Physiology & Behavior, Vol. 44, pp. 241–245. Copyright © Pergamon Press plc, 1988. Printed in the U.S.A. 0031-9384/88 $3.00 + .00

Event Related Potentials Recorded From Rats Performing a Reaction-Time Task

ELI BRENNER AND MAJID MIRMIRAN

Netherlands Institute for Brain Research, Meibergdreef 33, 1105 AZ Amsterdam, The Netherlands

Received 16 February 1988

BRENNER, E. AND M. MIRMIRAN. *Event related potentials recorded from rats performing a reaction-time task.* PHYSIOL BEHAV **44**(2) 241–245, 1988.—We recorded evoked potentials during performance of a reaction-time task, in which rats had to release a lever quickly in response to either a visual or an auditory stimulus for a food reward. We found two distinct peaks in their cortical evoked potentials. The first peak appeared at a fixed time after the stimulus, irrespective of the time it took the rat to release the lever. Its amplitude decreased with increasing reaction time. The second peak's latency was always longer when the rat took more time to release the lever, but its amplitude did not change. We believe that the first peak's amplitude is determined by the rat's "attention" to the stimulus, whereas the second peak's latency is related to the rat's "intention" to release the lever.

Evoked potentials Fluctuations in performance Sensory processing Attention Reaction time Rat

SENSORY processing is believed to consist of two stages. First, a "preattentive" stage in which sorting of sensory input occurs simultaneously for several features. Second, an "attentive" stage in which features are examined serially. These two stages can be demonstrated using textures embedded in larger similar textures. If the two textures differ in certain properties (e.g., colour), the embedded texture is seen directly. However, for other properties one has to examine the stimulus carefully before one can detect the embedded pattern (8,10). This requires an active search, usually by moving one's eyes. Such results have been quantified by determining changes in human reaction times with increasing numbers of items for qualitatively different stimuli (4).

Hillyard (7) demonstrated that "attention" affects the amplitude of human sensory evoked potentials. When subjects were instructed to attend to either one of two stimuli, the response evoked by that stimulus was greater than that evoked by the other. As the latency did not change (changes in latency are found when manipulating the ease with which the stimulus is discriminated), and as the stimuli were easy to detect, it is unlikely that the serial stage of sensory processing was involved. This suggests that the "preattentive" stage is also affected by changes in attention.

In a previous study we trained rats to press a lever in response to a visual stimulus (1,3). We found visual evoked potentials that increased in amplitude when performance improved; i.e, as the rat started selectively attending to the relevant cues. The response did not depend on the intensity of the stimulus. Similarly to the above-mentioned results for human subjects, only the peaks' amplitudes changed; their latencies remained unaffected. We could not be sure that the increase in amplitude was not simply due to the rat chosing a more strategic position for observing the stimulus or a more appropriate orientation of its eyes. To decrease this problem in the present study, we trained rats to hold down the lever until the stimulus was presented, and then to respond to the stimulus very quickly (2). In this way we can be certain both of the rat's position and of its attention to the stimulus. Furthermore, we also tested the rats with an auditory stimulus, in which case their precise orientation is less crucial. Assuming that fluctuations in the rats' response rates are partly due to fluctuations in attention (9), we examined whether there were any systematic differences between peaks in the sensory evoked potential for different reaction times. With this we hope to have a direct method of studying sensory attention in rats.

By averaging many periods of brain potential at each temporal relationship with a stimulus, all fluctuations related directly to stimulus detection maintain their amplitude, whereas the amplitude of unrelated fluctuations decreases with the number of periods that are averaged. Although we averaged in relation to the stimulus, this was done separately for different behavioural response latencies, so that response related fluctuations in the evoked potential could also be expected.

METHOD

We recorded brain potentials of six mildly food deprived male Brown Norway rats performing a reaction-time task for a food reward. For electrode implantation rats were anaesthetised with 0.15 ml Hypnorm (fentanyl; Duphar B.V.). Brain potentials were recorded differentially between stainless steel screws (0.75 mm diameter) implanted above the right occipital (3 mm anterior to lambda and 3 mm lateral to the sagittal sinus) and right frontal cortices (2 mm anterior to bregma and 1 mm lateral to the sagittal sinus). Interference by muscle potentials—especially during chewing—was reduced by attaching a ring of uninsulated wire to the skull around the socket and grounding this wire via the connector during recordings. We have previously shown that this allows us to record from freely moving rats while they are performing a behavioural task (1,3).

