THE EFFECT OF HYPOCAPNIA ON EXTINCTION OF CONDITIONED FEAR RESPONSES

G. M. van der Molen¹, M. A. van den Hout², H. Merckelbach²,
A. C. van Dieren² and E. Griez³

¹Department of Medical Psychology, ²Department of Mental Health Sciences and ³Department of Clinical Psychiatry, Limburg University, 6200 MD Maastricht, The Netherlands

(Received 13 May 1988)

Summary—Conditioning models have been very useful in the understanding of the etiology and maintenance of anxiety. Such laboratory models, however, leave unexplained why in many cases of naturally occurring anxiety, as in the case of agoraphobia, the fear responses do not extinguish. Literature on experimental anxiety provocation suggests that a systemic alkalosis might play a role in the maintenance of phobic fear. It was hypothesized that a subject in a state of respiratory alkalosis would show delayed extinction to classical conditioned anxiety. In a differential classical conditioning paradigm, consisting of a habituation-, an acquisition-, and an extinction-phase, slides and electric shocks were used as conditioned stimuli (CS) and unconditioned stimuli (US) respectively. The skin conductance response was taken as (U)CR. Subjects were randomly assigned to two groups: hyperventilation or control. It was shown that the extinction was not delayed when subjects were hypocapnic during the extinction. These data support the view that a respiratory alkalosis per se is not a sufficient condition for the maintenance of neurotic fears. The data of the present study are discussed in the context of existing literature on a psychological interpretation of the maintenance of anxiety.

INTRODUCTION

Concerning the explanation of naturally occurring phobias learning theory has enjoyed considerable prominence. Although laboratory models have been very useful, they leave some central clinical observations unexplained. In laboratory settings, extinction of the conditioned response will occur in the absence of the unconditioned stimulus (US). Clinical phobias, however, are highly resistant to extinction and even increases of fear can be noted in the absence of any US.

To account for an increase in fear responses in a period when extinction would be expected to occur, Eysenck developed the incubation theory of anxiety/fear responses (Eysenck, 1968). This theory states that in some cases the conditioned response (CR) can be aversive in itself. The aversive properties of the CR can act as a US and conditioning continues in the absence of the original US. This account seems highly plausible concerning the explanation of non-situational panic or fear-of-fear (Evans, 1972). Experimental evidence to confirm the notion of incubation is sparse, however. The question by what mechanism the extinction of fear is inhibited, is still open. Literature on experimental anxiety provocation and on hyperventilation provides some interesting suggestions.

Firstly, intense anxiety is common in the hyperventilation syndrome (HVS), and profound hyperventilation (HV) plays a role in the maintenance of complaints in approx 66% of the agoraphobic patients (Garssen, van Veenendaal and Bloemink, 1983). Symptoms characteristic of the HVS are, at least partly, the result of hypocapnia and respiratory alkalosis (Gelder, 1985). When asked to voluntarily overbreath the majority of panic patients experience physical symptoms and negative affect, which they rate similar to the experience of clinical panic (Bonn, Readhead and Timmons, 1984; Clark, Salkovskis and Chalkley, 1985; Salkovskis and Clark, 1986).

Secondly, a comparable phenomenon occurs in experimental panic-provocation interventions, such as lactate infusions (Pitts and McClure, 1969; Liebowitz, Fyer, Gorman, Dillon, Appleby, Levy, Sanderson, Levitt, Palij, Davies and Klein, 1984; Liebowitz, Gorman, Fyer, Levitt, Dillon, Levy, Appleby, Anderson, Palij, Davies and Klein, 1985; Margraf, Ehlers and Roth, 1986) and bicarbonate infusions (Grosz and Farmer, 1969; 1972). The experimentally induced metabolic alkalosis is accompanied by a number of physical symptoms typical of anxiety, such as palpitations, dyspnea, dizziness, etc. Most panic patients react with extreme anxiety to these triggers while normals do not.
Finally, a fair amount of research has also been done on the relationship between the effects of the inhalation of a 35%CO₂–65%O₂ mixture and panic (Grič, Lousberg, van den Hout and van der Molen, 1987; Fyer, Uy, Martinez, Goetz, Klein, Fyer, Liebowitz and Gorman, 1987). The inhalation of this mixture reliably induces panic symptoms comparable to those of lactate infusions or of HV provocation and also elicits high anxiety in panic patients. Somewhat paradoxically, the physical sensations do not occur during the initial hypercapnia but during the subsequent pCO₂ drop and hypocapnia that follows the 35%CO₂ challenge (van den Hout and Grič, 1985).

Summarizing, there are three reliable experimental procedures for eliciting anxiety and panic symptoms under controlled conditions, all of which have a systemic alkalosis, reflected in lowered pCO₂, in common.

