venously) (Fig. 1) and this effect was readily reversed by intravenous haloperidol (0.1 mg/kg). In contrast, none of the control lesions diminished the ability of *d*-AMPH to markedly depress these cells at low doses (Fig. 1A). Destruction of the median forebrain bundle, which contains the ascending axons of A9 cells, led to an increase in their spontaneous rate but did not prevent *d*-AMPH–induced depression of these cells.

Thus discrete lesions in the crus cerebri and the vicinity of the tail of the caudate nucleus effectively blocked the depressant effects of *d*-AMPH on DA cell firing rate even when it was given in nearly lethal doses. These findings, coupled with the relatively weak effect of microiontophoretically administered *d*-AMPH on DA cell activity (*5*), strongly suggest that the depressant effect of *d*-AMPH on these cells is mediated predominantly by a neuronal feedback pathway rather than as a direct or indirect action on DA receptors located on A9 DA cell bodies or dendrites. The finding that such lesions cause an increase in the spontaneous rate of firing of A9 cells suggests that they have been freed from an inhibitory input. The degree of block induced by the lesions varied from almost total to 50 percent. When *d*-AMPH did induce a partial depression of A9 cell activity in lesioned animals, it did so usually at a relatively low dose (0.8 to 1.6 mg/kg). The depression seen under these circumstances may be due either to an incomplete lesion that missed some feedback pathway fibers or to an action of *d*-AMPH either directly or indirectly on dopaminergic autoreceptors on the dendrites of A9 cells, as suggested by Groves *et al.* (*10*). In animals with chronic lesions of the crus cerebri, preliminary studies showed, in a few cases, some return of the ability of *d*-AMPH to depress A9 cells. The mechanism responsible for this return is unclear, but it could be due to the development of supersensitivity in some portion of the feedback pathway or some other compensatory mechanism.

Although in this study we have considered mainly feedback effects in the nigrostriatal system, the presence of DA-sensitive autoreceptors on DA neurons appears well established (*8, 18*) and it is intriguing to speculate on the possible physiological significance of DA receptors on dopamine cell bodies or dendrites. If present, dendro-dendritic synapses between DA neurons would imply a physiological role for DA receptors at such junctions. The published evidence for such synapses is, as yet, not conclusive (*19*). The pharmacological significance of DA autoreceptors appears much clearer. Directly acting DA receptor agonists and antagonists have been shown to interact at these receptors, thereby inducing changes in the activity of DA neurons (*7, 8*). At least one behavioral effect has been attributed to an action of a drug at this site (*20*). As we suggested previously, when considering the mechanism and site of action of a drug that affects the DA system, one must now take into consideration its effects on presynaptic receptors or autoreceptors as well as its postsynaptic actions. However, in the specific case of *d*-AMPH it would appear that in a pharmacological dose its ability to induce depression of A9 DA neurons is mediated largely through its effect on a neuronal feedback pathway whose cells of origin are in the caudate nucleus and whose axons travel by way of the crus cerebri to the substantia nigra.

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Stable and Plastic Unit Discharge Patterns during Behavioral Generalization

Abstract. *A movable microelectrode was implanted in adult cats trained to respond differentially to two different frequencies of light flicker. Unit responses were recorded along cortical and thalamic trajectories. The late components of the poststimulus response of 29 percent of the cells examined showed statistically significant differences when data from different behavioral outcomes to the same neutral generalization stimulus were compared.*

Numerous reports from human as well as animal experiments have established that the same physical stimulus can elicit diverse evoked response waveshapes. While the actual features of the stimulus seem to be represented by exogenous, stimulus-bound components of short latency, these waveshapes show differences usually manifested in relatively long latency components. Such phenomena have been observed in situations where the same stimulus is interpreted in different ways (*1*), or where the information delivered by the stimulus depends upon the features considered relevant by the subject, the relative probability of the stimulus, or its relationship to other events (*2*). The endogenous nature of these processes is most unequivocally established by potentials which appear when an expected event fails to occur (*3*).

