Steady Potential Responses from the Rat Cortex During Conditioning[1]

WALTER, COOPER, ALDRIDGE, MCCALLUM and WINTER[2] first described a negative potential shift (contingent negative variation, CNV) recorded from the human scalp during the interval between warning and response signals in reaction time experiments. Subsequent experiments by several other investigators have suggested a functional relationship between the CNV and central processes of attention, expectancy, and motivation[3–5]. Steady potential (SP) shifts associated with meaningful stimuli have also been recorded from cortex and other brain areas of experimental animals including cats, rabbits, rats, and pigeons[6–10]. The fact that psychoactive drugs influence processes of attention and motivation in man as well as conditioned behavior in animals suggests that drugs may be useful tools for learning more about the functional significance of brain steady potentials. Relatively few studies have attempted to examine the influence of centrally acting drugs on SP-behavior relationships[11–15]. The purpose of this investigation was to develop a test procedure to generate reproducible SP response patterns against which drug effects can be studied.

Methods. Six adult female albino rats (Sprague-Dawley descent obtained from Texas Inbred Mice Co.) were implanted with 22-gauge non-polarizable silver-silver chloride electrodes according to procedures described previously[14, 15]. The electrodes were in contact with cortex or bone via an agar-saline bridge. The active electrode was over parietal cortex (3–4 mm posterior to the bregma and 3–4 mm to the right of midline) and the reference electrode was in occipital bone. 5 to 7 days were allowed for recovery before recording began.

Cortical steady potential recordings were obtained with a Grass Model 7 polygraph using 7P1 d.c. preamplifiers. The animals were placed in a plexiglass cage within a ventilated, sound-attenuating box. A 4-inch speaker provided background white noise as well as the conditioned stimulus (CS), which was a 5-second sine wave tone at 25,000 cps. Tone intensity was kept constant for all experiments.

Initially the animals underwent 5–6 daily habituation sessions, each of which consisted of 20 trials of tone presentation at variable intervals of 45, 60 or 90 sec. Habituation was followed by 4–5 pairing sessions in which the tone was followed after 0.5 second by a 0.5 mA grid shock of 1.5 sec duration. Animals were then subjected to 4–6 extinction sessions.

Using the SP level at the onset of the tone as baseline, the SP change was measured at each 1-second interval throughout the 5-second stimulus period. The values obtained at each time point were averaged and the averaged SP response was utilized for further statistical comparisons.

Results. During the first 20 habituation trials, negative SP shifts were associated with the tone. These SP changes gradually diminished and reversed polarity during succeeding trials so that by the end of habituation SP responses were essentially positive (Figure 1). A paired *t* comparison demonstrated a significant difference between the first 40 and last 40 habituation trials at the 2nd, 3rd and 4th sec (Table).

With initiation of pairing, negative SP shifts developed rapidly and the averaged responses were significantly different from responses during habituation (Figure 1, Table).

Responses during the first 40 extinction trials were not significantly different from those observed in the pairing sessions (Table). With subsequent extinction trials, the negative SP response amplitudes gradually decreased, and even reversed polarity during the 4th and 5th sec in 4 animals (Figure 1, Table).

Figure 2 illustrates averaged SP responses of 4 rats during 80 habituation trials, 80 pairing trials, and the first 80 extinction trials.

Discussion. The results of this study may be summarized as follows: a) During habituation trials the initially negative SP responses to a tone stimulus gradually diminished in amplitude and became largely positive responses in the last 20 trials. b) When a foot shock was paired with the tone, negative SP responses developed with the first few trials and remained essentially unchanged during succeeding pairing trials. c) SP responses during the first 20–40 extinction trials were not statistically different from pairing trials, but thereafter the negative responses gradually decreased in amplitude and a positive component developed in 4 of 6 animals. In general, these studies are in agreement with those of ROWLAND[10], DURKOVIC

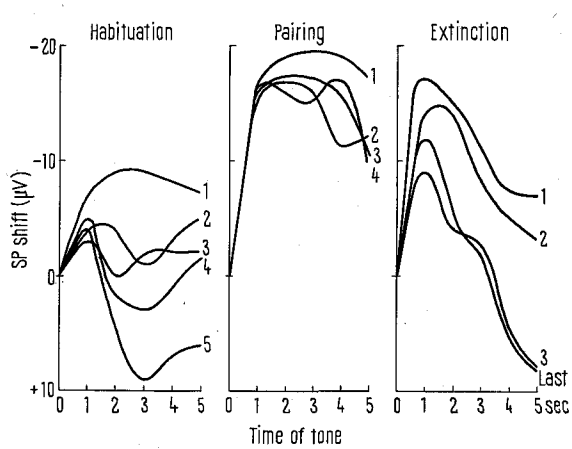

Fig. 1. Cortical steady potential shifts in response to a 5-sec tone. Each curve represents an average of the responses of 6 rats obtained during a single session of 20 trials. For statistical comparisons, see Table.

