Quantification of cortical arousal: Correlation with locomotor activity

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Cortical arousal has been assumed to be a continuous rather than "all or none" phenomenon. Few studies using quantitative techniques for the examination of cortical activity have been sensitive enough to detect such an arousal continuum, if one does exist. Typically, these studies have quantified cortical activity by using period analysis or amplitude analysis. A technique is presented which incorporates both of these types of analysis and yields a derived measure sensitive to alterations in cortical arousal. This derived measure was found to be significantly correlated with locomotor activity.

Cortical activation, or arousal, has been assumed to underlie enhanced performance on a number of behavioral tasks such as reaction time, fixed interval responding, and locomotor and open-field activity (Goethe & Isaac, 1977; Isaac, 1960; Isaac & Reed, 1961; Joseph, Forrest, Fiducia, Como, & Siegel, 1981). It has been suggested (Duffy, 1962; Hebb, 1955; Lindsley, 1952) that cortical arousal (i.e., low-voltage, high-frequency, desynchronous activity as defined by Morruzzi & Magoun, 1949) follows a continuum similar to the continuum found in behavioral arousal. Unfortunately, evidence for the existence of an EEG activation continuum is rare. Some investigators have discussed an EEG arousal response, or alpha-blocking reaction, in relation to behavioral arousal (Brazier, 1977; Motokizaw & Furuga, 1973). Such discussions have led many researchers in this field to the view that arousal in the EEG is either present or absent and is, in essence, "digital" in nature rather than following the proposed arousal continuum (Bouyer, Montaron, Rougeul-Buser, & Buser, 1980).

Relatively few investigations have attempted to detect alterations in the EEG of the awake, behaving subject. The studies that have attempted to determine the relationship between EEG and behavior have generally led to qualitative rather than quantitative results, and most have been concerned with the occurrence of hippocampal theta activity rather than low-voltage, high-frequency cortical activity characteristic of cortical activation (Arnold & Lopes da Silva, 1977).

A number of automated EEG scoring techniques have been devised which might prove useful in the detection of levels of cortical arousal and their relationship to behavior. Some of these methods have greater applicability than others. For instance, cross-correlational analysis is used to identify harmonic frequencies in the EEG. Since the activated EEG is desynchronous, this technique may

be of limited value. Spectral analysis may also be of limited value since the EEG is considered outside of its real time frame and thus, outside the time frame of the behaviors being observed. Amplitude analysis, however, has enjoyed some success in the detection of drug effects on the EEG (Drohocki, 1968; Goldstein, 1975; Harner, 1977). The same is true for period analysis (Fink, 1975; Itil, 1975). In a recent study, Etevenon and Giannella (1980) found that amplitude and period analysis differentiated the presleep EEG better than either spectral analysis or correlational analysis. Although both amplitude and period analysis have been shown to be useful in some situations, they both suffer from the fact that they ignore certain aspects of the EEG signal. Amplitude analysis ignores frequency and period analysis ignores amplitude. Since the unaroused EEG is described as consisting of high-voltage, low-frequency activity and the activated EEG as consisting of low-voltage, high-frequency activity, we might expect an EEG arousal continuum to vary on both amplitude and frequency parameters. Thus, either of the aforementioned techniques might prove useful. Additionally, since the changes in the frequency and amplitude of the EEG appear concurrently, a single measure that incorporates both amplitude and frequency information would have the advantage of greater sensitivity, since neither aspect of the signal is ignored. The circuit and study presented here are an attempt to provide and validate a measure sensitive to alterations in cortical activation.

