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Habituation and Conditioning of the Defence Reactions and Their Cardiovascular Components in Cats and Dogs

JANE MARTIN, COLIN J. SUTHERLAND*, and ANDRZEJ W. ZBROŻYNA**

Department of Physiology, Medical School, University of Birmingham, Birmingham B15 2TJ, Great Britain

Summary. Cardiovascular and behavioural responses elicited by novel, noxious or aversive stimuli have been studied in dogs and cats. Hindlimb blood flow, heart rate and arterial blood pressure increased in dogs when an orienting response was elicited by a novel stimulus (a sound). Similar cardiovascular responses occurred in dogs to mild noxious stimulus and in cats displaying a threatening posture when confronted by a dog. The cardiovascular components of the orienting response to a sound habituated with repetition of the sound. In two dogs however sensitization (increase) of the response occurred with repetition of the sound. The cardiovascular response in cats confronted by a dog was modified by repetition of the confrontations: the vasodilation in the muscles waned and eventually was replaced by vasoconstriction while the cardiac acceleration and pressor response persisted. The threatening response was the most persistent. The modification of the behavioural and cardiovascular aspect of the response was not developing in parallel. The cardiovascular pattern was altered before any apparent changes of the behavioural pattern occurred. The cardiovascular responses to the noxious stimulus in dogs and cardiovascular components of the defence reaction in cats were readily conditioned to a sound. The possible role of the modification of the cardiovascular pattern in defence reactions in pathogenesis of hypertension is discussed.

Key words: Cardiovascular – Habituation – Conditioning – Defence reactions.

INTRODUCTION

The emotional response elicited by a sudden, loud noise or by noxious stimulation involves a characteristic pattern of cardiovascular changes. Such a response has been described in dogs by Caraffa-Braga et al. (1973); the cardiovascular pattern consisted of vasodilatation in skeletal muscles, vasoconstriction in the mesenteric and renal vascular beds and increase in the heart rate and arterial blood pressure. Forsyth (1972) described similar cardiovascular responses in rhesus monkeys. This pattern of cardiovascular changes is known to be produced by electrical stimulation in well defined areas of the brain-stem in cats (Eliasson et al., 1951; Abrahams et al., 1960; Feigl et al., 1964), in dogs (Bolme et al., 1967) and in monkeys (Forsyth, 1972). In non-anaesthetized cats mild electrical stimulation in these brain-stem areas induced increased alertness with a postural response resembling the orienting reaction, more intense stimulation produced a full threatening reaction (Abrahams et al., 1960).

Thus the orienting reaction, startle, response to noxious stimuli and the defence reaction are a continuous family of responses differing in their intensity but identical in the cardiovascular response accompanying them. That the threatening reaction and response to noxious stimulation are closely related has been shown by Hutchinson, Renfrew and Young (1971) and by Hutchinson (1973) who demonstrated in a wide range of species that noxious stimulation elicits aggressive behaviour. However, the naturally elicited responses and their cardiovascular components in the intact animal show an important degree of variability, while the defence reaction to electrical stimulation in the defence area of the brain stem or that occurring in the decerebrate animal are stereotyped (Bard and Macht, 1958; Abrahams et al., 1960).

That the cardiovascular components of the defence reaction can be modified by habituation or conditioning has been shown by Abrahams et al. (1964). Furthermore there is a large body of evidence showing that cardiovascular responses may be conditioned and that

* Present address: Department of Chemistry and Biology, Preston Polytechnic, Preston, Lancashire
** To whom offprint requests should be sent

also in this way the original pattern of the response may be altered (Menzies, 1937; Pshonik, 1952; Dykman and Gantt, 1958; Shmavonian, 1959; DiCara and Miller, 1969; Bølme and Novotny, 1969). In the present study an attempt was made to show how the cardiovascular participation in orienting reaction, in response to a mild noxious stimulus and in the threatening response, may be modified by simple forms of learning. In particular the effect of habituation (waning of the response with repetition), sensitization (waxing of the response with repetition) and conditioning was studied. The results of this work have been briefly reported elsewhere (Sutherland and Zbrożyna, 1971, 1974a, 1974b).

METHODS

Twenty dogs (18 beagles and 2 mongrels) of both sexes, 9 adult female cats and 7 kittens of both sexes were used in this investigation. Three types of experimental series were carried out, conditioning experiments in which dogs and 3 adult cats were used, confrontation experiments in which cardiovascular responses were recorded on 4 adult cats and confrontation experiments on 5 adult cats and kittens in which no cardiovascular responses were recorded. In the experiments on the conditioning of the flexor reflex in dogs the animal was placed in a soundproof cabin (Amplifon, Milan, Italy) and could be viewed clearly by the experimenter through a one way treble glazed window. The animals were conditioned to a sound. The sound, which at the later stage was used as the conditioned stimulus, was increased in intensity in a stepwise fashion from 33–83 dB in each session and repeated until the behavioural and cardiovascular responses waned at each intensity level (habituation). Then the conditioning was commenced, the sound now being followed after a 2–10 s delay by electrical stimulation of the front paw. The electrical stimulation was delivered via two electrodes secured between the front limb toes. A constant current of up to 3 mA was so adjusted for each dog so that it would elicit a small flexor reflex of the front limb without involving general movements of the body. On average 10 trials were carried out during each experimental session.

In confrontation experiments cats were placed in a small box, facing a grill through which the animal could clearly see. The box was covered with a cloth while a dog was brought into the room and placed in front of the grill. The cloth was then removed.

The surgery was carried out in strictly aseptic conditions under pentobarbitone anaesthesia (30 mg/kg i.p.). After surgery the cats were given daily subcutaneous injections of 5.0 mg/kg Engemycin (oxytetracycline) for 5 days on average. Dogs required this treatment only occasionally. For blood pressure measurement a pvc crystal tube (Portex), filled with heparin solution (1000 i.U./ml in saline), was inserted via the common carotid artery into the aorta.

