Brief Report

neuroscience

P300- like event related potential amplitude in rats is a correlate of conditioned reinforcement

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We have developed a methodology for recording a robust P300 event related potential (ERP) in rats. In these experiments a contingency shaped model of the human "oddball' paradigm was employed in which rats were shaped to press a lever for food reinforcement signaled by the click of the pellet dispenser. A target tone cued the insertion of the lever that retracted after 1-sec or immediately following a single reinforced response, while a non-target tone was randomly presented. Brain activity was recorded through stainless steel electrodes implanted 1-mm below the skull. Here, we compared the amplitude of the P300 response to the click of the pellet dispenser to the amplitude of the P300 response to the target and non-target tones. We found that the amplitude to food click was significantly greater than the amplitude to the target tone that cued lever insertion. Since the food click is more proximal to the primary reinforcer than the lever tone, it is a stronger conditioned reinforcer than the lever tone that sets the occasion for the food click. Accordingly we suggest that the P300 in rats is a correlate of conditioned reinforcement.

Although an unambiguous P300 ERP model has been demonstrated in a few primates, the finding is more ambiguous in the rat[1,2,3,4]. Recent experiments have attempted to relate the P300 ERP to attention and arousal[5], depression[6] and animal models of schizophrenia[7]. In a pilot experiment we found rat P300 ERP amplitude to a cue for lever pressing decreased during extinction and increased rapidly during re-acquisition. Since the magnitude of the P300 ERP to the target tone diminished as the target tone's conditioned reinforcing properties were extinguished, we hypothesize that the P300 ERP may be a correlate of the brain's response to the occurrence of a conditioned reinforcer.

In backward chaining, discriminative stimuli that cue the next response in the chain become conditioned reinforcers for the response that produces them. The strength of a conditioned reinforcer is inversely related to its proximity to the primary reinforcer in the chain. In the rat oddball paradigm, the target tone cues the rat to press the lever that produces a click of the food magazine. The click of the food magazine is a conditioned reinforcer that cues the rat to approach the feeding tray and eat the primary reinforcer. If the conditioned reinforcement interpretation is correct, the magnitude of the P300 ERP to the click of the feeder should be greater than the P300 ERP to the target tone because the target tone is further removed from the primary reinforcer. Accordingly, the present experiment compared the magnitude of the P300 ERP to the target tone, click and non-target tone.

RESULTS

Fig. 1 shows the ERPs to the click, target and nontarget tones for each of the six rats. **Fig. 1** shows that for each rat, the P300 ERP amplitude to the click is substantially greater than the amplitude to the target tone. A repeated measures ANOVA of the peak voltage for each rat under click and target conditions revealed that the mean peak voltage (143.3 μV) for the P300 ERP to the click was significantly greater than the mean peak voltage (64.2 μV) to the target tone ($F1, 5 = 11.84$, $P < 0.018$). **Fig. 2** shows the grand average P300 ERP to the click, target tone and non-target tone averaged across all six rats. The insert shows the mean peak voltage with 95% confidence interval error bars.

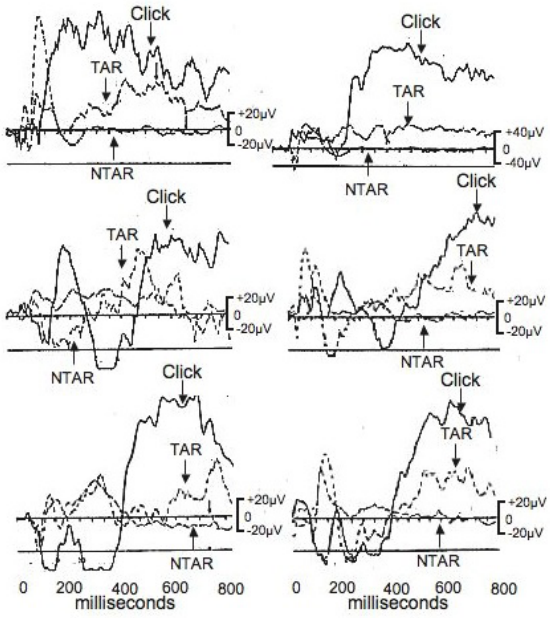

Fig 1: The P300 ERPs to the click, target and non-target stimuli for each of the six rats. The dark upper line is the ERP to the click, the middle dashed line is the ERP to the Target (lever) tone, the dotted lowest line is the ERP to the non-target tone and the solid straight line is the zero baseline. The amplitude bars to the right show the size for ±20 μV except the upper right panel where the amplitude is ±40 μV. The ERP to the click is consistently higher than the ERP to the target tone both of which are higher than the non-target ERP.