Considering systemic alkalosis as a characteristic feature of panic on the one hand, and the delayed extinction of natural phobias on the other, it was hypothesized that an alkalosis in itself might play an important role in the maintenance of phobic anxiety: the extinction of phobic fear may be inhibited by hypocapnia and alkalosis.

Seeing that Pavlovian approaches to phobic anxiety have proved quite successful, it was decided that a classical conditioning paradigm would be used for testing the issue under review. The set-up was a differential conditioning design comparable to the one commonly used by Öhman and co-workers (Öhman, Fredrikson, Hugdahl and Rimmö, 1976; Öhman, 1986), in which physiological factors were varied. Two groups, both in a state of normocapnia, were exposed to different pictures, one of which was consistently reinforced by an electric shock, whereas the other one was never reinforced. During extinction, however, in one group hypocapnia was introduced, whereas the other group remained normocapnic.

We were interested in pure hypocapnia effects on extinction, while the possibility that hypocapnia might induce fear in some subjects and that this fear could interfere with the processes under study, was outside the scope of the present investigation. Therefore we pre-tested all subjects for fear during respiratory alkalosis and those subjects expressing fearfulness during the pre-test phase were excluded from the experiment. It was hypothesized that in subjects in a state of respiratory alkalosis the extinction of classically conditioned skin conductance responses will be delayed.

METHOD

Subjects

The subjects were 32 undergraduate students (10 males and 22 females) with no current or prior history of phobic complaints. Their ages ranged from 19 to 34. The subjects were paid for their participation in the study. They were randomly assigned to either of the two groups: hyperventilation during extinction (HV-group) or control (C-group).

Before the actual experiment, the subjects filled out the Dutch version of the State-Trait-Anxiety-Inventory (STAI) [van der Ploeg, D'efares and Spielberger, 1981] to measure general anxiety level.

Apparatus and stimulus materials

SCR and skin conductance level (SCL) were recorded with a Beckman Skin Conductance Coupler (type 9844), and the method of constant voltage (0.5 V) was used. The coupler allowed for a maximum sensitivity of 0.05 micromho. Beckman Ag–AgCl electrodes (dia. = 8 mm) were attached to the distal phalanges of the second and third fingers of the subjects' left hand with adhesive collars.

An electric stimulus with a maximum capacity of 60 mA transmitted electric current (dc) to the subjects. Two shock electrodes were placed on the first finger of the subject's left hand, at the distal and medial phalanges.

The conditioned stimuli (CS) consisted of slides depicting a crowd and an escalator. A Kodak Carousel was used for the presentation of the slides. The slides were projected onto a white wall. The size of the projected image was approx 80 × 120 cm, 2.5 m in front of the subject.

Onset and offset of the stimuli, inter-trial intervals, occurrence of the electric pulses and response registration were controlled by a microcomputer (PDP Min-11).

End-alveolar carbon dioxide pressure (pCO₂) was measured continuously by means of a Gould Godart Mark-II® capnograph.
Design

A 2 (group) × 2 (reinforcement) factorial design with repeated measures on the last factor was used. For statistical analyses, a trial factor, in the form of a repeated measure, was added. The group factor refers to the condition to which the subjects had been assigned: HV or C. The reinforcement factor is a consequence of the fact that each subject saw two slides, one of which (CS*) was associated with electric shock (US) during the acquisition phase and the other one (CS-) never followed by an US.

Procedure

Subjects in the HV-condition came to the laboratory a few days prior to the actual experiment. They were fully explained what HV is and what they could expect. Then the experimenter demonstrated how to ventilate very forcefully and subjects were trained in reducing their pCO₂ rapidly and in keeping it reduced to 50% of their resting pCO₂. Finally they were instructed how to recuperate quickly. Most subjects could meet the criterion without difficulties in one training session. Subjects who could not and those experiencing anxiety during HV provocation were not allowed to participate in the actual experiment. Subjects in the control condition also came to the laboratory a few days before the actual experiment. They were ‘trained’ to do a mental arithmetic task for 2 min followed by a hand tapping task. These tasks were chosen as controls for distraction and motoric activity in comparison with the experimental group.

Some days after the training session subjects came to the laboratory for the conditioning procedure. Upon arrival in the laboratory, the subjects were asked to sit down in a comfortable chair which was placed in a dimly lit, sound attenuated chamber. Recording apparatus, microcomputer and Kodak Carousel were in an adjacent room. The slides were projected through a hole in the wall. The experimenter then explained that during the experiment electric shocks would occur. After the subjects had given their consent and the electrodes had been fastened, the experimenter started a shock work-up procedure in which the shock level was gradually increased until the subject indicated that the shock was “very uncomfortable but not painful”. The subjects were not instructed about the CS–US contingency.

