Evoked Response and Behavior in Cats

Abstract. *Electroencephalographic averaged evoked responses to flashing lights of four different intensities were recorded in ten cats and correlated with behavior. Animals showing a high degree of exploratory behavior, aggressiveness, and activity and little withdrawal showed relatively large increases in amplitude of the averaged evoked response with increases of stimulus intensity. Those showing opposite behavioral traits had small increases or decreases of average evoked response amplitude with increases of stimulus intensity. These findings are compatible with those reported for human subjects. Inference is made about a neurophysiological mechanism for stimulus intensity modulation.*

Individual differences in response patterns of the cortical averaged evoked response (AER) to flashing lights of varying intensities have been reported (*1, 2*). Of specific interest is the fact that at higher intensities of stimulation some human subjects show an increasing amplitude of certain components of the vertex-to-ear AER while others show decreasing amplitude. The former are referred to as augmenters, the latter as reducers (*3*). Among normal male subjects, reducers respond to stimulation of minimum intensity more readily and more strongly than augmenters (*4*). At high levels of stimulation, reducers attenuate input apparently in order to avoid overstimulation. From this response pattern an inference is made regarding the existence of a stimulus intensity control system in the central nervous system. This interpretation is consistent with both Freud's structural concept of stimulus barrier (*5*) and Pavlov's idea of protective inhibition (*6*). It also provides an explanation of the behavior of certain nonparanoid schizophrenics who are acutely aware of minimum intensity stimulation and who are in a state of hyperarousal. This presumably activates mechanisms of protection against overstimulation (*3, 7*). Other evidence has been provided which suggests that there are specific behavioral characteristics associated with individuals who are augmenters and reducers (*8*). Augmenters react in a prompt and marked way to sudden and novel stimuli. They are prone to respond in overt emotional ways to stressful situations. Their great sensory contact with the external environment can be called "attention-out" behavior (*3*). Reducers on the other hand tend to show relatively little external reaction to sudden and novel stimuli and, generally, little overt emotional responsiveness in stressful situations. Their greater orientation to internal processes can be called "attention-in" behavior (*3*).

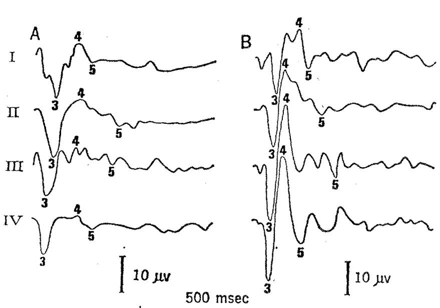

Fig. 1. Typical series of evoked response waveforms to four intensities of photic stimuli. Each trace is the averaged response to 112 randomized flashes (15 msec in duration) of the following intensities (in foot candles): I = 0.6, II = 2.4, III = 8.6, and IV = 39.0. Upward deflection indicates negativity at the vertex, referenced to the left ear. Peaks are identified by numbers corresponding in the cat (with allowance for shorter latencies) to the system used by Buchsbaum and Silverman (*1*) for human AER. (A) Amplitude reduction obtained from cat 8, especially between intensities II and IV. (B) Marked amplitude augmentation obtained from cat 6.

Based on these observations, reports, and theoretical considerations, this study of a common laboratory animal was undertaken to determine whether augmenter and reducer individuals could be found with the evoked response technique, and whether averaged evoked response patterns and behavioral characteristics are related.

Ten adult cats were used. They were placed separately in a box (0.36 m^3) containing several stimulus objects and illuminated with two 40-watt bulbs. The same five raters simultaneously made observations of each animal through "one-way" windows. During two successive 5-minute periods spontaneous activity and responses to a specific stimulus were observed. The stimuli presented were (i) three exposures to 1 second of a flashing strobe light (ten flashes per second); (ii) three light and three heavy knocks on the box presented alternately; (iii) 10 seconds of a rubber hose hissing and whipping about as the result of a low and high rate of oxygen flow, each presented three times, alternately; and (iv) three low (20 volts) and three high (100 volts) intensity square-wave single electric pulses (15 msec in duration) administered alternately at 10-second intervals through a floor grill. Behavior was independently rated immediately on the following seven-point scales which had been qualified with descriptor words in addition to the following titles: (1) exploration, (2) activity, (3) excitability, (4) withdrawal, (5) fear, (6) aggression, and (7) rage. The interrater correlations and their probabilities among raters for the scales were, respectively, (1) 0.86, $P = .003$; (2) 0.85, $P = .005$; (3) 0.57, $P = .045$; (4) 0.42, $P = .102$; (5) 0.26, $P = .394$; (6) 0.84, $P = .006$; and (7) 0.62, $P = .032$.