In some of these studies, the different endogenous processes were accurate fac-

similes of responses usually elicited by familiar but absent stimuli and were consistently and differentially associated with particular interpretations or behavioral outcomes. Numerous controls were included to rule out possible influences of unspecific factors such as orientation, changes in set, movement, or response bias. For these reasons, the endogenous processes were interpreted to reflect the readout of specific memories (*4*). In the other studies cited, the data were insufficient to determine whether these released processes represent specific items of information or constitute an unspecific reflection of the utilization of a central cognitive processor involved in matching representations of past and present events. Such studies refer to these endogenous processes variously as emitted potentials, late positive components, or $P_{\overline{300}}$.

As yet, it has not been possible to decide whether a common psychological denominator underlies these different manifestations of endogenous processes, whether they reflect the representation of specific information, or whether they are unspecific correlates of functions generally involved in the evaluation of information. Nonetheless, the rapid proliferation of research on these phenomena attests to the widespread recognition that in any event they provide a reflection of cognitive processes mediating the interpretation of incoming information in the context of previous experience. This realization necessarily directs attention to two questions: (i) Is it possible to identify distinctive neuronal activity related to the cognitive process? (ii) Are exogenous (stimulus-bound and endogenous (interpretative) processes mediated by different classes of neurons?

Our initial approaches to this problem used chronically implanted movable microelectrodes which provided multiple unit data (*5*). Neural ensembles in many regions displayed firing patterns closely correlated with the endogenous evoked potential components. For the present study, an improved microdrive was designed. Higher impedance platinum-iridium glass-insulated microelectrodes were used to permit resolution of the firing patterns of single cells (*6*).

Seven adult cats were implanted with a chronic microelectrode. In four of these animals, the microelectrode penetrated medial suprasylvian cortex (stereotaxic coordinates A10 L7) and was then extended to probe the lateral geniculate nucleus. In three other cats, the microelectrode penetrated the visual cortex 2 mm lateral to the midline (stereotaxic coordinates A2 L2) in area 17; the subsequent traverses then probed the cortical regions on the medial aspect of the hemisphere. In all seven cats, approach-approach discriminations were established between flicker stimuli at two different repetition rates, V_1 or V_2 (*7*). All procedures were carried out in a 2 by 2 by 2 foot (1 foot = 0.3 m) apparatus bearing pedals and dippers on the left and right sides of a work panel. Flicker was delivered from a silent fluorescent tube mounted in the roof of the apparatus. Training was carried out with conventional shaping techniques and a modified Gellerman schedule of stimulus

