had not caused any general sensitization, nor context conditioning effects.

Unconditioned odor effects

As a control on possible US-effects of the odor itself or of pre-existing associative effects of the odor on complaints or breathing behavior, explorative analyses were carried out on the first acquisition trial of the 14 *S*s that started with a CS- trial. Seven of them had ammonia first, 7 other *S*s had niaouli first, both mixed with room air. Their first CS- trial (which included an odor) was compared with the first context exposure (without the odor) result in a repeated measures ANOVA. Unconditional odor effects should appear as CS- Odor by Measurement interaction.

Subjective complaints. *S*s overall reported slightly more complaints in the CS- trial than in the context trial [$F(1,12) = 4.78$; $P < 0.05$; means are 18.6 (context) and 19.5 (CS-)], but no interaction with the type of odor appeared ($F < 1$).

Fig. 1. The conditioning effect on subjective complaints as a function of type of CS+ odor (ammonia or niaouli).

Respiratory behavior. Except for some general temporal effects replicating the context exposure effects on respiration, no significant effects appeared (F 's < 1 for all CS– Odor $\times$ Measurement interactions, except for V_E : $F(1,12) = 1.96$; $P = 0.18$). Thus, the introduction of the odors themselves did not change respiratory behavior.

Acquisition

Subjective complaints. Apart from a gas mixture main effect [$F(1,26) = 47.79$; $P < 0.001$] and a main effect of Trial [$F(2,52) = 5.88$; $P < 0.01$], a Mixture $\times$ Trial interaction appeared [$F(2,52) = 5.17$; $P < 0.01$]: the CO₂-enriched air produced more complaints than air, but S s habituated across CO₂ trials showing a decreasing complaint score. The mixture main effect appears for arousal [$F(1,26) = 69.5$; $P < 0.001$], cardiac/warmth [$F(1,26) = 39.3$; $P < 0.001$], respiration [$F(1,26) = 21.1$; $P < 0.001$] and for unclassified complaints [$F(1,26) = 16.2$; $P < 0.001$], but not for tingling complaints (see Table 1). No CS+ Odor main effect or Mixture $\times$ CS+ Odor emerged, which supports the conclusion that the odor producing substances themselves had no additional effects on complaints.

Respiratory behavior. Minute ventilation, frequency and end-tidal fractional concentration of CO₂ were all affected strongly by the inhaled gases. The following effects appeared for these measures: Mixture [$F(1,26) = 69.6$, 16.3 and 73 respectively]; Time Block [$F(3,78) = 56.7$, 16.8 and 21.9] and a Mixture $\times$ Time Block interaction [$F(3,78) = 51.7$, 7.8 and 5.97]. All probabilities were $P < 0.001$ or smaller, except for the last mentioned $F(\text{FCO}_2; \text{Mixture} \times \text{Time Block}, P < 0.05)$. The interaction shows a steep increase in V_E and frequency only with CO₂ inhalation. The interaction for FCO₂ shows stable values over time while breathing CO₂, while there is a rising trend from 4.58 to 4.80% in the room air condition. Again, no CS+ Odor main effect or Mixture $\times$ CS+ Odor emerged, indicating that the smelling substances themselves are unlikely to have had additional effects on breathing behavior.

Test

Subjective complaints. There was no overall conditioning effect (Conditioning: $F(1,26) = 2.48$; $P = 0.12$). A CS+ Odor main effect appeared when ammonia was the CS+: S s had more complaints for both ammonia and niaouli conditions than when niaouli was the CS+ [$F(1,26) = 8.89$; $P < 0.01$]. However, this was specified by a significant Conditioning $\times$ CS+ Odor interaction [$F(1,26) = 5.45$; $P < 0.05$; see Fig. 1]. Only when ammonia served as CS+, a significant conditioning effect emerged [$F(1,26) = 7.64$; $P < 0.05$], but not when niaouli was the CS+ [$F(1,26) < 1$].