Beginning 1 to 2 hours later, AER's were recorded on tape (FM Ampex SP 300). Silver–silver chloride electrodes (Grass Co.) were placed at the scalp vertex and, for reference, on the left ear. The signal was amplified with a Tektronix 122 preamplifier and RCA CA 3033A integrated circuits used for later amplification. Filtering was used to provide a passband of 3 to 38 hz (− 3-db voltage points). All AER data were obtained with the animals' eyes mostly open while the animals were restrained in a small chamber which

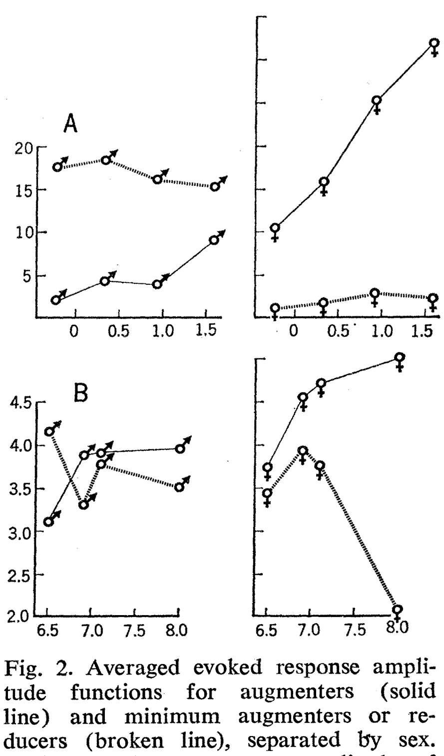

Fig. 2. Averaged evoked response amplitude functions for augmenters (solid line) and minimum augmenters or reducers (broken line), separated by sex. Ordinate values represent amplitude of excursion from peak 3 to peak 4 in microvolts. (A) is from the present study and shows the individual cats of either sex which had the greatest and least slopes. Abscissa is log intensity in foot candles. (B) is from Buchsbaum and Silverman (*1*) and shows nonpsychiatric human augmenter and reducer groups. Abscissa is log intensity in millilamberts.

Table 1. Behavior ratings and slopes of amplitude of AER response to flashes of four intensities. Flash intensities were 0.6, 2.4, 8.6, and 39.0 ft-c. Cats are listed in order from lowest to highest slope. Behavior ratings are given as the rating sum of the same five raters on each scale (maximum 30). Male, M; female, F.

Cat No.	Sex	Slope (μv/ft-c)	Behavior						
			Exploration	Activity	Excitability	Aggression	Rage	Withdrawal	Fear
8	M	−0.075	5.9	3.4	5.9	2.5	0.3	14.2	7.4
2	M	0.013	2.3	1.8	12.1	3.7	3.8	24.7	16.8
5	F	0.013	15.9	14.0	21.0	5.5	1.2	22.5	17.0
3	F	0.016	22.4	18.0	18.2	4.9	17.1	18.0	13.8
1	F	0.043	21.5	12.3	12.0	1.1	1.7	13.7	9.8
4	M	0.141	4.4	3.0	4.7	1.2	0.8	14.0	5.9
7	M	0.160	2.7	1.9	12.6	4.2	0.1	20.7	10.9
9	M	0.273	14.6	13.1	12.6	22.8	7.3	11.1	10.1
6	F	0.412	28.8	28.1	8.5	19.9	3.0	6.3	11.0
10	F	0.471	23.0	23.7	23.0	1.8	1.4	12.2	8.8
Correlation with slope			0.64	0.78	0.38	0.85	0.12	−0.59	−0.14
P			.025	.005	>.05	.005	>.05	.05	>.05