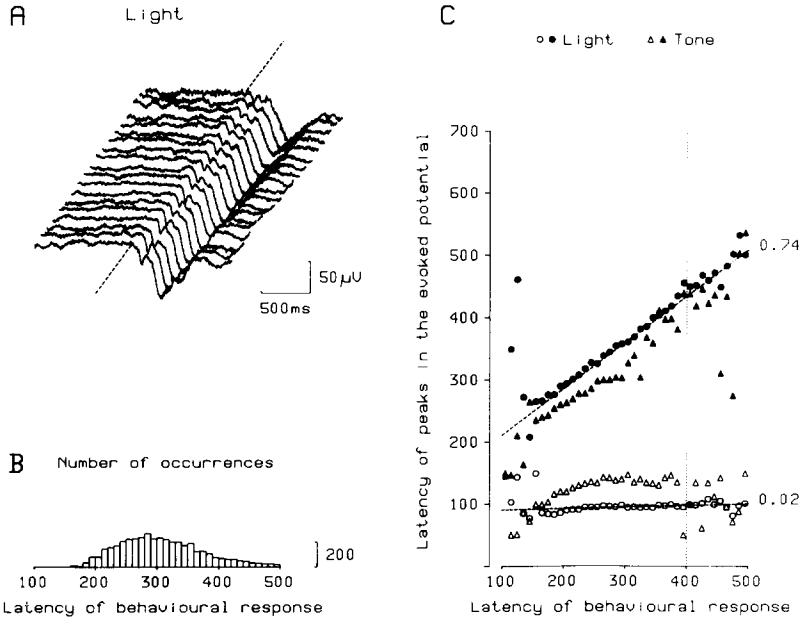

FIG. 1. Data are shown for one of the six rats. (A) Visual evoked potentials for behavioural response latencies falling into consecutive 10 msec response latency categories (bottom trace=shortest latency). Dashed line shows stimulus onset. Downward deflection indicates positivity of the occipital screw. The decline in the amplitude of the first peak as the behavioural latency increases is clearly visible. (B) Distribution of the latencies of the behavioural response. (C) Relationship between the latency of the behavioural response and that of the two peaks in the evoked potential (open and filled symbols; both latencies in msec). Responses later than 400 msec after stimulus onset are not rewarded (dotted vertical line). Dashed lines are drawn through the results for visual stimulation (circles). The second peak (filled symbols) clearly shifts with behavioural performance, but the slope is clearly below one (0.74).

The recording equipment has been described in more detail in a previous paper (3). Relevant to this study is the fact that recordings took place under subdued light (5 cd/m) in a shielded box with a lever, 3 standard green 5 mm light emitting diodes (visual stimulus) above this lever, a loudspeaker (auditory stimulus) well above the light emitting diodes, and a feeder for rewarding the rats with food pellets. All stimulation, analysis of behavioural performance, rewarding of appropriate responses, brain potential acquisition and selective averaging was regulated automatically be a computer. We recorded for 1 sec before and 1 sec after stimulus onset, at a sampling rate of 1 kHz (bandpass filtered at 0.1–1000 Hz). Stimulus onset was determined to the nearest msec, and behavioural response latencies were divided into 10 msec time bins. Potentials were averaged separately for each time bin of behavioural response, so that both peaks related to the stimulus and peaks related to the response could be expected.

Rats started each trial by pressing the lever. A tone (1.35 kHz; 75 dB) sounded whenever the lever was pressed down far enough. The lever had to be held down until a stimulus appeared, which occurred after an interval that varied at random between 2 and 6 seconds from the beginning of the trial. If the lever was then released within 400 msec, the rat was rewarded with a food pellet. In order to avoid possible electrocortical responses to the disappearance of the stimulus, the stimulus always remained ON until acquisition of the brain potential was completed. For the same reason, releasing the lever did not terminate the tone which indicated that the lever was being held down during the second after stimulus onset.

All 6 rats were first tested with the first visual stimulus. Four of these rats were then tested using a change in pitch of the tone (from 1.35 to 3 kHz) as the stimulus. Two rats that had been tested with this auditory stimulation were later subjected to two more short tests. In the first test, they were subjected to the same change in tone, but it now had no relevance to food reward. In the second test, the rats were trained to hold down the lever for at least 1 sec, and then to release it although no stimulus appeared.