CIRCUITRY

The circuit presented in Figure 1 consists of an amplifier, comparator, and voltage to frequency converter. The subjects' EEG was amplified by a Grass Instrument Co. 7P5 preamplifier. This amplified EEG signal was filtered so that frequencies of less than 2 Hz were attenuated. The signal was then passed through a voltage-dividing network and was differentially filtered. This produced one signal that was representative of the ongoing EEG and another

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Figure 1. Analog-to-digital conversion circuit.

that presented a moving baseline for the ongoing EEG. Both of these signals were then directed to a differential amplifier and an operational amplifier configured as a comparator. The comparator detected differences between the two signals. When the ongoing EEG signal was greater than the baseline signal, a pulse equal to the duration of the half wave of the EEG signal was output. This was then converted to the TTL-compatible signal (zero-crossing out).

The differential amplifier (TL084C), mentioned earlier, “subtracted” the baseline from the EEG signal. This result was then half-wave rectified (1N4148) so that only the positive-going portions of the signal were allowed to pass. This half-wave-rectified signal was converted into a series of pulses. The frequency of this pulse train was linearly proportional to the amplitude of the half-wave-rectified signal. Thus, the greater the amplitude of the signal, the greater the number of pulses at “voltage out.” This voltage to frequency conversion was accomplished by a Teledyne Semiconductor 9400 integrated circuit.

The frequency range of this pulse train was set by R5, C3, and C4. With the values shown in Table 1, a 60-Hz sine wave with a peak-to-peak voltage of 2 V (measured at pin 1 of the TL084C) produced a mean frequency of 25 Hz. In general, the frequency of the pulse train at “voltage out” is given by the equation:

$$f = \frac{V_{in}}{2R5} \times \frac{1}{(V_{ref}) (C4 + 12pf)},$$

where f is the output frequency, V_{in} is the voltage at pin 1 of the amplifier (TL084C), and V_{ref} is the voltage at pin 7 of the voltage-to-frequency converter (9400).

To test the effectiveness of this circuit in detecting alterations in cortical arousal, the following experiment was conducted.

EXPERIMENT

Method

Subjects. The subjects were four Long-Evans-derived rats 120-160 days of age. They were individually housed and maintained on a 12-h-light, 12-h-dark cycle. All subjects had free access to food and water over the course of the experiment.

Table 1	
Component	Value
R1	1 kΩ
R2	50 kΩ
R3*	10 kΩ
R4	1 MEGΩ
R5	47 kΩ
R6	100 kΩ
D1	1N4148
C1	35 μF
C2	1 μF
C3	.01 μF
C4	.0033μF
U1	9400
U2	TL084C
U3	7404

Note—All resistors are 1/4 W. *Subscripts in Figure 1 indicate matched components.

Apparatus. The apparatus consisted of the circuit mentioned above interfaced to a Grass 7P5 wide-band EEG preamplifier situated in a Grass Model 7 polygraph. The J6 output of the driver amplifier provided the input to the circuit. The outputs of the circuit were interfaced to the SYM-1 microcomputer used for data acquisition.

The subjects were tested in an activity chamber that consisted of a $30 \times 59 \times 28$ cm aquarium with the length bisected by an infrared beam. Beam breaks were detected and counted by the SYM-1. The floor of the chamber was covered by bedding material (Sanicel), and the walls by white paper to increase reflectance and, consequently, ambient illumination. The light source used in one of the experimental conditions was provided by a battery-powered 6-V sealed beam headlight.

Stainless steel screws (1.1 mm in diameter) were used as cortical recording electrodes and were connected by stainless steel wires to a socket (Winchester Type SM3S). A three-conductor ribbon cable was used to connect the subject to the preamplifier. The cable and plug assembly were suspended above the subject and chamber by a counter-weighted beam, thus, allowing freedom of movement while providing slight, constant tension on the electrode cable. This arrangement proved to be durable and essentially artifact free.

Surgery. The subjects were anesthetized with sodium pentobarbital (50 mg/kg). After the incision was made and the skin and muscle covering the skull reflected, three small burr holes were made. Stainless steel jeweler's screws were implanted. These electrodes were connected to a Winchester Type SM3S socket which was attached to the skull with dental acrylic. The active bipolar electrode sites were over the parieto-occipital cortex. The third electrode served as a reference and was placed just anterior to the suture nasofrontalis.