This tube was led out through a skin button between the scapulae. The end of the tube was fitted with a three way tap (K-75 sterile, three way stopcock, Pharmoseal Laboratories, Glendale, California). During the experiment a P37 miniature transducer (Statham Instruments) was plugged into the tap. The output was amplified by a DC2D Devices amplifier and a continuous record of blood pressure was obtained on a Devices pen recorder. The signal from the output of the blood pressure preamplifier was fed to a Devices Instantaneous Ratemeter (Type 2751) which computed the heart rate. The output of the Ratemeter was fed to the Devices pen recorder and a curve of the heart rate was recorded. A record of the blood flow was obtained with an electromagnetic flow probe (Micron, Nycotron) implanted on the external iliac artery, the deep femoral branch being tied off. A pvc occluding device (Debley, 1971) was implanted downstream on the external iliac artery for determining zero flow. The zero flow was established after each experiment. During the experiment the flow probes were connected to a flow meter (Medical and Biological Instrumentation Ltd., Nycotron) and the output was amplified and displayed on the pen recorder (Devices Ltd.) as pulsatile flow (DC3 amplifier, Devices Ltd.) and mean flow (DC2 amplifier, Devices Ltd.). The mean signal of flow and pressure from the amplifiers outputs were fed to an electronic divider (Analog 4, Quadrant Multiplier A.D. 246 in the feedback of an A.D. 410 operational amplifier) to compute conductance $\frac{\text{mean flow}}{\text{mean pressure}}$ wich was recorded on the pen recorder.

Chest movements (respiration, vocalization) were recorded with a strain gauge secured on the animals thorax. Gross limb movements were recorded by a capacitance displacement transducer attached to the paw. The output of the transducer was amplified (DC2D Devices Ltd.) and recorded. The lag between the movements and the pen deflection was less than 0.5 s. The amplitude of the pen deflection was proportional to the vertical component of the movement. The recording of limb movement was supplemented by direct observation and by a record of EMG of the quadriceps of the limb in which the blood flow was being monitored.

RESULTS

The Orienting Reaction. The behavioural response to the first auditory stimulus of moderate or low intensity (60 dB or below) was that the dog stopped whatever it was doing, pricked up its ears and then turned its head towards the source of the sound. In 12 dogs cardiovascular changes accompanied the orienting reaction. In all but one the hindlimb blood flow and heart rate increased. The hindlimb blood flow increase ranged from 15–280% of the resting flow rate while the heart rate increase varied from a few beats/min to maximum of 2.5 fold. In 9 dogs the blood pressure increased by 5–20 mmHg and in 3 dogs the blood pressure dropped by 10–25 mmHg. On Figure 1 an example of cardiovascular changes accompanying the orienting response is shown.

Cardiovascular participation in the orienting reaction was dependent on the intensity of the stimulus; the tendency was for the cardiovascular response to increase with an increase of the intensity of the stimulus e.g. increases of the sound intensity by 10 dB within the range of 50–80 dB were sufficient to produce in dogs increases in the iliac blood flow by 20–100%, in the heart rate by 10–20% while the blood pressure increase did not exceed 5–10 mmHg.

Habituation of the Orienting Reaction. The cardiovascular and behavioural response to a stimulus gradually diminished with repetition of the stimulus. The speed of cardiovascular habituation varied from individual to individual: in some dogs the response disappeared after only one presentation, in most dogs,

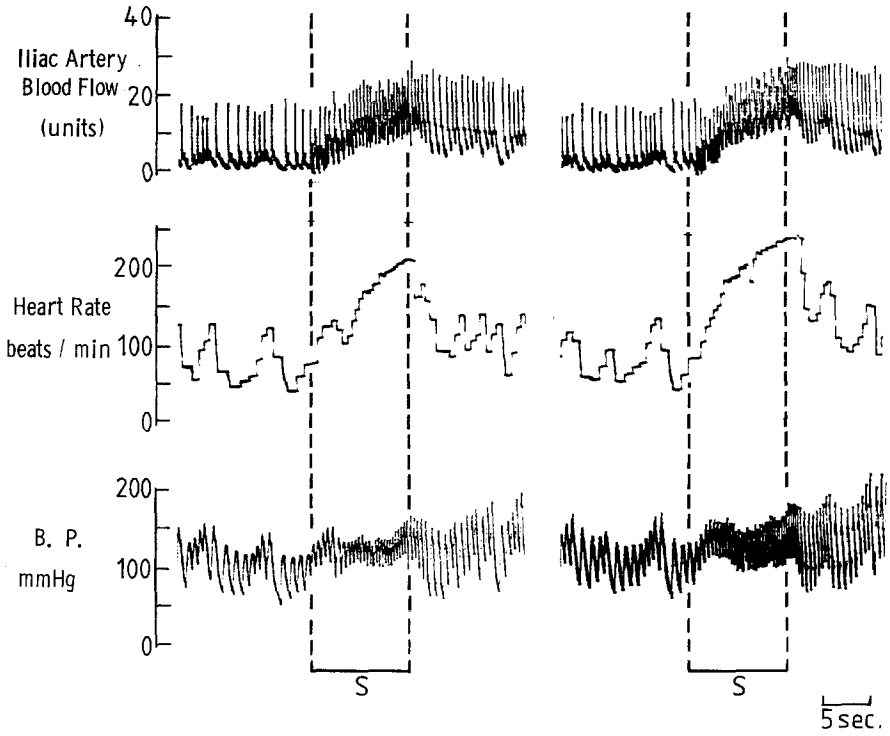

Fig. 1
The cardiovascular response of a dog to 2000 Hz 60 dB sound (*S*) presented to the animal for the first and second times. The response was accompanied by a slight head movement

however, complete habituation was achieved after 3–6 presentations of the stimulus of a moderate intensity (60 dB). The increases of blood pressure and heart rate habituated much more readily than the increases in hindlimb blood flow. Habituation of the behavioural response also varied and often bore no relation to the course of habituation of the cardiovascular responses. In two dogs the behavioural orienting reaction was not accompanied by cardiovascular changes.

Sensitization. In two dogs under study repetition of a sound (2000 Hz) of moderate intensity (70 dB) produced increasing restlessness leading to struggling with a gradual intensification of the cardiovascular changes. An example of such sensitization is shown in Figure 2. In this example the sound of 60 dB intensity evoked the usual behavioural orienting response together with a deep inspiration on the onset of the stimulus. When the intensity of the sound was increased to 70 dB a large increase in the hindlimb blood flow appeared.