For each stimulus modality, rats were tested until they had made at least 4000 adequate behavioural responses. This usually took about 25 sessions, with rats obtaining 150–200 food pellets per session. In order to follow how peak latencies shift with changes in behavioural performance, we shifted the sweeps (see Fig. 1A) along the time axis until we found the best fit for each peak (see Fig. 3 for the second peak). We then used the amount by which each sweep was shifted to determine the shift in peak latency. In practice, each peak's latency was first determined in a smoothed version of the average evoked potential at the modal behavioural response time (for each rat). A section of the evoked potential at the modal response time that included the peak was then fit to the average response at all other behavioural latencies (i.e., all other sweeps). A least squares procedure was used to find the best fit, with sections being shifted along the time axis and being adjusted to the optimal offset for the potential. The actual peak latencies were then

TABLE 1

LATENCY AND AMPLITUDE OF THE TWO PEAKS IN THE EVOKED POTENTIAL FOR BEHAVIOURAL RESPONSES AT 300 msec AFTER STIMULUS ONSET (MEAN±SD)

Stimulus	Number of Rats	First Peak	Second Peak
Latency (msec)			
Visual	6	96 ± 7	414 ± 58
Auditory	4	140 ± 18	369 ± 71
Amplitude (μV)			
Visual	6	21 ± 9	68 ± 22
Auditory	4	24 ± 2	69 ± 15

TABLE 2

CHANGES IN LATENCY AND AMPLITUDE OF THE TWO PEAKS IN THE EVOKED POTENTIAL PER msec INCREASE IN THE LATENCY OF THE BEHAVIOURAL RESPONSE (MEAN±SD)

Stimulus	Rats	First Peak	Second Peak
Latency (msec/msec)			
Visual	6	0.05 ± 0.07	0.69 ± 0.16‡
Auditory	4	0.23 ± 0.10†	0.64 ± 0.24†
Amplitude (μV/msec)			
Visual	6	−0.05 ± 0.04*	0.02 ± 0.15
Auditory	4	−0.03 ± 0.03	0.00 ± 0.14

Increase in peak latency and decrease in amplitude with increasing behavioural latency: *$p<0.05$, †$p<0.01$, ‡$p<0.005$ (deviation from zero).

calculated from the peak determined for the modal behavioural latency and the relative shift in position on the time axis that gave the best fit. Slopes in the relationship between each peak in the evoked potential and behavioural performance were determined by linear regression including all values at behavioural latencies which occurred at least 100 times. The figures also only include averages of at least 100 sweeps. Amplitudes were determined relative to the average potential during the last 100 msec before stimulus onset. Changes in amplitude with fluctuations in behavioural performance were determined by linear regression (in μV per msec).

For each rat, the relationships between behavioural performance and peak latencies and amplitudes were determined (see previous paragraph and Fig. 1). The "slopes" of these relationships and the values calculated for a behavioural latency of 300 msec were used for further evaluation. One-tailed t-tests were used to determine whether peak latencies increased and whether peak amplitudes decreased with increasing behavioural latency; i.e., whether the different slopes found within our group of rats deviated significantly from zero. For the second peak, two-tailed t-tests were used to determine whether there was a direct relationship between behavioural and peak latencies; i.e., whether the slope was significantly larger or smaller than one.

RESULTS

We found two reproducible positive peaks in the evoked potential (Fig. 1; Table 1). The first had a latency of about 90–100 msec for visual stimuli and 120–160 msec for auditory stimuli. The latency did not shift significantly with behavioural performance for visual stimulation, but did do so for auditory stimulation. The amplitude decreased significantly with increasing behavioural reaction time for visual stimulation, and just failed to do so for the auditory stimulus (Table 2). The change in amplitude with behavioural performance (the slope) was not significantly different for the two modalities. As previously found for the visual stimulus, the auditory stimulus also failed to produce a detectable evoked potential when it was not related to the task (Fig. 2). The second peak's latency varied with behavioural performance. Its amplitude did not change significantly, nor were there significant differences between the test situations. Furthermore, this peak could be found when the rats were trained to perform the same behavioural "response" in the absence of stimulus (Fig. 2).