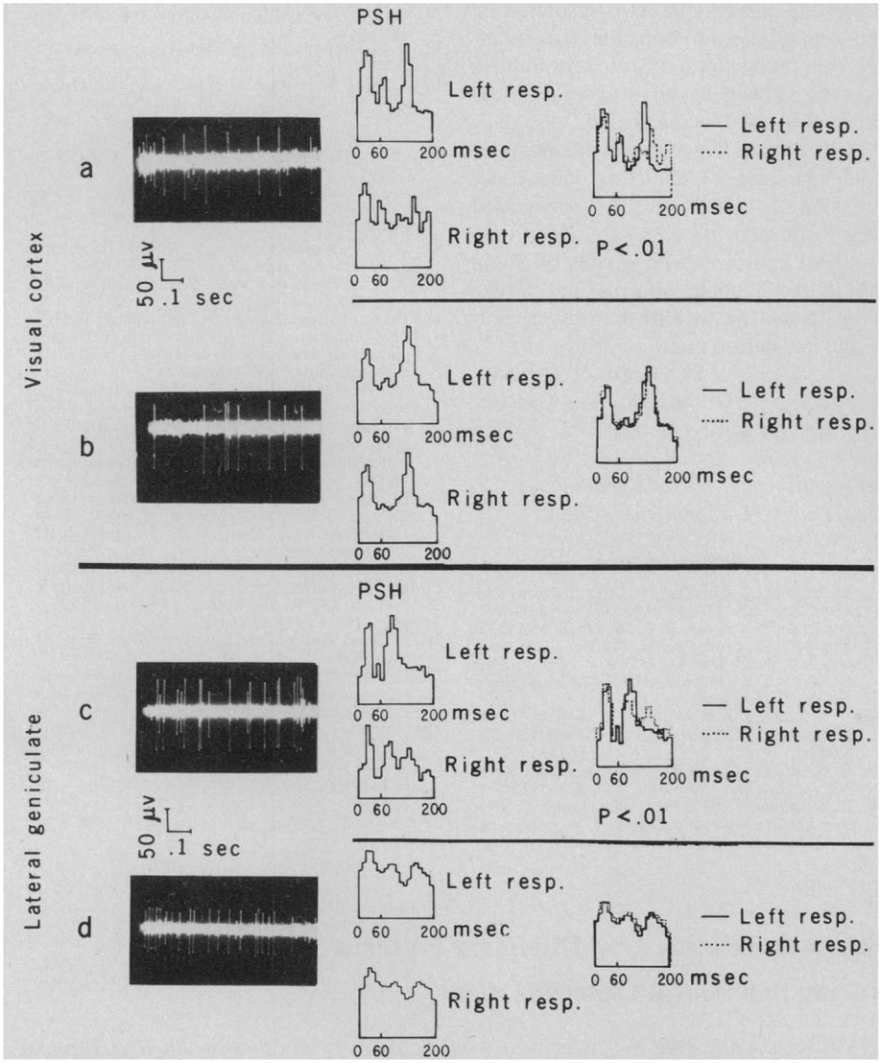

Fig. 1. Examples of both "stable" and "plastic" cells recorded during microelectrode traverses of visual cortex and lateral geniculate. (a) "Plastic" cell recorded from visual cortex. The post-stimulus histograms (*PSH*) prepared from equal numbers of triggers from whole behavioral trials ending in left and right responses (*resp.*) to the identical generalization stimulus are shown in the center of the figure. The superposition of these PSH's is shown on the far right. The early components (0 to 60 msec) are seen to be isomorphic, whereas there are clear differences in the late components (60 to 200 msec). Both early and late components were tested independently. As in the case of this cell, the early components showed no significant difference (with a single exception) in each of the 56 cells studied, whereas 16 of these cells (29 percent) showed statistically significant ($P < .01$) differences in the late components. The choice of latencies in the definition of "early" and "late" was made a priori, on the basis of previous work with evoked potentials (*4*) as well as typical primary component latencies. Adherence to this a priori characterization is to avoid possible bias in the statistical analysis (*9*). (b) "Stable" cell recorded in visual cortex showing isomorphic early and late components. The majority of cells studied in lateral geniculate and visual cortex (71 percent) were in this category. (c) "Plastic" cell recorded from lateral geniculate, again showing late component differences and early component isomorphism. In the oscilloscope tracing on the left, it can be seen that there are two cell amplitudes present. The PSH's are computed for this example for the larger of the two cells. Cell identity was determined by the presence of clearly defined, normally distributed peaks in the computer-calculated amplitude histogram, as well as by unit waveshape. (d) "Stable" cell from lateral geniculate.

presentations, with an average interval of 1 minute between trials. Presentation of flicker stimulus V_1 was established as the cue to obtain a dipper of blended tuna fish and milk by pressing the lever on the left side of the work panel (CR_1), while the same reinforcement was delivered if the lever on the right side of the panel was pressed (CR_2) if V_2 were presented. Self-correction of errors was not permitted.

After substantial overtraining, the microelectrode was slowly advanced until a well-resolved unit was encountered. A series of differential generalization trials was then presented, in which a flicker stimulus V_3 at a frequency intermediate between V_1 and V_2 was occasionally interspersed into the random stimulus sequence (*7*). Sometimes the cat responded to V_3 as if it were V_1, pressing the lever on the left side of the work panel (V_3CR_1), while on other occasions V_3 elicited the opposite form of generalization and the cat pressed the lever on the right side (V_3CR_2). These interspersed presentations of V_3 continued until a sufficiently large sample of both types of generalization had been obtained.

At times, the microelectrode was left in the same position for periods as long as 14 days, while repeated observations were obtained of the response patterns displayed by the same cell. Amplitude, spike waveshape, and post-stimulus histogram contour were used to confirm that the same cell was held throughout this period of observation. A more complete discussion of our criteria and methods for classifying single cell responses in chronic preparations may be found elsewhere (*8*). If the cell was lost or the period of observation was deemed adequate, the microelectrode was advanced until another well-resolved unit was encountered.