With repetition of the sound the animal became restless and the hindlimb blood flow increase was each time more and more enhanced while the blood pressure and heart rate were only slightly elevated. The response was eventually habituated when the intensity of the sound was reduced to 60 dB. The first component to habituate was the behavioural response. Already on the third repetition of the sound the dog was completely quiet while the iliac blood flow was still increased by 60%, conductance by 50%, blood pressure by 10% and heart rate by 30%. On the sixth repetition of the sound the blood pressure and the heart rate remained steady and did not change on further repetition of the sound while the hindlimb blood flow increased again but now for the last time on the seventh presentation of the stimulus.

The Flexor Reflex and Accompanying Cardiovascular Changes. In this series of experiments the front limb flexor reflex was recorded in response to electrical stimulation of the paw. The threshold electrical stimulus to the front paw eliciting a flexor reflex of the front limb consistently produced an increase in the hindlimb blood flow. This increase of flow was blocked by intra-arterial injection of 0.2–0.4 mg atropine sulphate. It was therefore concluded that it was due to active vasodilatation in the skeletal muscles produced by activation of the cholinergic sympathetic nerve fibres. Usually the muscle vasodilatation was accompanied by fluctuations in the arterial blood pressure and the heart rate. In two dogs the threshold stimulus for the flexor reflex did not elicit any changes in the monitored cardiovascular parameters.

Conditioning. After habituation of the cardiovascular responses to the sound conditioning procedure was introduced. The auditory stimulus (usually 2000 Hz 60–80 dB) sounded for 2–10 s and simultaneously with its termination an electrical stimulus was applied to the paw. Usually all the cardiovascular changes

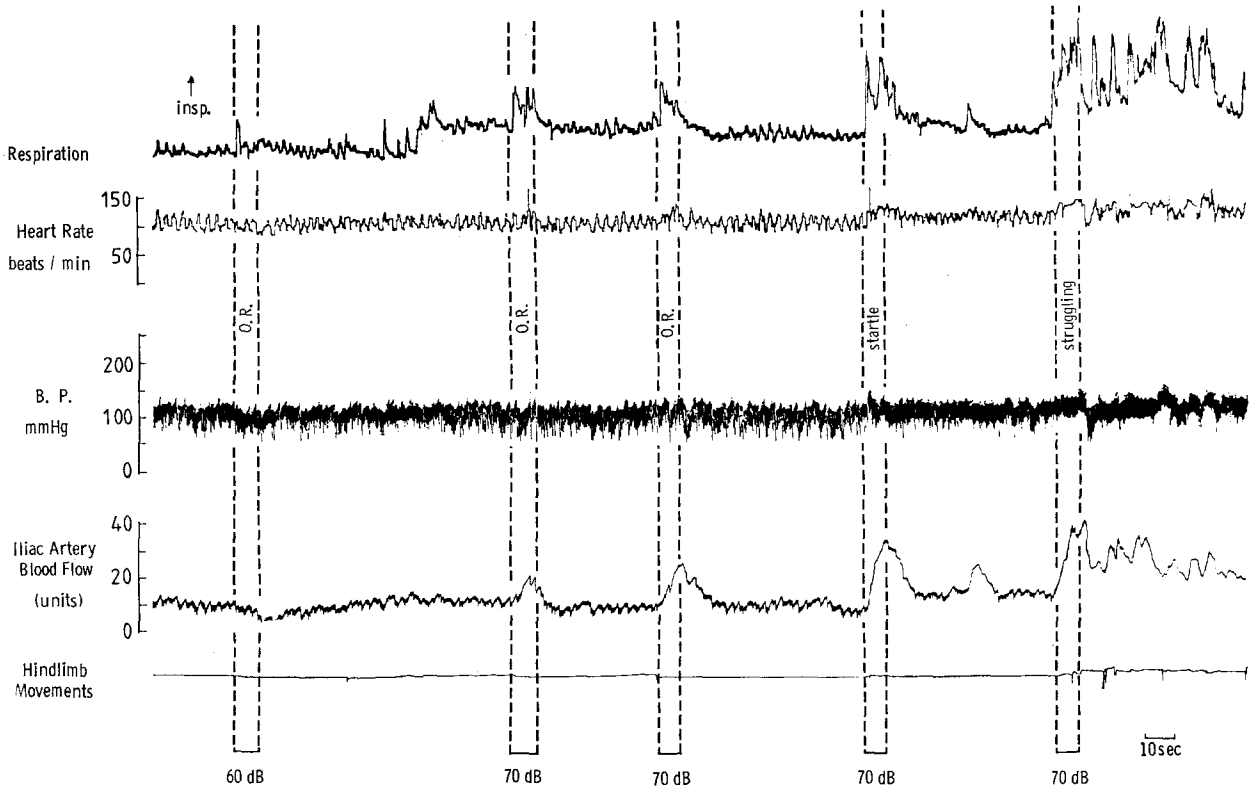

Fig. 2. Sensitization of the cardiovascular response in a dog to a 2000 Hz sound alone after its intensity was increased from 60–70 dB in the second trial. The arrow indicates inspiration

elicited by noxious stimulation of the paw were conditioned to the preceding sound. The first conditioned responses to develop were the cardiovascular and respiratory changes, they consisted of vasodilatation in the skeletal muscles, heart rate increase and change in the respiratory pattern. They appeared after 1–4 combinations of the sound with the noxious stimulus. The conditioned flexor reflex appeared after 6 or more combinations. The conditioned increase of the external iliac artery flow was due to active vasodilatation in the skeletal muscles of the hindlimb produced by activation of the cholinergic sympathetic nerve fibres, since it was blocked by injection of 0.2–0.4 mg atropine sulphate intra-arterially (Fig. 3). The atropine test was repeated at least once or twice on each dog with the same result. The conditioned hindlimb vasodilatation was not correlated with gross limb movements or with EMG activity of quadriceps muscle.