Training. After a 10-day recovery period following surgery, the subjects were placed in the activity chamber for 50 min each day for 20 days. Light (50 fc) and dark (less than 1 fc) conditions were alternated each day.

Following this 20-day habituation period, both EEG and locomotor activity data were collected for 10 5-min intervals on each day of the two replications of the light-dark conditions.

Results

Three measures were obtained for each subject in each interval: locomotor activity, cortical voltage, and cortical frequency. Additionally, a fourth derived measure was obtained by dividing the cortical voltage in an interval by the associated cortical frequency. The data were analyzed using separate three-way analyses of variance.

Results of the analysis for locomotor activity indicated that the rats were significantly more active in the dark than in the light [$F(1,117) = 11.74, p < .01$]. Locomotor activity also decreased over the 10 5-min intervals of the test session [$F(9,117) = 1.99, p < .05$]. This decrease was greatest in the second replication in the light condition, producing a significant interaction between these variables [$F(9,117) = 1.97, p < .05$].

The results of the analysis of cortical voltage also revealed a significant effect produced by the illumination conditions [$F(1,117) = 9.37, p < .01$] and a decrease over the duration of the test session [$F(9,117) = 4.81, p < .01$]. The voltage was higher under the light condition and during the latter portion of the test session.

The effects of illumination conditions and time in the apparatus were both detected in the analysis of the frequency of base-line crossings seen in the cortical potentials. Zero crossings were more frequent in the dark [$F(1,117) = 7.03, p < .01$] and during the earlier part of the test session [$F(9,117) = 5.97, p < .01$]. In addition, a three-way interaction of illumination conditions,

Figure 2. Total locomotor activity and the derived EEG measure (amp./zero cross.) across intervals of the test sessions.

periods within the test session, and replications was found to be significant [$F(9,117) = 2.56, p < .05$]. These data indicated a lower number of base-line crossings in the latter portion of the test session in the light during the second replication.

The analysis of the derived measure (cortical voltage divided by base-line crossings), or mean voltage, detected the illumination effect [$F(1,117) = 11.53, p < .01$], with the higher measures occurring in the light. An increase was seen during the test session [$F(9,117) = 6.44, p < .01$]. In addition, the interaction of illumination condition, periods within the test session, and replications was also significant [$F(9,117) = 3.23, p < .01$], indicating an increase in this measure during the test session that was greatest in the light during the second replication.

With respect to locomotor activity changes within the test session, significant correlations were obtained when they were compared with cortical voltage ($r = -.75, p < .01$), base-line crossings ($r = +.725, p < .01$), and mean voltage ($r = -.735, p < .01$). These relationships are apparent in Figure 2.

DISCUSSION

The results of the present study indicate that both locomotor activity and electrophysiological activity of the cerebral cortex differ in the light and dark, with light

producing a reduction in both measures in the nocturnal rat. These findings lend support to the hypothesis that level of illumination is important in determining both behavioral and cortical arousal in the rat (Isaac, 1971). The variables that had a significant effect upon locomotor activity also produced significant differences on the measures of cortical electrophysiological activity.

Although the subjects had experienced the handling procedures and were exposed to the experimental situation before data were gathered, it is apparent that habituation to these procedures and the apparatus was not complete. The reduction in both behavioral and electrophysiological measures of arousal within the test sessions and between the replications demonstrate this.

While all of the electrophysiological measures detected effects of the experimental conditions, there appeared to be differences in the sensitivity of the individual measures. This is suggested by the detection of a greater number of higher order interactions by the derived measure, which combined measurements of amplitude and frequency. This would seem plausible, since cortical arousal includes both frequency and voltage changes (Morruzzi & Magoun, 1949). Thus, a measure that incorporates both aspects of the response might be expected to have greater sensitivity than the individual measures.

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