The experiment consisted of three phases. The first was a habituation procedure. This phase involved 8 CS-only trials (4 CS- and 4 to be CS*). Then the acquisition phase followed, in which 6 reinforced presentations of CS* and 6 unreinforced presentations of CS- occurred. Before the start of the final, extinction phase the subjects in the HV-condition were asked via the intercom to HV forcefully for two minutes reducing pCO₂ to circa 1/3 (or lower) of the resting pCO₂ and then to lower the frequency and/or depth of ventilation so that pCO₂ was reduced to 50%, of resting value. At that point the experimenter gave feedback of their performance and subjects were asked to keep ventilation continuously at that rate/depth, as was learned in the training session. (Subjects in C-condition were at this point asked to do the mental task and to start hand-tapping). Then the extinction continued, consisting of 10 unreinforced presentations of both slides. At the end of this phase subjects were asked to breathe at their own pace, or to stop hand-tapping respectively.

Slides were presented for 8 sec. The duration of the shock was 0.5 sec and it was delivered exactly upon removal of CS*. Inter-trial intervals varied between 20 and 40 sec, in steps of 5 sec, and with a mean of 30 sec.

Throughout the experiment, the order of presentation of the two slides was quasi-random; no more than two successive presentations of the same slide occurred. CS* and CS- slides were counterbalanced across the two groups.

Response definition and analysis

An 8 second CS–US interval allowed for the recording of multiple response forms of the SCR (Prokasy and Kumpfer, 1973). Like Öhman et al. (1976), differentiations were made between FAR-, SAR- and TOR-components of the SCR. The first-interval anticipatory response (FAR) pertains to a maximal deflection with a latency of 1–4 sec after CS onset. The second-interval anticipatory response (SAR) is defined as a maximal deflection at 4–8 sec after CS onset. Maximal deflections occurring at 1–4 sec after CS offset during the habituation and extinction phases are regarded as
third-interval omission responses (TORs). The SCR components were measured in micromho and square-root transformed (Venables and Christie, 1973). Data were analyzed as response magnitudes.

Separate analyses of variance were carried out for FARs, SARs and TORs during the three phases of the experiment. The comparisons of interest are a group × reinforcement (G × R) interaction and a group × reinforcement × trials (G × R × T) interaction. A rejection level of \( P < 0.05 \), with Greenhouse–Geisser corrections was adopted for all comparisons.

RESULTS

The mean of the US level was 26.7 mA in the HV group and 26.4 mA in the control group. This difference did not reach significance. Neither were there any significant differences in anxiety level, or initial SCL-level. The data on FAR, SAR and TOR during the three phases of the experiment are depicted in the Fig. 1. The mean SCRs are represented in blocks of two trials.

Habituation

There was a significant main effect Trial for SAR and TOR \( (F(4, 120) = 4.78 \) and \( F(3, 90) = 5.97 \) indicating that habituation occurred in the case of SAR and TOR only. No other effects of interest reached significance in this phase.

Acquisition

Data for FAR and SAR are presented only. A strong main effect Reinforcement was found \( (F(1, 30) = 42.79, F(1, 30) = 35.83 \) for FAR and SAR respectively), as well as a Trial effect for FAR \( (F(5, 150) = 3.19 \), and a R × T interaction \( (F(5, 150) = 3.44, F(5, 150) = 3.19 \), for both FAR and SAR. This indicates that the procedure was highly effective and that a reliable differentiation between CS+ and CS− took place. No difference between the groups or a G × R interaction emerged.

Extinction

During extinction significant Reinforcement \( (F(1, 30) = 6.86, F(1, 30) = 37.08, F(1,30) = 13.83 \) and Trial effects \( (F(8, 240) = 2.13 \) and \( F(9, 270) = 360 \), for FAR and TOR respectively) emerged. No R × T interaction reached significance, which indicated that although responsiveness decreased on the whole, differential responding was maintained and thus no substantial extinction occurred. No significant G × R or G × R × T interactions were found, which means that there was no difference in the process of extinction between the groups. An unexpected significant main effect group showed up, \( (F(1, 30) = 7.52, F(1, 30) = 6.31, F(1, 30) = 6.48 \) indicating that the SCR in HV-group was, on the whole, lower than in the C-group.

DISCUSSION

In the present study no evidence was found that suggested that resistance to extinction is specific in those subjects who hyperventilated during the extinction of fear reactions.

Thus the data obtained did not confirm our hypothesis that subjects in a state of respiratory alkalosis during extinction will show a delayed extinction of a classical conditioned electrodermal response, as compared to normocapnic subjects. Quite unexpectedly, HV-subjects had smaller SCRs than C-subjects during extinction. It is possible that this difference is inherent in the HV task. Proper control will consist of "normocapnic hyperpnea". However, there are no a priori reasons to assume that this decreased SCR might have influenced the occurrence of delayed extinction.