As the cardiovascular and somatic responses were followed throughout the process of conditioning it was observed that with development of the conditioned vasodilatation in the hindlimb the vasodilator response to the noxious stimulus was gradually diminishing. Eventually the noxious stimulation of the paw did not produce vasodilatation in the hindlimb, but instead the vascular tone returned to prestimulus level (Fig. 4B). When the duration of the conditioned stimulus was prolonged and the application of the noxious stimulation was postponed vasodilatation continued until the noxious stimulus was administered (Fig. 4). Conditioned tachycardia of 10–40% and pressor response of 10–30% developed to the sound in 3 experimental sessions while the responses to the noxious stimulus waned in parallel with the vasodilator changes. The flexor reflex to the electrical stimulation of the paw was always present.

Once the conditioned response was established to 2000 Hz sound, a 1000 Hz tone elicited the same pattern of somatic and cardiovascular response. This response included hindlimb vasodilatation which was at the beginning of this series identical to both sounds i.e. lasted as long as the duration of the sound (Fig. 4B). During differentiation, however, in which repeated presentation of the 1000 Hz sound alone and the 2000 Hz sound paired with the noxious stimulus was carried out a gradual fading of the conditioned responses to the 1000 Hz sound occurred. It often happened in the initial stage of the process of such differentiation that the conditioned flexor reflex still

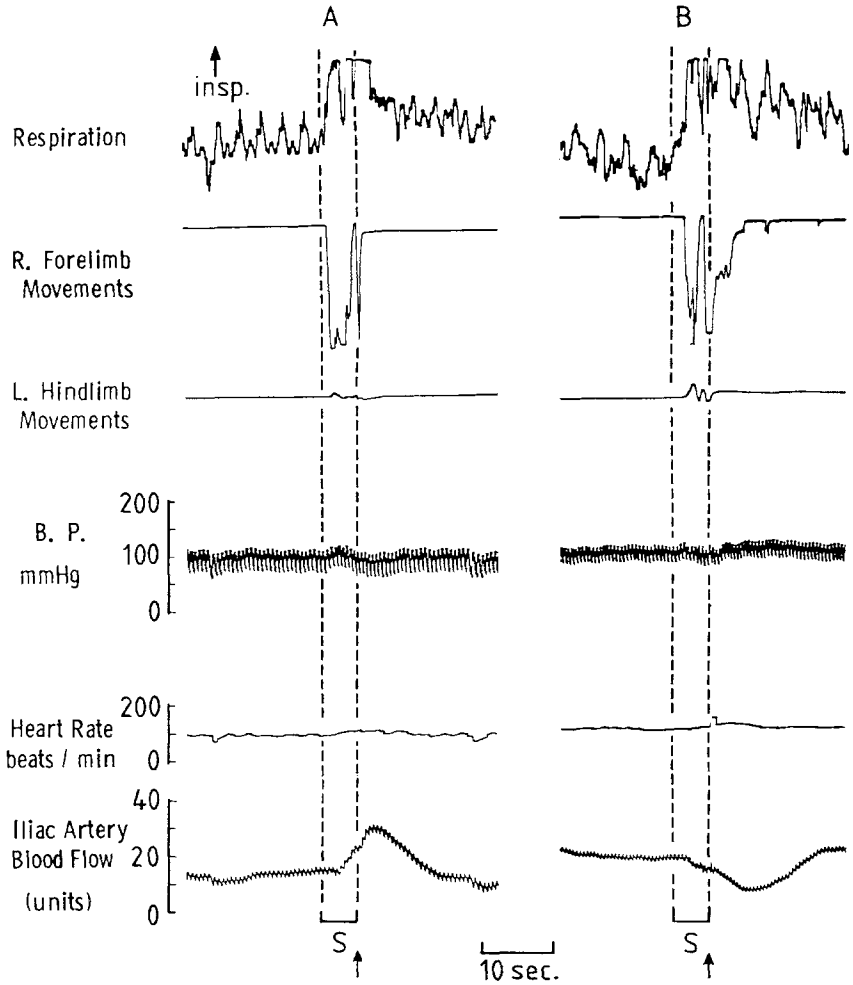

Fig. 3A and B
The effect of systemic intra-arterial injection of 0.2 mg/kg atropine sulphate on the conditioned and unconditioned hindlimb blood flow increase in dog 18. *S* – sound 2000 Hz, 51 dB, arrows indicate forepaw stimulation. (A) before, (B) after administration of atropine

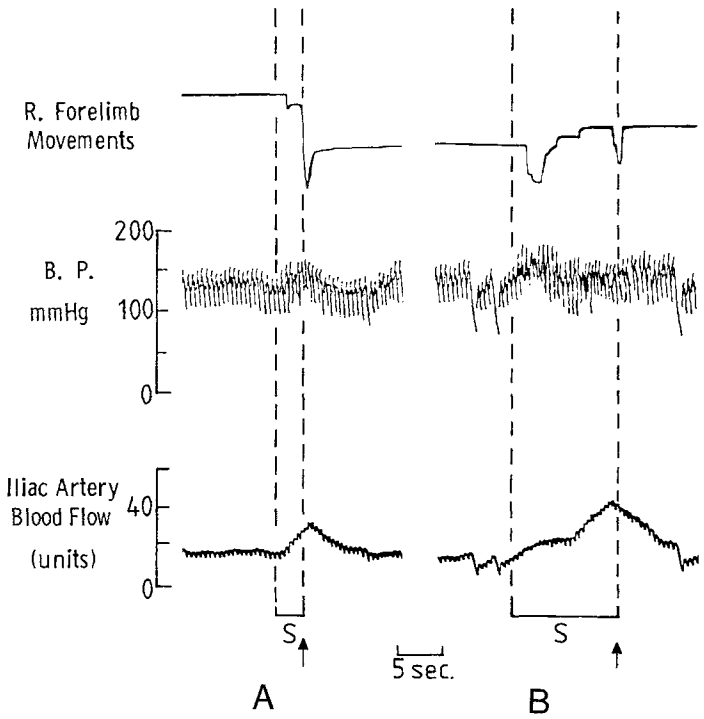

Fig. 4A and B
The effect of prolongation of the conditioned stimulus and delay of the noxious stimulus on the hind limb vasodilatation. In the first panel the electrical stimulation (indicated by an arrow) was given after 2.5 s duration of the conditioned stimulus, the blood flow was increasing during the sound, until the electrical stimulus to the front paw eliciting flexor reflex was administered. The electrical paw stimulation coincided with the reversal of the flow curve. The same happened when the conditioned stimulus lasted 10 s. *S* – 2000 Hz sound, 60 dB, arrow indicates noxious stimulation of the forepaw