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DISCUSSION

The finding that the p300 ERP amplitude is substantially greater to the click than it is to the target tone is consistent with the interpretation that the P300 ERP is a correlate of the brains response to the occurrence of a conditioned reinforcer. Since the click is more proximal to the primary food reinforcer it has greater conditioned reinforcing properties than the tone that predicts the lever insertion that enables the response leading to the click-food reinforcer. Although we had predicted the increased P300 ERP to the click, we were surprised at the magnitude of the increase that was more than double the amplitude of the P300 ERP to the tone. It is possible that the ERP to the click is a compound of the click as a predictive stimulus and the virtually immediate delivery of the food pellet. Further experiments will be needed to separate the possibility of the click ERP merging with an ERP to sensing the food pellet. Nonetheless, these results clearly demonstrate that the amplitude of the P300 ERPs was a function of their proximity to the primary food reinforcer in the chain of behavior. Accordingly, it would be interesting to train the rats on a longer backward chain of behavior and test the hypothesis that P300 ERP amplitude to conditioned reinforcers in the longer chain would be a decreasing function of the distance backward from the primary reinforcer.

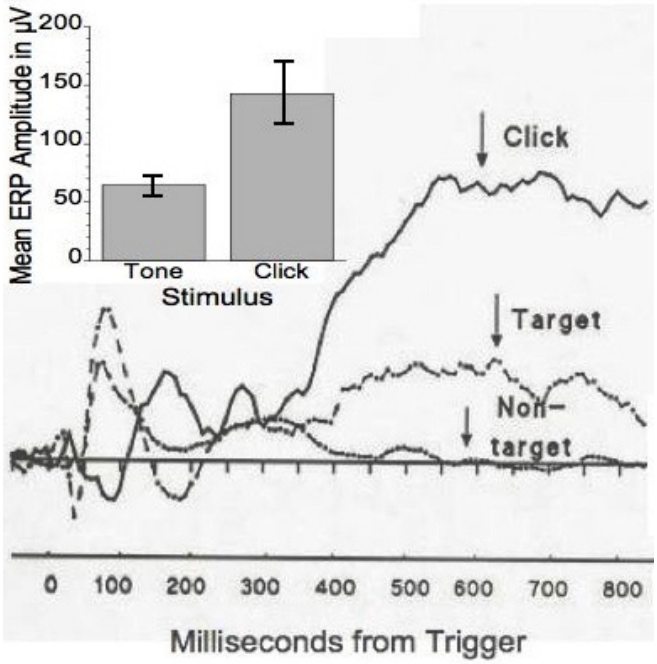

Fig 2: The grand average P300 ERP to the click, target tone and non-target tone averaged across all six rats. Note that the click and target tone ERPs have similar latencies (about 500-600 msec) and that the amplitude of the click ERP is more than twice the amplitude of the Target ERP. These latencies are similar to latencies found in other research with rats. The insert shows the mean peak amplitude for the click and target tones with the error bars delineating the 95% confidence interval.

METHODS

Electrode Placement

Six female Blue-Spruce hooded rats were reduced to and maintained at 80% of their free feeding weight by restricted feeding. The tip of a formvar insulated stainless steel electrode, was placed 1mm below the skull, 1.5 mm left of the midline and 1-mm caudal to lambda. One electrode 3-mm rostral to bregma served as an indifferent and a contralateral electrode 5-mm rostral bregma served as the isoground.

Behavioral Training and Testing

One week after surgery, the rats were trained to press a retractable lever for food reinforcement (45 mg Noyes pellets) in a standard operant chamber. A target tone (4.4 kHz, 40 msec and 90 dB SPL) signaled the insertion of the lever which retracted following either a single reinforced response, or one second after insertion. The target tone was presented on a variable time (VT) 32-sec schedule, while a non-target tone (2.0 kHz, 40 msec and 90 dB SPL) was presented on a truly random VT 4-sec schedule. Each daily session was terminated after 50 reinforcements had been earned. Throughout the experiment, the rats were required to maintain a criterion of obtaining 90% of all programmed reinforcers during training sessions prior to testing. All training and test sessions were conducted using an 8:1 nontarget to target ratio. Target and click recording were conducted in separate sessions.

ERP Testing Procedures

The EEG was filtered using a bandpass of .03 to 35 Hz (12 dB/octave rolloff). During the recording rats were behaving freely without constraints. ERP epochs for each channel were digitized at 256 Hertz over 50 millisecond before to 850 milliseconds after stimulus onset. Processing of individual epochs occurred off-line. Single trial epochs from any channel having voltages in excess of + 350 mV were excluded. ERP averages were constructed separately for target and non-target tones. ERPs to the click were averaged over a mean of 36 trials (with not less than 20 trials). ERPs to the target and non-target tone were based on a means of 65 trials (with not less than 30 trials) and 498 trials (with not less than 113 trials) respectively.

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AUTHOR CONTRIBUTIONS

W.D.K. designed the experiments. W.D.K. and S.F. conducted the experiments and analyzed the data. W.D.K. wrote the paper.

PROGRESS AND COLLABORATIONS

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