To further differentiate the conditioning effect on complaints, it was tested separately on the different subsets. For the arousal, respiration and unclassified complaints, a significant conditioning effect appeared when ammonia was the CS+ [$F(1,26) = 15.29$, $P < 0.001$ for arousal; $F(1,26) = 6.22$; $P < 0.02$ for respiration; $F(1,26) = 4.47$; $P < 0.05$], and not when niaouli was the CS+ (all F 's < 1). It should be noted that for both the respiration and unclassified complaints, a main effect of the CS+ Odor appeared (more complaints overall when ammonia was the CS+ compared to niaouli; $F(1,26) = 14.6$; $P < 0.001$ for respiration; $F(1,26) = 6.86$; $P < 0.02$ for unclassified), and a CS+ Odor $\times$ Conditioning interaction that just failed to reach statistical significance [$F(1,26) = 3.62$, $P = 0.06$ for respiration; $F(1,26) = 3.54$; $P = 0.07$]. For the arousal complaints, however, no CS+ Odor main effect was apparent, but a strong CS+ Odor $\times$ Conditioning interaction [$F(1,26) = 9.51$, $P < 0.005$] was observed. There were no effects on tingling and cardiac/warmth complaints (see Table 1).

Respiratory behavior. Breathing frequency was also affected by a significant Conditioning $\times$ CS+ Odor interaction [$F(1,26) = 5.24$; $P < 0.05$; see Fig. 2]. A significant conditioning effect appeared only when the CS+ was ammonia [$F(1,26) = 4.60$; $P < 0.05$], but not when it was niaouli [$F(1,26) = 1.19$, NS].

Across CS+ and CS- there was in addition a significant linear rising trend over time in V_E when ammonia was CS+ [$F(1,26) = 9.24$; $P < 0.01$], but not when niaouli was the CS+ ($F < 1$). FCO₂ showed only reliable effects of Time Block, generally replicating the context exposure pattern. A summary of the respiratory data can be seen in Table 2.

Correlational analysis of respiratory behavior, negative affect and subjective complaints

The conditioning manipulation had no effect on state anxiety: there was a general decrease from the first to the second day (cf. *supra*), and this effect did not interact with CS+ Odor. Collapsing Ss across conditions, Pearson correlations between NA-state and total complaints scores were significant only on the second day for the context exposure and for each of the three CS- only trials (r s between 0.45 and 0.55; $P < 0.02$). These correlations appear to rely mainly on the arousal ($r = 0.49$), cardiac/warmth ($r = 0.48$) and the unclassified set ($r = 0.36$). No significant correlations were found between complaints on CS+ only trials and any of the NA measures.

In order to investigate the relationship between somatic complaints caused by the conditioning manipulation on the one hand and NA and somatic responses on the other hand, stepwise regression analyses were run with forward inclusion of variables and 'F to enter' set at 1. The difference between subjective complaints during CS+ and CS- trials was the criterion variable,

Fig. 2. The conditioning effect on respiratory frequency as a function of type of CS+ odor (ammonia or niaouli).

Table 2. Respiratory frequency, minute ventilation (l/min) and fractional concentration of expiratory CO₂ (means across trials and time blocks)

	<i>f</i>	<i>V_E</i>	F CO ₂
Context exposure			
Day 1	11.9	8.11	4.72
Day 2	13.0	8.57	4.74
Acquisition			
Ammonia CS+			
CS+	16.4	15.00	6.83
CS-	14.6	8.10	4.52
Niaouli CS+			
CS+	15.0	17.06	7.04
CS-	13.0	8.15	4.92
Test			
Ammonia CS+			
CS+	15.3	10.00	4.55
CS-	14.2	8.98	4.59
Niaouli CS+			
CS+	12.0	6.52	4.82
CS-	12.5	6.38	4.77

NA (trait and state of the particular day), and the difference between CS+ and CS- (means per trial) for the respiratory parameters and heart rate served as predictors. Table 3 provides an overview of the significant contributions to the increase in subjective complaints, both during acquisition (trial 3) and test (trial 1-3). Also for each set of complaints, a regression was run using the difference between the mentioned parameters after averaging across the three CS+ or CS- trials.