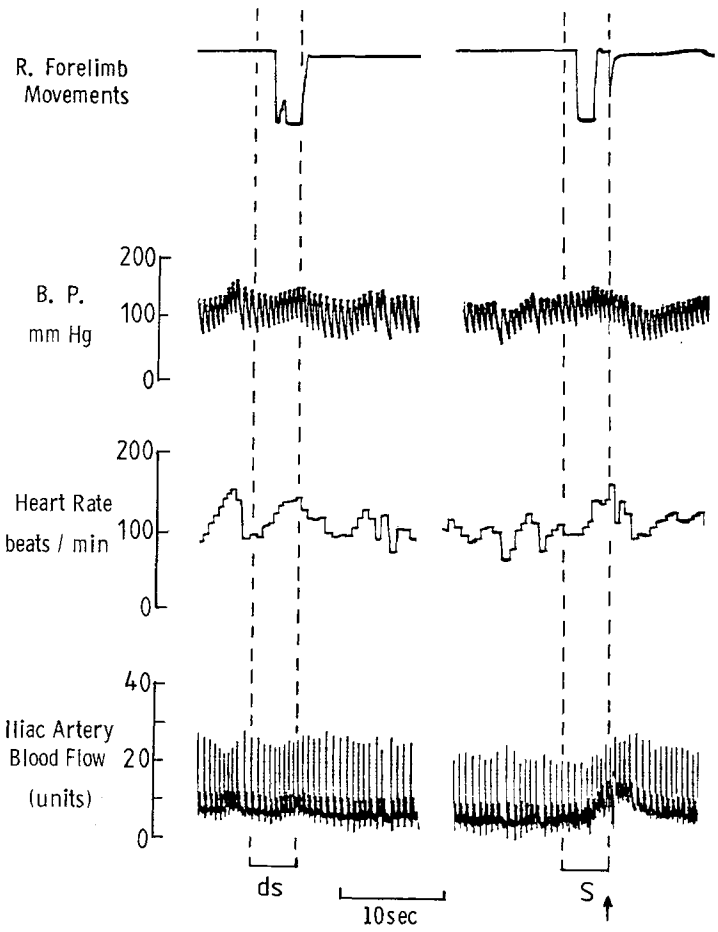

Fig. 5
Transitional stage of differentiation: the response to differential stimulus (*ds*) no longer elicits cardiovascular changes while conditioned flexor reflex is still present. The positive stimulus (*s*) evokes the full conditioned reaction. *ds* – 1000 Hz sound, 60 dB, *S* – 2000 Hz, 60 dB. Compare with similar experiments published elsewhere (Sutherland and Zbrożyna, 1974, Fig. 4, p. 385)

persisted although the vasodilator response has already faded. This interesting dissociation of the conditioned vascular and flexor responses is illustrated in Figure 5.

Confrontation Experiments. Three series of confrontation experiments were carried out on cats. The purpose of the first two series was to establish to what degree the threatening response in cats can be habituated and whether it is present in "naive" kittens. The third series was performed to investigate whether the cardiovascular components of the threatening response in cats would be modified by the process of habituation and conditioning.

Confrontation experiments were carried out on 6 adult cats of unknown life history (two male and four female). In these experiments the cats were confronted in their home cage with a non aggressive dog. Each session consisted of ten face to face confrontations. There was usually one session a day. Two of the cats did not respond with the threatening reaction when confronted by a dog on the first day. All other cats displayed a threatening response to various degrees. In 3 cats the threatening reaction was completely habituated within 2–7 confrontation sessions. In the other three the threatening response was reduced. The longest series consisted of 310 confrontations carried out during 47 days. At the end of the series most of the outward components of the threatening response in this cat disappeared (hissing, growling, arching back, piloerection) but it was still showing some signs of threatening behaviour.

Experiments on Kittens. Seven kittens of 3 different litters of age 4–6 months were used in these experiments. Special care was taken that the kittens did not see or have any sensory experience of any other animals but mother or littermates. During the confrontation session a non-threatening dog was brought into the room face with the kitten which had previously been placed in the cage. This procedure was repeated ten times on each session and no physical contact between the kitten and the dog was allowed. During the first session all kittens reacted with a threatening response of varying degree, usually showing pupillary dilatation, pricking up ears, hissing, growling, arching back and piloerection. The kitten with the lowest score of the threatening response during the first day developed a response on the sixth confrontation con-