[1] Supported by a grant from the Medical Research Foundation of Texas.

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Statistical comparisons of steady potential responses

Time of Stimulus (sec)	Habituation (first 40 trials) vs. Habituation (last 40 trials)		Habituation (last 40 trials) vs. Pairing (first 40 trials)		Pairing (first 40 trials) vs. Extinction (first 40 trials)		Pairing (first 40 trials) vs. Extinction (last 40 trials)	
	t[a]	P[b]	t	P	t	P	t	P
1	1.991	NS	3.153	<0.05	0.306	NS	3.790	<0.02
2	3.505	<0.02	7.446	<0.001	0.600	NS	3.939	<0.02
3	2.824	<0.05	4.398	<0.01	1.318	NS	3.064	<0.05
4	3.245	<0.05	3.508	<0.02	1.381	NS	4.203	<0.01
5	2.540	NS	2.786	<0.05	1.508	NS	3.414	<0.02

[a] Paired t comparison using each animal as its own control. $n = 6$. [b] NS indicates $P > 0.05$ based on 5 degrees of freedom.

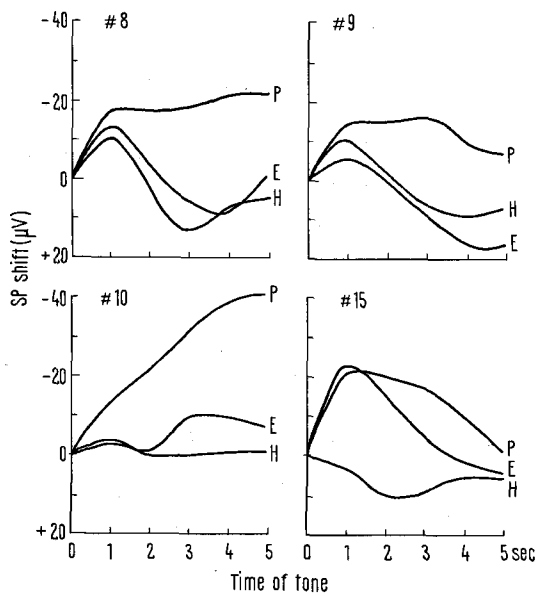

Fig. 2. Averaged steady potential shifts recorded from individual animals during 80 habituation trials (H), 80 pairing trials (P) and 80 extinction trials (E).

and COHEN[7] and CHIORINI[6] regarding the types of SP response changes which occur during habituation, conditioning and extinction.

The results with this experimental procedure suggest that the SP response to tone during pairing with foot-shock is related to the animal's anticipation or expectancy of the impending shock. This idea is further supported by the fact that the SP response was unchanged during the early extinction trials but then gradually diminished as the animals 'learned' that the shock was no longer imminent. Previous studies have shown a relationship between the SP response associated with lever-pressing for a food reward and the 'anticipation' of the number of rewards that would be received[15].

In the present experiments the SP response during pairing could also be considered a correlate of the conditioned emotional response. This would suggest that it may be worthwhile to study the effects of psychoactive drugs on such SP responses. The possible similarity between these SP responses to warning stimuli and the human CNV, which is known to be influenced by psychological state[16], further indicates the importance of a thorough examination of SP-behavior relationships.

In conclusion, this experimental procedure provides reproducible SP response patterns, similar to those observed by other investigators, which can be utilized in an investigation of the role of brain steady potential changes in the action of psychoactive drugs.

Zusammenfassung. Während Versuchsreihen an Ratten über Gewöhnung, Paarung und Auslöschung wurden jeweils signifikante Veränderungen des kortikalen Bestandespotentials (Gleichspannung) als Antwort auf Schallreiz gemessen.

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Inhibitory Effect of Bile Acids on Renin Angiotensinogen Reaction System

We have already reported that the naturally occurring renin inhibitor in ox bile was taurodeoyxcholic acid[1] and that synthetic sodium deoxycholate was also a potent competitive inhibitor of renin[2]. In this investigation, we examined the effect of various synthetic bile acid derivatives on the activity of renin in the formation of angiotensin in vitro.

Materials and methods. Taurocholic acid, glycocholic acid, taurodeoxycholic acid, glycodeoxycholic acid, chenodeoxycholic acid, taurochenodeoxycholic acid and