None of the NA measures contributed significantly to the rise in complaints in any of the regressions that were run. In contrast, increases in complaints were only significantly predicted by differences in somatic responding of the Ss.

DISCUSSION

The present study provided evidence for classical conditioning of respiratory behavior and of subjectively expressed somatic complaints. The conditioning effect could not be explained by context conditioning, (selective) sensitization or by unconditioned or pre-existing responses to the CSs. A number of interesting elements in the data deserve further attention. First, although the inhalation of CO₂-enriched air during acquisition affected all measured respiratory parameters, Pavlovian conditioning affected mainly respiratory frequency. Gallego and Perruchet (1991) also found that the conditioning effect was confined to temporal parameters of the ventilatory responses. However, they found an increase in total cycle time to the CS+ (i.e. the respiration rate slowed down), whereas we found the opposite. It may be that the observed difference exemplifies the

Table 3. Stepwise multiple regressions of respiratory frequency, minute ventilation, end-tidal fractional concentration of CO₂ and heart rate (CS+ minus CS- trials) and negative affect on total complaint scores per trial and on complaint subsets (averaged across 3 trials) (CS+ trials minus CS- trials). The order of predictors per criterion reflects the sequence of steps

	Criterion	Predictor	Beta	<i>R</i>	<i>R</i> ² change	<i>P</i>
Acquisition	Trial 3	<i>V_E</i>	0.45	0.41	0.17	0.02
Test	Trial 1	HR	0.40	0.60	0.36	0.0007
		<i>f</i>	0.36	0.70	0.14	0.01
	Trial 2	<i>f</i>	0.35	0.34	0.12	0.07
	Trial 3	<i>f</i>	0.33	0.35	0.12	0.06
	Respiration	HR	0.53	0.65	0.42	0.0002
	Arousal	<i>f</i>	0.58	0.60	0.36	0.0006
		HR	0.43	0.63	0.04	0.19
		<i>V_E</i>	0.39	0.70	0.09	0.04
	Cardiac	—	—	—	—	—
	Tingling	<i>V_E</i>	0.66	0.44	0.44	0.0001
	Unclassified	—	—	—	—	—

distinction between a stimulus-stimulus (S-S) and a stimulus-response (S-R) type of learning, made in the animal learning literature (Rescorla, 1988), or the distinction between "signal learning" and "intrinsic learning" (Levey & Martin, 1987; Baeyens, Eelen, Van den Bergh & Crombez, 1992) in the human learning literature. The CR in the Gallego and Perruchet study (frequency decrease) may imply a learned attentional response of an S-S type: the tone signalling that the hypoxic US was about to be introduced may have increased attentional responding. A decrease of the respiratory rate is indeed compatible with such a response: both the tone alone and the hypoxic stimulus alone in the control condition of the acquisition phase induced slower breathing in their Ss. The CR in the present study (frequency increase) may point to an S-R type of learning where the CS has become a substitute for the US (i.e. the ammonia with air was itself experienced as a bad suffocating gas). The fact that the conditioning effect was confined to the "bad" odor (ammonium) and did not develop to the "fresh" odor (niaouli) supports this interpretation.