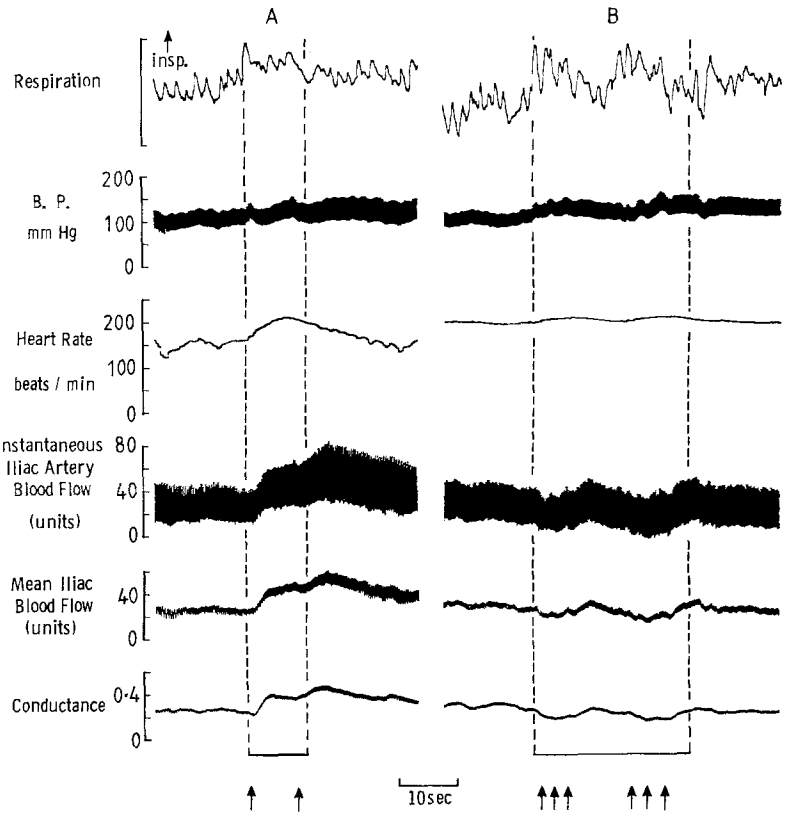

Fig. 6A and B
The response of a cat confronted by a dog and the effect of intra-arterial infusion of atropine (0.2 mg/kg) on the vasodilatation in the hind limb. (A) before injection of atropine, (B) after injection of atropine. The bars at the bottom of the figure indicate the period of confrontation, the arrows – cats hissing

sisting of pupillary dilatation, pricking up ears, piloerection on the back, arching the back and hissing. Often sniffing at the dog was followed by a burst of threatening behaviour. Confronting kittens with a rabbit did not produce a threatening response in the kittens. Repeated confrontations with a dog over days or weeks led to diminution of the threatening response. The speed of habituation varied from 4–11 days. There were individual differences in the way each kitten responded during the first confrontation and in the course of habituation. The general tendency, however, for the threatening response to decline was obvious.

Cardiovascular Response in Naturally Elicited Threatening Reaction. Three female cats were used in this series of experiments and they all responded with the characteristic feline threatening reaction when confronted by a dog. This threatening reaction was initially accompanied by an increase in the heart rate, blood pressure and in the blood flow in the external iliac artery. During the confrontations the cats remained in the sitting position and their hind limbs were usually immobile throughout the experiment. The increase in the hind limb blood flow was due to an active vasodilatation in the skeletal muscles effected via the sympathetic cholinergic nerve fibers since it was abolished by systemic intra-arterial injection of 0.2 mg/kg atropine sulphate or methatropine (Fig. 6).

Habituation of the Cardiovascular Components of the Naturally Elicited Defence Reaction. The cardiovascular component of the threatening reaction in cats confronted by a dog gradually diminished with the repetition of the confrontations in which no physical contact between the animals was allowed. In Figure 7 the course of habituation of the cardiovascular components is shown. The conductance in the external iliac artery was greatly diminished during the third experimental session and in the fourth a reduction in conductance occurred in 8 out of 14 trials indicating that in these instances vasoconstriction had replaced the hindlimb vasodilatation during the threatening response of the cat. An overall pressor response persisted suggesting that vasoconstriction in other vascular beds (most likely renal, cutaneous and mesenteric) did not habituate as quickly. Similarly tachycardia persisted longer although bradycardia occurred on some occasions towards the end of these series. In all three cats of this series the threatening reaction habituated rather slowly and even at the end of the series (on the 8th session) growling and striking with the paw still occurred while cardiovascular response