allowed the head to project through an opening. The eyes were positioned 10 cm from the center of an opening (30 by 30 cm) in the front side of a chamber (50 by 50 by 50 cm) lined with foil to reflect the flashes produced by tubular lamps inside the front wall adjacent to the opening. This arrangement made it extremely difficult for the animal to avoid retinal illumination. Four intensities [I = 0.6, II = 2.4, III = 8.6, and IV = 39.0 foot candles (ft-c) (1 foot candle = 10.8 lumen/m^2)] of flash were randomly presented at a rate of 1 flash/sec over an 8-minute period. The random presentation minimized the possibility of selective avoidance of a given stimulus intensity. To examine whether the AER data were stable for testing and retesting, each cat was retested four times. The retests were done at the same time of day at intervals of 2 to 3 days. A Mnemotron computer of average transients (CAT 900) and X-Y plotter were used to obtain AER curves for the cat tested for 500 msec after 112 flashes of each intensity. After each test the system was calibrated by introducing a 15-μv (peak to peak), 10-hz sine wave into the amplifier inputs; a pulse for triggering of the CAT at a fixed-phase angle was produced by feeding the sine wave into a Schmidt trigger.

The largest excursion in 36 (90 percent) of the 40 AER traces was between what was identified as positive peak 3 to negative peak 4, after the peak identification method used by Buchsbaum and Silverman (*1*) for human AER analysis was adapted to the cat. Criteria for peak identification, which produced consistent results in all traces, were as follows: peak 3, the largest positive peak in the latency interval of 35 to 120 msec and peak 4, the largest succeeding negative peak occurring at a latency of no more than 170 msec. For the four flash intensities the mean amplitudes and standard deviations of the excursion between peaks 3 and 4 were (in microvolts): I, 9.6 ± 6.8; II, 12.3 ± 8.3; III, 15.0 ± 10.6; and IV, 16.9 ± 12.6. The corresponding mean latencies and standard deviations of peak 3 for the four flash intensities in milliseconds were: I, 64.4 ± 6.3; II, 58.0 ± 6.6; III, 52.8 ± 9.5; and IV, 49.8 ± 9.4. The corresponding latency values for peak 4 were: I, 111.9 ± 11.6; II, 105.0 ± 9.6; III, 101.1 ± 11.1; and IV, 98.5 ± 12.2. The above latencies were shorter than those shown by Buchsbaum and Silverman (*1*) in humans (75 to 100 msec for peak 3 and 125 to 170 msec for peak 4). This seems compatible with the probable greater retinal illumination produced by the eyes-open condition used in the present study in contrast to the eyes-closed condition used by Buchsbaum and Silverman since it has been shown (*9*) that latency is reduced by higher flash intensity. Also the shorter neural pathways in the cat would be expected to cause the earlier appearance of an equivalent peak. Slopes of AER amplitude over the four stimulus intensities were obtained by the least squares method and expressed as microvolts per foot candle.

Typical AER curves are shown in Fig. 1; Fig. 1A shows the AER curve from cat 8, the greatest reducer, and Fig. 1B shows the curve from cat 6, a marked augmenter. Figure 2A shows the amplitude plotted against log intensity for the minimum and maximum augmentation by cats of either sex. The greater response to low level stimulation of the male reducer as compared to the male augmenter coincides with the finding in human males (*1*). There is strong similarity of these curves to those in Fig. 2B, similarly plotted curves of human reducer and augmenter groups reproduced from Buchsbaum and Silverman (*1*).

Slope and behavior results are summarized in Table 1. Positive slopes strongly predominated, occurring in nine of ten cases, a significant finding ($P = .01$, sign test) that suggests that augmentation may be much more prevalent than reduction in the cat. However, the AER data from this day of behavior rating show a wide variation of augmentation among cats, positive slopes ranging from 0.013 to 0.471 μv/ft-c. An examination of test-retest data showed no significant difference. This suggests that there is slope stability for each individual.