Post-stimulus histograms from each cell were constructed separately during the differential generalization trials in which V_3 presentation resulted in left bar response (V_3CR_1) or right bar response (V_3CR_2). Under each of these conditions, two different post-stimulus histograms were constructed: (i) using cellular responses to all stimuli that occurred during the behavioral trial, and (ii) using only cellular responses to the stimuli that occurred during the latter half of each trial (see Fig. 1).

Quantitative assessment of whether the post-stimulus histograms obtained from a given cell were significantly different during V_3CR_1 and V_3CR_2 was carried out by testing the hypothesis that the two post-stimulus histograms were derived from the same parent distribution of cell firing probability. The test statistic followed the χ^2 distribution, and was derived specifically for histogram data; it afforded the important advantage of allowing an a priori partition of the histogram into an early (0- to 60-msec) segment and a late (60- to 200-msec) segment, each of which could be tested independently as well as jointly (*9*). Histograms were not normalized, and thus represented absolute neuronal response, rather than relative probability of firing. The choice of the intervals chosen to represent the early and late segments of the histogram was made based on previous experience with evoked potential data, as well as on the basis of typical primary and secondary response latencies (*4*).

Table 1. Firing pattern of brain cells. Cortical placements were made with sufficient exposure of the cortical surface to confirm the area traversed by the microelectrode by direct examination. Lateral geniculate placements were made according to stereotaxic coordinates. Latency and waveshape of the unit discharge were used to confirm the placement. The criterion used to define significant difference between two post-stimulus histograms was $P < .01$. If a criterion of $P < .05$ had been used, 11 cortical and 7 lateral geniculate cells would be defined as "plastic." Thus, the labels "stable" and "plastic" are not sensitive to the precise statistical cuts made.

Structure	Cats (*N*)	Cells (*N*)	Number of cells with different firing pattern (post-stimulus histogram) when same stimulus elicits two different behavioral responses	
			0 to 60 msec	60 to 200 msec
Cortex	4	26	0	9
Lateral geniculate	4	30	1	7
Total	7†	56	1	16

*Of the 26 cortical cells, 22 were in visual cortex and 4 were in medial suprasylvian cortex. †In one cat, data were obtained from both association cortex and lateral geniculate body.

A stable cell was defined as one which showed no significant difference in the pattern of cell activity when the post-stimulus histograms obtained during V_3CR_1 and V_3CR_2 trials were compared, while a plastic cell was defined as one for which such comparison indicated a statistically significant difference in cell response. Table 1 shows the results obtained from this analysis. Of the 26 cortical cells for which adequate data (*10*) were obtained during differential generalization, none showed significant difference (at the $P < .01$ level) in the early segments (0 to 60 msec) of the post-stimulus histogram, whether whole or half trials were examined. However, nine cells showed a significant difference in the late segment of the histogram (60 to 200 msec) when trials resulting in different behavioral outcomes to the same stimulus were compared. Of the 30 cells in the lateral geniculate nucleus for which adequate data were obtained, one cell showed a significant difference both in the early and late segments of the histogram, while six others showed a significant difference only in the late segment. Thus, a total of 16 of the 56 cells examined (29 percent) were identified as plastic (see the legend of Table 1). This population of 56 cells, recorded over a period of 2 years, is sufficient to establish the existence of these two classes of cells, since the observed incidence of plastic cells far exceeds that which might be expected to arise from chance statistical fluctuations.

In the present work, evoked potential data were obtained simultaneously with unit data, and were separated by analog filtering with subsequent computerized digitizing. These evoked potential data were analyzed by sorting methods used in previous work, cited above, as well as by newer, cluster analytic methods (*11*). The results obtained were qualitatively and quantitatively similar to those obtained earlier. In the case of the neuronal data obtained in the present study, it was not possible to perform pattern recognition analysis that was analogous to the methods used in our evoked potential studies. These methods have not yet been extended to the unit level. Nevertheless, several examples of the facsimile property described above were found in the unit data of this experiment. Due to the lack of appropriate pattern recognition techniques, the facsimile property at the unit level could be only tentatively explored in this work. This analysis is described in a more detailed report (*12*).