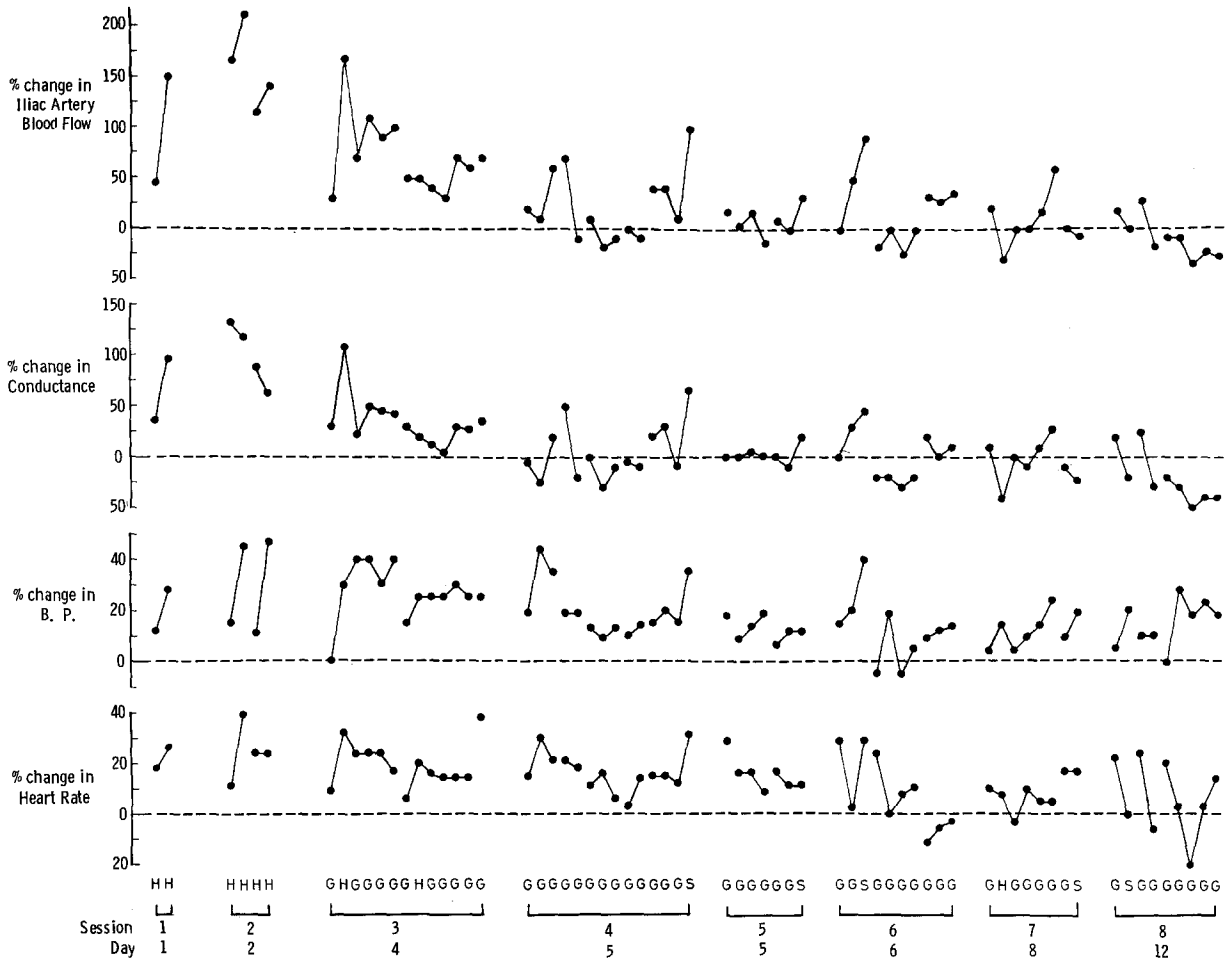

Fig. 7. Habituation of the cardiovascular components of the threatening response elicited in a cat confronted by a dog. Each point corresponds to one bout of rage during confrontation. The points linked by a line refer to one confrontation when a dog was taken in to the room and brought closely to the cat. On the 5th day there was a morning and afternoon session. *H* – hissing, *G* – growling, *S* – striking with a front paw in the direction of the dog

was greatly altered. In all cats muscle vasodilatation was the first to wane.

Conditioning of the Naturally Elicited Cardiovascular Components of the Defence Reaction. In the confrontation experiments in which a cat was confronted by a dog, the confrontation was preceded by 2000 Hz sound. The response to tone alone was previously completely habituated by repeating the sound 14 times. A conditioned response to this stimulus developed after one pairing and it consisted of muscle vasodilatation, tachycardia and increased alertness (Fig. 8). However the response to the tone faded as the response of the cats to the dog became habituated.

DISCUSSION

It has been shown in the present experiments that the same pattern of cardiovascular response occurs in orienting reaction, in response to noxious stimulus, and in the defence reaction in cats confronted by a dog. This pattern of response consists of vasodilatation in the skeletal muscles, increase in the heart rate and in the arterial blood pressure. This is essentially the same cardiovascular response as obtained by electrical stimulation in the brain stem areas for the defence reaction in cats (Abrahams et al., 1960). Furthermore it was found that this pattern of response undergoes modification with repetition of the stimulus eliciting it or during the process of conditioning. The original cardiovascular response accompanying a new sound diminished when the stimulus was repeated and finally vanished.

This process of habituation has also been observed in the defence reaction elicited in cats confronted by a dog. The behavioural response is not a reliable index of the degree of the cardiovascular changes since it takes longer to habituate. In some circumstances

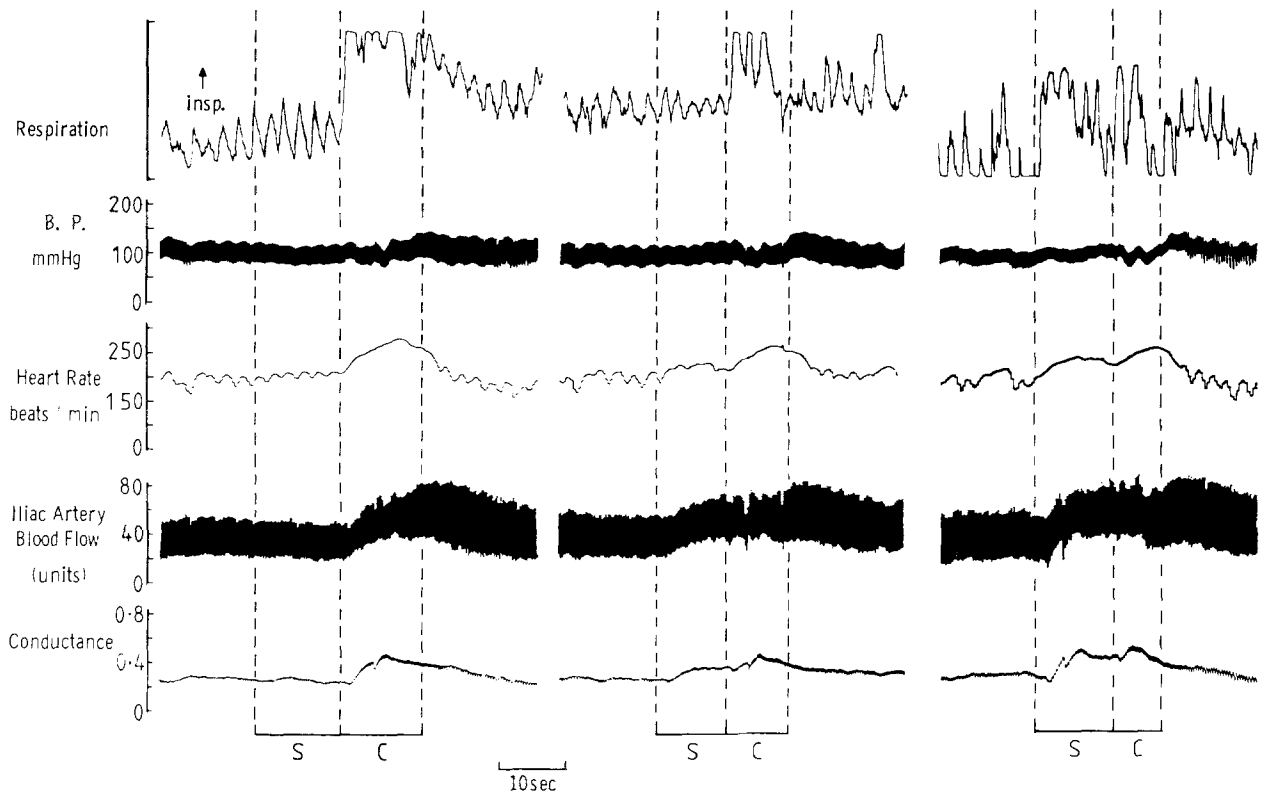

Fig. 8. Conditioning of the cardiovascular components of the threatening response in the cat confronted by a dog. The first and second panel show the cardiovascular response to first and second combination of the sound and the confrontation, the third panel shows the response two days later. The first sound elicited a very slight orienting reaction with small pupillary dilatation, the second time sound elicited in the cat increased alertness with larger pupillary dilatation, the third time the cat looked alarmed and had larger pupillary dilatation. *S* – sound 2000 Hz, 70 dB, *C* – confrontation with the dog

sensitization occurred instead of habituation. Sensitization reverses the effect of habituation and may bring back in full the whole pattern of the cardiovascular response. This is consistent with Scholander's (1960) finding that "increased attentiveness" in human would prevent habituation and lead to sensitization of the electrodermal response and tachycardia to a sound. However in a "relaxed" state the same subjects would habituate these responses readily. This suggests that the level of background activity of the defence centres may be determining whether habituation or sensitization will ensue in the course of repetition of a sensory stimulus. This is supported by the fact that in anxious patients habituation of EMG and electrodermal responses was found to be impaired (Lader, 1970). Furthermore in severely anxious patients these responses have shown an increase with repetition of the stimulus indication that sensitization took place. As in confrontation experiments on cats, socially provoked aggression in normal human subjects leads to increases in the blood pressure (Hokanson et al., 1963).