The prediction that degree of augmentation would be positively correlated with exploration, activity, and aggression ("attention-out" behavior) and negatively correlated with withdrawal ("attention-in" behavior) was supported by the significant Pearson correlation coefficients seen in Table 1. Of particular interest is comparison of the animals at the extremes of slope. It is seen that the strongest augmenters, cats 6 and 10, both showed very much larger ratings on exploration, activity, and aggression than did cats 8 and 2 who had the lowest slopes. On the withdrawal scale the two cats with minimum slopes showed higher ratings, and there was no overlap with the lower ratings of the two extreme augmenter cats. It is of considerable interest that manic patients, who are clinically well known to also show much exploration, activity, and aggression and little withdrawal, have likewise been shown (*10*) to be strong augmenters. In connection with further cross-species comparison, it is to be noted that the two greatest augmenter animals (cats 6 and 10) are females while the two least augmenter animals (cats 2 and 8) were males, suggesting that the sex differences in cats may be the same as those previously found in humans (*4*).

These data suggest that at least one

common laboratory animal may have a very similar though less pronounced stimulus intensity control system to that previously observed in humans and that relation of the control system to behavior may also parallel that found in people. The ability of these neurophysiological data to predict individual differences in animal "personality" was rather striking. This opens the possibility that common laboratory animals may be used for extensive experimental study of these phenomena.

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Criteria of Brain Death

I suggest that it is important, in regard to the experiments of Hossmann and Sato (*1*), to elucidate the reasons for the recovery of brain function after presumably prolonged anoxia under their experimental conditions, since this is contrary to the experience of other investigations on the effects of cerebral anoxia, beginning with the classic experiments of Sugar and Gerard (*2*). Furthermore, the conclusion that this "raises serious questions about the reliability of criteria currently used for the determination of brain death" is unwarranted. Experimental anoxia must approximate the clinical situation in man to have relevance to the problem of criteria for brain death; even at that, species differences must always be considered, as well as the fact that the human condition defies precise measurement of the degree and length of anoxic insult.

The ultimate answers to the criteria for brain death must come from the human experience. The clinical criteria evolved thus far (*3*) are eminently conservative: totally unresponsive coma, loss of all motor function (including respiration), loss of reflexes and electrocerebral silence (defined as no electrical activity over 2 μv when recording from scalp electrode pairs ten or more centimeters apart with interelectrode resistances under 10,000 ohms but over 100 ohms) existing for a 24-hour period, except in the instances of initial overdose of a central nervous system depressant drug, or hibernation, when the observation period must be extended. Evidence is accumulating that spinal reflexes may be preserved despite brain death. Whether shorter observation periods in specific clinical situations, as has been suggested by some, are appropriate has yet to be determined by systematic research in man.

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We agree that an important aspect is to elucidate why, in our experiments, neuronal recovery occurred after more than 1 hour, in contrast to earlier investigations. In most of the experiments to which Silverman refers (*1*) the pneumatic cuff method was used, which produces an interruption of both the arterial blood supply to the brain and the venous outflow from the brain. Ames *et al.* (*2*) showed that this may cause an impairment of the blood recirculation (no reflow phenomenon) after a few minutes of ischemia. In our experiments, in which the venous outflow was not blocked, a "no reflow phenomenon" did not occur, and this was possibly one of the reasons for the improved recovery.

We have discussed the reliability of the criteria on brain death mainly because in our experiments the electroencephalogram (EEG) was still isoelectric when membrane excitability and synaptic transmission had already recovered for a long time. Furthermore, the reappearance of the EEG seemed to depend on a relatively high blood pressure and could be delayed at normotensive levels. We have noticed the sudden recovery of EEG activity after many hours of electrocerebral silence when the blood pressure was increased. This suggests that even prolonged electrocerebral silence does not prove the irreversible loss of neuronal function. We do not deny that the human brain is irreversibly damaged when the criteria elaborated by Silverman *et al.* (*3*) are fulfilled, but we feel that this is due to the current limitations of therapeutic measures rather than to the reliability of these criteria themselves.

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Amino Acid Synthesis in Simulated Primitive Environments

In reference (*10*) of their report Bar-Nun *et al.* (*1*) stated: "H. R. Hulett (*2*), by confusing meteorites with meteoroid and micrometeorite fluxes, reached an erroneous value of 4×10^{-5} cal cm^{-2} yr^{-1}" for the energy flux of meteoric material on the earth. I should have used some term other than meteorite to refer to the incoming material. However, in one of the references I cited there appears the statement: "The total mass of meteoric material that enters our atmosphere per day may be something of the order of 100 tons" (*3*). This refers to all incoming solid material, not just material that