All the cells that met our criteria of "plasticity" did so whether whole trials or only the latter halves of trials were examined. This fact indicates that the differential response of these cells is manifested long before any overt behavioral

response occurs, and provides reassurance that these findings do not arise from nonspecific sources such as movement, direction of gaze, and so forth. Similar reassurance is derived from the fact that 39 of the 56 cells examined showed no significant differences either early or late in the post-stimulus response. Perhaps the most convincing support for the statement that these findings are not attributable to nonspecific causes comes from the fact that 15 of the 16 plastic cells showed no significant differences during the early segment of the post-stimulus histogram. The latency span of the early segment of the histogram corresponds to the sensory-specific or exogenous portion of the evoked response, and should reflect changes in the afferent input that might derive from changes in the direction of gaze or level of arousal. All 16 plastic cells showed changes in the long-latency segment of the histogram that corresponds to the latency region of the endogenous components described in the introduction to this report.

The body of data presented in this report indicates that two classifications of cells exist in the thalamus and cortex. We have called "stable" those cells whose average firing patterns are determined by the parameters of the physical stimulus, and "plastic" those cells whose response patterns vary, in their late components, depending upon the meaning attributed to the afferent input. Our findings suggest that the endogenous processes observed in the brain are related to the activity of a subset of cells, which we term plastic cells. The fact that both stable and plastic cells exist within a given recording site indicates that the set of stable cells may fulfill the role of providing a stable, afferent input, while the set of plastic cells, through differential late responses, may mediate operations on the afferent input that are correlated to the cognitive process of the animal. Establishing whether stable and plastic cells represent different types of neurons would seem to merit high priority.

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18 November 1975

Hydrogen Produced from Decomposition of Methanol During Engine Compression?

Reed and Lerner discussed methanol as a fuel for internal combustion engines (*1*). They reported improved acceleration, lower levels of CO in the exhaust, better fuel economy (miles per gallon), and improved octane rating for a fuel consisting of 5 to 15 percent (by volume) methanol in gasoline. Further, Reed and Lerner proposed a mechanism "to account for the disproportionate effects of methanol on the octane value and other properties of gasoline." Additional information on the performance attributes of methanol-gasoline blends has recently been presented (*2*).

According to the Reed and Lerner hypothesis, methanol can decompose into CO and H_2 during the compression stroke of an internal combustion engine. Since this decomposition is endothermic, heat would be absorbed, the cylinder charge cooled, and premature combustion reactions quenched. They further relate that "the CO and H_2 formed on dissociation increase the flame velocity of the charge, giving more complete and efficient combustion."

To support their methanol decomposition mechanism Reed and Lerner calculate from data in Kirk and Othmer [reference 7 in (*1*)] that "at 10 atmospheres methanol is 18, 85, and 99.7 percent dissociated at 100°, 200°, and 300°C, respectively," However, these results are misleading because (i) they apply to equilibrium conditions only and (ii) they apply to the CH_3OH, CO, H_3 system and not to a system that includes air. No reason was given to indicate that decomposition is fast enough for high CO and H_2 levels to be established during the compression stroke of an operating engine. Furthermore, if it is assumed that the reaction rate is relatively fast, Reed and Lerner did not explain what effect carbureted air may have on any CO or H_2 generated in the combustion chamber prior to ignition.

To explore the validity of Reed and Lerner's mechanism, we investigated methanol decomposition experimentally by measuring the amount of CO and H_2 in the unburned charge of a single-cylinder engine operated at equivalence ratios (ϕ) equal to 0.82 (lean) and 1.2 (rich). Pure methanol was tested rather than a gasoline-methanol blend since the Reed and Lerner proposal does not depend on the presence of gasoline, and we expected the use of pure methanol to increase decomposition product levels.

A poppet valve (*3*) was used to extract gas samples from the combustion chamber prior to flame arrival at the sampling

Table 1. Combustion chamber CO and H_2 concentrations.

Fuel	ϕ	H_2 (% by volume)		CO (% by volume)	
		Observed	Corrected	Observed	Corrected
Following compression, prior to ignition					
Methanol	0.82	0.4	−0.1	0.0	0.0
Indolene	0.82	0.4	0.0	0.0	0.0
Methanol	1.2	0.6	0.0	0.4	0.0
Indolene	1.2	0.5	−0.1	0.5	0.1
In unburned charge, near end of combustion					
Methanol	0.82	0.4	0.2	0.2	0.1
Indolene	0.82	0.0	−0.1	0.1	0.1