A second important finding was that also subjective complaints were conditioned in this procedure. A similar pattern of effects appeared as was found with regard to the respiratory effects: it was confined to ammonia, exemplifying the selective association phenomenon. Furthermore, the conditioning effect on complaints was not confined to complaints related to general arousal, but involved specific respiratory and other complaints (headache, dizziness) as well. However, the subsets of complaints showed a slightly different pattern: the arousal related complaints were specifically conditioned to the ammonia CS+, whereas the respiration and unclassified complaints tended to generalize more: when ammonia was CS+ more complaints were reported to the niaouli CS- as well. A parallel was found in the breathing behavior in that Ss showed rising V_E 's over time across both ammonia and niaouli odors, but only when ammonia was CS+. It seems that once Ss had learned that "a bad suffocating gas" could be given, their discriminative capabilities in responding to the CSs were impaired, as indicated by their breathing behavior and related complaints. This effect is peculiar and warrants further research in light of the phenomenon of multiple chemical sensitivity (MCS), a condition of somatic complaints attributed to low levels of environmental chemicals in the absence of known toxicological mechanisms (Schusterman, 1992; Ziem & Davidoff, 1992; Bolla-Wilson, Wilson & Bleeker, 1988). Indeed, it may mean that Ss having had a bad US-experience (e.g. a toxicological challenge or hyperventilation) in the context of a specific odor seem vulnerable to rapid generalization to other odors, even when they have not been paired with the bad experience itself. The fact that acquisition and test were on separate days may be important because the loss of memory for specific stimulus attributes may have contributed to this effect (Riccio, Ackil & Burch-Vernon, 1992).

Both the selective conditioning effect and tendency to generalize to CS- trials are at odds with the fact that the Ss have undoubtedly consciously noticed the simple contingency relationships equally well in both CS+ odor conditions. Despite the easy discriminability of the odors and the strong US effects during acquisition, the Ss' somatic responses and complaints are governed by basic associative processes that do not simply reflect these consciously noticed contingencies. The selective association phenomenon is consistent with the suggestion that belongingness is facilitated by affective response matching between the involved stimuli, suggesting that they may evoke similar primary response tendencies (Hamm *et al.*, 1989). However, other explanations for the observed differences may be taken into consideration as well. For example, although there were no unconditioned effects of the odors themselves, differences in previous experiences with the CSs may have facilitated learning the "ammonia CS- shortness of breath US" combination.

A third important finding is that NA is related to a basic level of psychosomatic complaints, but not to an increase in complaints as caused by the conditioning procedure. NA, as measured by the STAI, therefore likely reflects a response style rather than an attentional style. This interpretation is consistent with some other findings. In an earlier study we found that NA had a main effect regardless whether Ss were breathing CO₂ or room air (Van den Bergh *et al.*, 1993). If it would be an attentional style, the difference between complaints of high and low NA Ss would increase when somatic responses were induced. Also, when normals were observed during rest, it was found that STAI-measured NA explained most of the variance in psychosomatic complaints, while respiratory parameters added only minimal explained variance (Wientjes & Grossman, 1994). But when stress manipulations were applied, Steptoe and Vögele (1992) found no correlation between STAI-measured NA and accuracy of bodily perception. However, even though

in the present case, the increase in complaints due to conditioning is better predicted by changes in somatic functioning, there is no clear link between type of somatic responding serving as the more prominent predictor and type of somatic complaints. So, paradoxically interoceptive feedback is likely to serve as a basis for complaints, but not through accurate perception of one's own bodily responses.

The present study is also relevant to an hyperventilation based account for panic symptoms (Garssen *et al.*, 1992). Although one may doubt the ecological validity of the present approach with odors, it has been previously documented that exposure to organic solvents may trigger panic (Dager, Holland, Cowley & Dunner, 1987). Furthermore, the belongingness aspect similar to that found in this study may mediate the learning of combinations like hot or crowded places and shortness of breath as is found in agoraphobia. In any case, the present findings have relevance for findings that panic patients may show somatic complaints whether or not they hyperventilate in terms of induced hypocapnia. Assuming that the subjective experience caused by CO₂ inhalation compares with the experience of an episode of hyperventilation, it appears that bodily responses and complaints may be triggered by CSs in the absence of USs like CO₂ or hypocapnia. Furthermore, this may occur through associative processes that to some extent may appear irrational (Seligman, 1988). In this respect, it may be interesting to note that Lynch, Bakal, Whitelaw and Fung (1991) found chest EMG during CO₂ inhalation to correlate better than any other physiological measure with the occurrence of frightening cognitions and sensations in panic patients. This points to the importance of replicating this study with panic patients.

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