Before the possible implications of the findings of the present research are speculated on, some methodological comments should be given. First, there was, on the whole, a strong conditioning effect, both during acquisition and still during extinction. This could possibly have overruled the effect of hypocapnia. Furthermore, it is hard to interpret the extinction data, because in both groups there was hardly any extinction. Therefore it is difficult to decide whether extinction was delayed or not. This is quite contrary to what is found in existing literature. In most studies on prepared conditioning, 20 extinction trials proved to be sufficient for documenting differential
extinction (see Öhman, Fredrikson and Hugdahl, 1978) as a function of stimulus type. However, as the study by Dawson, Shell and Banis (1986) makes perfectly clear, differential extinction effects as a function of stimulus type become more pronounced when an extensive extinction procedure is used (i.e. 48 instead of 20 trials). It may well be that delayed extinction as a result of hypopacnia only emerges when an extensive extinction procedure is used. Future research should preferably employ more extinction trials and weak conditioning paradigms, e.g. trace conditioning and low US intensities, to prevent such ceiling effects.

A second issue of interest is formed by the differences between the three components of the skin conductance response. The phobic anxiety reaction is often seen by learning theorists as a
conditioned emotional response in which sympathetic activity is most pronounced. Therefore SCR has played a prominent role in experimental anxiety research (Katkin and Deitz, 1973). Nowadays it has become clear, however, that attention and arousal can affect SCR to a considerable extent (Spinks, Blowers and Shek, 1985). In the work of Öhman and colleagues (see Öhman, 1986) FAR was usually the component of interest. Contrary to what is reported most in this kind of research, in our experiment, not FAR, but SAR and TOR showed pronounced effects. This is in line with the findings of Merckelbach, van der Molen and van den Hout (1987) who also found better conditioning effects for SAR than for FAR in a comparable study. There are plausible theoretical arguments to explain that effect. The FAR has a latency of 1–4 sec after stimulus presentation. The FAR may be considered as an orientation reaction to CS while the SAR, with a latency of 4–0 sec prior to CS-offset, c.q. expected US-onset, can be considered as the anticipation to US (Gray, 1981).

Another problem in the present experiment is the extent to which slide-shock associations can be considered as a laboratory model for conditioning processes in agoraphobia. One might question the "belongingness" between the slide content and the shock. To draw a parallel again with the preparedness research: the conditioning study by Cook III, Hodes and Lang (1986) has shown that a resistance to extinction, after having been shown slides of snakes and spiders does only occur when shock rather than white noise is used as the US. Thus it is possible that a different US (e.g. an interoceptive US such as tachycardia) would have facilitated delayed extinction in the present experimental procedure.

Finally, it might be argued that a decrease in pCO₂ to 50% of resting value is hardly ever noted during naturally occurring panic. However, this circumstance should have been an a fortiori argument in favour of our hypothesis.

Apart from these methodological considerations the question is left open why we could not demonstrate an influence of respiratory alkalosis on the extinction of fear responses. In recent literature, psychological explanations of the maintenance of anxiety are considered (Ackerman and Sachar, 1974; van der Molen and van den Hout, 1987; Clark, 1986). These explanations share the opinion that the perception and interpretation of bodily symptoms lead to panic, and suggest that the development of fear can best be described as a self-maintaining positive feedback loop. Both the presence of certain bodily sensations and the catastrophical misinterpretation of these sensations form the very crucial point of these models. The present study sought to isolate the bodily symptoms from the interpretation of these symptoms and to investigate the role of alkalosis per se. Therefore, subjects were selected who did not have problems with hyperventilation in itself, or with the accompanying bodily sensations, such as palpitations, tingling hands etc. These subjects did not show or report any signs of overt subjective anxiety. The subjects indicated afterwards that they had not experienced fear during the experiment, due to HV. According to a cognitive physiological model of panic, the panics that occur in situations when an alkalosis is induced (lactate, bicarbonate, HV-provocation) can be accounted for by the fact that subjects mislabel the sensations accompanied by the alkalosis. Insofar as one can assume that the absence of group differences was not caused by methodological factors, the validity of this view is enhanced by the findings of the present study, that alkalosis per se does not influence the acquisition or extinction of fear.

Acknowledgements—This study was supported by a grant from the Netherlands Organization for Scientific Research (NWO-Psychon 560-268-001). The authors are grateful to Mrs R. Gierlings for her help in the study, to Mrs M. van der Horst for editing the English text, and to Mrs I. van Neppen who typed the manuscript.

REFERENCES