In the confrontation experiments described here the cardiovascular response was diminishing with repetition of the confrontations. Among cardiovascular components the vasodilatation in the muscles was most readily extinguished and a transient stage of hypertension in a defence response to a repeated stimulus is therefore likely to occur as a result of increased total peripheral resistance. The persistence of the hypertensive state would depend on the rate of habituation of vasoconstriction in renal, mesenteric and cutaneous vascular beds and on the degree of abrogation of the baroreceptor reflex. The latter effect has been found to occur as a component of the cardiovascular response to stimulation in the defence area of the hypothalamus (Hilton, 1963; Coote and Perez-Gonzalez, 1972), and it is reasonable to suspect suppression of the baroreceptor reflex when the defence reaction was activated naturally. Furthermore Zbrożyna (1976) reported that a renal vasoconstriction occurs in baboons confronted by a snake, indicating the important role this response may be playing in the development of hypertension. The renal vasoconstriction in the naturally elicited defence reaction reduces renal blood flow to a considerable degree and in some instances may lead to a prolonged shutting off of renal blood circulation (von Holst, 1972; Lauson et al., 1944; Trueta et al., 1940; Mancia et al., 1974).

It has been shown that renal vasoconstriction in the naturally elicited defence reaction may not habituate and may lead to death in tree shrews (von Holst, 1972) or as it has been shown in experiments on baboons it may spontaneously reappear (Zbrożyna, 1976).

There is a large body of evidence already aacumulated suggesting that the defence reaction (fear, aggression) plays an important role in the development of essential hypertension in human. For instance Reiser et al. (1951) described 12 representative patients with malignant hypertension and found correlation between the precipitation of malignant hypertension and the occurrence of "emotionally charged life situations". Harris and Singer (1968) suggest that hypertensive patients have shown pronounced characteristics of hostility, "nervous tension" and anxiety. The fact that by conditioning (Elder et al., 1973; Benson et al., 1971) or by yogic exercise (Datey et al., 1969; Patel, 1973) the blood pressure in some hypertensive patients can be lowered supports the concept of neurogenic origin of hypertension in these cases.

Conditioning may be playing an important role in the everday regulation of the cardiovascular responses to environmental stimuli. It has been shown here and by other workers (Menzies, 1937; Dykman and Gantt, 1958; Shmavonian, 1959; Abrahams et al., 1964; Bølme and Novotny, 1969; Hothersall and Brener, 1969; DiCara and Miller, 1969; Harris et al., 1973; Bleecker and Engel, 1973; Wells, 1973; Schwartz and Shapiro, 1973) that cardiovascular responses may be readily conditioned. In the present experiments vasodilatation in the hind limb muscles elicited by noxious stimulation of the forelimb was conditioned to a sound. This vasodilatation could not be due to the hindlimb muscle contractions occasionally accompanying forelimb flexor reflex since the blood flow increase occurred independently of the hind limb movements. Moreover in repeated tests the hindlimb vasodilatation was abolished by atropine (0.2 mg/kg). Furthermore in the stage of incomplete differentiation of the conditioned response the differential stimulus continued to elicit a forelimb flexor reflex while the vasodilator response was absent (Fig. 5 and Sutherland and Zbrożyna, 1974, Fig. 4).

During the process of conditioning the hindlimb vasodilatation elicited by noxious stimulation of the forelimb skin was gradually diminishing. When conditioned vasodilatation to the sound was well established the noxious stimulus no longer elicited its original vasodilator response (Fig. 4). The conditioned vasodilator response may have been related to the delay of the administration of the noxious stimulus, therefore tests were carried out varying the delay between the onset of the sound and the noxious stimulus (Fig. 4). These experiments have shown that the timing of the noxious stimulus had an effect on the conditioned vasodilator response but also confirmed beyond any doubt that this stimulus lost its original effect of eliciting muscle vasodilatation. In spite of it the noxious stimulation appeared to be essential for maintaining the conditioned vasodilatation. This last property has been clearly demonstrated in the differentiation series, when the vascular response to 1000 Hz sound, which was not paired with the noxious stimulus faded away, while the response to 2000 Hz sound, which was consistently combined with the noxious stimulus, was maintained (Fig. 5, see also Sutherland and Zbrożyna, 1974, Fig. 4). During conditioning there was a general tendency towards a gradual decline of the cardiovascular components of the response to the noxious stimulus but the flexor reflex remained unaltered.

It is noteworthy that pairing of a sound with confrontation by a dog produced in the cat a very swift conditioning of the cardiovascular response (Fig. 8). This conditioning was quicker than conditioning with the use of the mild noxious cutaneous stimulation. The cardiovascular response to the sound paired with the sight of a dog was eventually extinguished while the conditioned response to the sound paired with the noxious stimulus was maintained (see also Sutherland, 1973).

In conclusion it may be stated that central control of the cardiovascular system is closely related to the control of behavioural responses. The "naturally" elicited cardiovascular response in defence reactions are modified according to the experience of the animal. In the process of habituation single elements of these responses may be habituated while some others might be more persistent. Sensitization might increase cardiovascular participation particulary in anxious individuals. Conditioning processes may modify cardiovascular response in more permanent fashion. Thus experience has a profound influence on cardiovascular responses and may produce haemodynamic imbalance leading to hypertension.

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