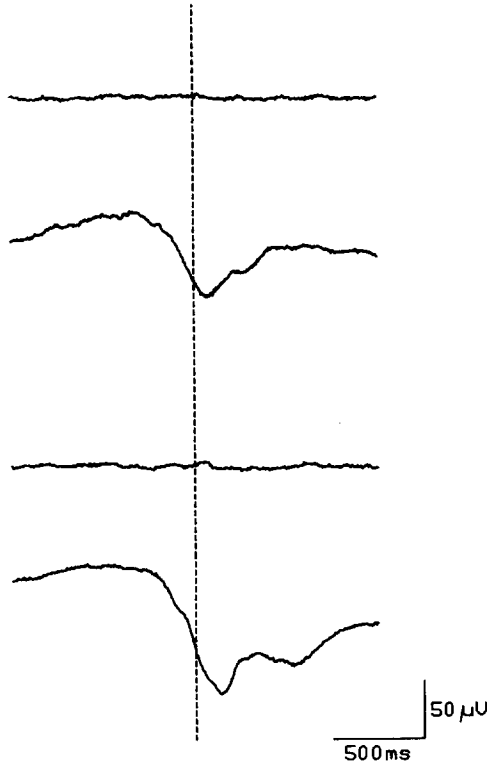

FIG. 2. Responses to the tone when not performing the task (first and third plot) and to releasing the lever after holding it down for at least one second (no stimulus; second and fourth plot). The dashed line indicates the moment the tone changes (from 1.35 to 3 kHz) and the moment that the lever is released. Each plot is based on about 800 recordings. The first two plots are for the rat of Fig. 1. The last two are for another rat. The change in tone gave no response when unrelated to the task. Only the second peak we had found in the presence of a stimulus was evident in response to releasing the lever without a stimulus.

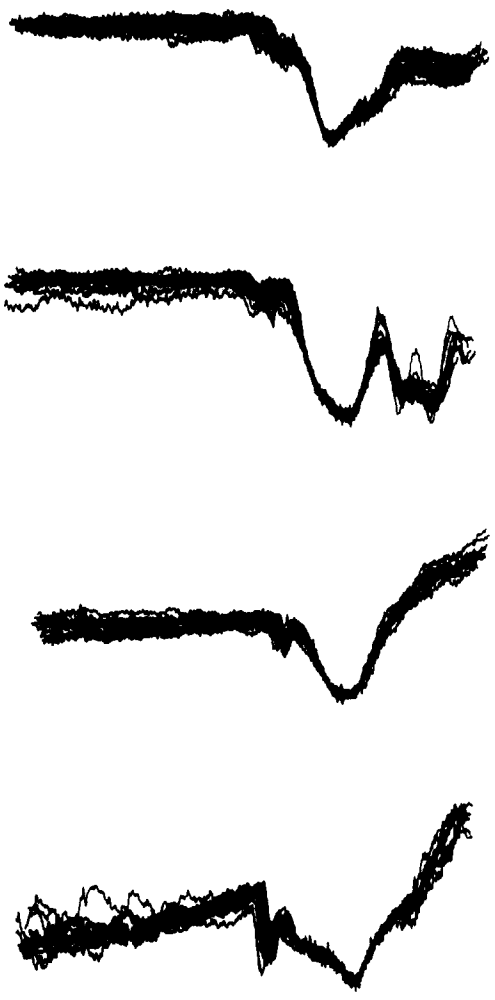

FIG. 3. Reproducibility of the second peak. Evoked potentials at different behavioural latencies superimposed so that they are synchronous with respect to the second peak. Note that the first peaks are not superimposed, because the whole evoked potentials were shifted along the time axis to synchronize the second peak. The stimulus is not shown because it is obviously also at a different position for each trace. The top plot is for the rat of Fig. 1. Each of the other plots is for a different rat.

DISCUSSION

We found two distinct peaks in our task-related potentials. The first peak was different for the two stimulus modalities and was absent when no stimulus was presented. It was also absent when the stimulus was presented, but the latter was irrelevant to the task. In that case the rat presumably paid no attention to the stimulus. This does not mean that such responses may not be found at other sites (5) or in response to other, stronger stimuli [e.g., the flash evoked potential recorded from the same sites in our previous study; (3)]. In our previous study (3) we demonstrated that this peak is picked up by the occipital screw.

The first peak's latency increases slightly with behavioural response latency for auditory stimuli, but does so very modestly—if at all—for visual stimulation. The increase in the peak's latency for auditory stimulation mainly occurs at low behavioural response latencies (e.g., open triangles in Fig. 1), making it difficult to interpret. It may be related to recognition of the tone. It is worth taking note of the fact that the visual stimulus consists of light onset whereas the auditory stimulus is a change in tone. In the latter case a distinction has to be made. The reduction in latency at the fastest response rates may somehow be related to the time taken to make this distinction (11).

The amplitude of the first peak in our evoked potentials is smaller when the rat is slow to respond than when the rat responds quickly. This confirms that although early stages of sensory analysis take a certain amount of time, the extent to which such analysis is allowed to take place may differ from time to time. The variations in the extent of the response suggest that part of the fluctuation may be accounted for by changes in sensory attention. However, the variations were rather modest, and were not significant for the auditory stimulation. For the visual stimulus alone, the effect was not large enough to exlude the possibility that the fluctuations in response amplitude result from the rat's orientation; particularly that of its eyes. However, the volume and source of the auditory stimuli, within the closed space in which testing occurred, make it unlikely that orientation affects the response to auditory stimulation. When the auditory stimulus was presented independently of the task, no evoked potential was observed at all. We believe that attention does affect this peak, but that quite a high level of attention is necessary for performing this task at all, so that the fluctuations we find are quite small. Despite this, we consider this technique suitable for comparing evoked potentials under conditions which affect the response (e.g., drug treatment), and hope it will help us in determining what aspect of performance is delayed.

For the second peak we find quite a different picture. This peak does not depend on the stimulus modality. Moreover, it can be found when no stimulus is presented, by averaging the brain potential in relation to the moment the lever is released. Its latency always shifts with the latency of the behavioural response, while its amplitude never does. Superimposing evoked potentials for different behavioural latencies in such a way that they are synchronized relative to the second peak (Fig. 3), clearly demonstrates the peak's reproducibility, allowing us to exclude the possibility that the peak is built up of several components with different relationships to the stimulus and the behavioural response. Although we have no evidence of the origin of the second peak, its relationship with the response suggests that it may depend on activity in the frontal area.

As the peaks and the behavioural latencies are presented on the same time scale, the slopes we find can give us direct estimates of the contribution of the processes underlying the peaks to the latency of the response. To begin with, the second peak cannot be a response to the movements required for releasing the lever, because its latency does not increase to the same extent as does the behavioural response latency. Although the slope was significantly above zero, it was significantly below one, both for visual ($p<0.005$) and auditory ($p<0.05$) stimulation. Its reproducibility and the fact that its latency does not shift fully with the behavioural response suggest that it reflects an "intention," rather than a direct command of the required muscles. The rest of the increase in reaction time must originate after the processes underlying this peak. Possibly they are related to the rat's not being in an ideal position for performing the response Note that we do not measure movement onset, but use the moment that the lever is release as our measure of behavioural response latency [see (6)].

When drugs affect performance in behavioural tests, it is usually difficult to determine which aspects of information processing are delayed. By not only measuring changes in reaction time, but also examining how peaks in the evoked potentials related to these reaction times fluctuate with performance, we hope to be able to distinguish between drug effects on early sensory processes or sensory attention (latency and amplitude of the first peak), brain processes involved in determining the appropriate response (shift in second peak), or more peripheral aspects of the performance itself (shift in reaction time with no corresponding shift in the peaks). We are at present examining whether this method can really be of help in specifying the stage at which drugs affect performance.

REFERENCES

1. Brenner, E.; Mirmiran, M. Sensory evoked potentials during food-motivated operant behaviour in the rat. Soc. Neurosci. Abstr. 12:520; 1986.
2. Brenner, E.; Mirmiran, M. Temporal relationships between stimulus, response and evoked potentials in a reaction-time task in rats. Neuroscience 22(Suppl):705; 1987.
3. Brenner, E.; Mirmiran, M.; Overdijk, J.; Timmerman, M.; Feenstra, M. G. P. Effect of noradrenergic denervation on task-related visual evoked potentials in rats. Brain Res. Bull. 18:297–303; 1987.
4. Dick, M.; Ullman, S.; Sagi, D. Parallel and serial processes in motion detection. Science 237:400–402; 1987.
5. Dyer, R. S.; Clark, C. D.; Boyes, W. K. Surface distribution of flash-evoked and pattern reversal-evoked potentials in hooded rats. Brain Res. Bull. 18:227–234; 1987.
6. Goodin, D. S.; Aminoff, M. J. The relationship between the evoked potential and brain events in sensory discrimination and motor response. Brain 107:241–251; 1984.
7. Hillyard, S. A. Electrophysiology of human selective attention. Trends Neurosci. 8:400–405; 1985.
8. Julesz, B. Texton gradients: the texton theory revisited. Biol. Cybern. 54:245–251; 1986.
9. Posner, M. I.; Snyder, C. R. R.; Davidson, B. J. Attention and the detection of signals. J. Exp. Psychol. 109:160–174; 1980.
10. Posner, M. I.; Presti, D. E. Selective attention and cognitive control. Trends Neurosci. 10:13–17; 1987.
11. Ritter, W.; Simson, R.; Vaughan, H. G.; Macht, M. Manipulation of event-related potential manifestations of information processing stages. Science 218:909–911; 1982.