$\dot{\eta}_T \simeq \dot{\eta}_R$ for long waves, the shear motion becomes $\dot{\eta}_{SI} \simeq \dot{\eta}_R(C_R - C_T)$. Depending on whether $C_T = C_R$, $C_T < C_R$ or $C_T > C_R$, the shear motion may vanish, be in phase, or in phase opposition with the motion of the RL. In the last case, maximum excitation of the inner hair cells and of the primary neurons ending on them should occur during the displacement of the BM toward scala tympani. Such phase reversals occurred systematically in Mongolian gerbils (*15, 16*).

We modeled the shear motion at the inner hair cells, through the use of both digital and analog simulation. In the latter, an electrical network was constructed for the TM on the basis of electromechanical analogies of the second kind ($V_R \rightarrow \dot{\eta}_R$, $Z_{electrical} \rightarrow Y_{mechanical}$) and connected to a network analog of the cochlea (*21*). The results obtained for one point along the cochlea as a function of log frequency are shown in Fig. 2 by means of oscilloscopic traces. The trace with the broad envelope corresponds to the amplitude of the BM, and that with the narrow envelope, to the amplitude of the shear motion. The maximum is sharpened toward both low and high frequencies, in qualitative agreement with the tuning curves obtained on mammalian cochlear nerve fibers. A direct quantitative comparison of a model tuning curve and an average neural tuning curve is shown elsewhere (*22*). In Fig. 2A the ratio of constants C_T/C_R was so chosen as to make the model shear motion practically disappear at low frequencies; in Fig. 2B the ratio was slightly increased to show the phase reversal at these frequencies. The reversal can be seen by comparing the oscillation phases of the two traces. The phase reversal is accompanied by a minimum in the model shear motion below the main maximum. The minimum may correspond to a notch sometimes observed in neural tuning curves below the characteristic frequency (*23*).

Only experiments can determine whether sharpening of cochlear frequency analysis involves the mechanism we have described. What our model results demonstrate is the availability of such a mechanism, given appropriate physical constants. The results are in agreement with the recordings of receptor potentials and transmembrane impedance changes in the inner hair cells (*5*). Furthermore, they are consistent with response phases observed in the cochlear nerve at low sound frequencies (*15, 16*) and with an earlier conclusion that these phases arise from an interaction of two components that nearly cancel each other (*4*). The linear mechanism described does not replicate the well-known nonlinear phenomena in the cochlea, however, especially the phenomenon of two-tone suppression (*24*). In preliminary experiments we have demonstrated that two-tone suppression is produced in our model when the model coupling between the organ of Corti and the TM is made to increase with the magnitude of the shear motion. Such an increase appears plausible in a mechanical system.

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Hippocampal Afterdischarges: Differential Spread of Activity Shown by the [^{14}C]Deoxyglucose Technique

Abstract. *Differential spread of afterdischarge activity initiated electrically in ventral and dorsal parts of the hippocampal formation was studied by the* [^{14}C]*deoxyglucose technique in rats. Afterdischarges initiated in either the ventral or dorsal hippocampal formation, without activation of the ventral subicular cortex, increased glucose utilization in the lateral septum. In contrast, afterdischarges initiated by direct activation of the ventral subicular cortex increased glucose utilization in extensive areas of the ipsilateral amygdala, claustrum, hypothalamus, preoptic region, and basal forebrain.*

The hippocampal formation (*1*) has been implicated in various functions including memory, spatial orientation, and the neuroendocrine control of specific hormones (*2*). It is also the structure most frequently showing pathology in patients with temporal lobe epilepsy (*3*). Related to this finding is its extremely low threshold to electrical stimulation for eliciting afterdischarges (AD's), paroxysmal bursts of intense activity involving the synchronous firing of many neurons.

MacLean's suggestion in 1949 (*4*) of functional differences between ventral and dorsal hippocampal formation has been supported by a growing body of anatomical (*5, 6*) and physiological (*7, 8*) evidence showing significant differences in the projections of ventral and dorsal parts of the hippocampal formation. Recently, a unit study in the awake primate demonstrated that while the dorsal hippocampus projects almost exclusively via the fornix system, the ventral hippocampus influences hypothalamic and basal forebrain nuclei primarily via nonfornix pathways (*8*).

It seemed appropriate to study these differential projections by using the [^{14}C]deoxyglucose (DG) technique, developed by Sokoloff and colleagues (*9, 10*), to metabolically map the spread of AD's electrically initiated in the ventral and dorsal hippocampal formation. Our results show markedly increased metabolic activity throughout the amygdala, hypothalamus, preoptic region, and basal forebrain associated with hippocampal AD's only when there is direct activation of the ventral subicular cortex (*1*). In contrast, hippocampal AD's initiated in either the ventral hippocampus or dorsal hippocampal formation resulted in a

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much less extensive pattern of increased DG uptake, confined primarily to the lateral septum.

Twenty-five male Sprague-Dawley albino rats had monopolar stimulating and recording electrodes stereotactically implanted under anesthesia in either the ventral or dorsal hippocampal formation. After a recovery period of at least 3 days, rats were transferred to individual Plexiglas holders and the threshold for eliciting an AD was determined. A bolus of DG (10 μCi per 100 g) was then injected into the tail veins of these unanesthetized animals, followed by 45 minutes of electrical stimulation (0.2 to 0.4 mA, 1-msec pulses, 16 per second) (*11*) except in controls, in which no stimulation was used. Electrical stimulation was periodically interrupted to detect AD activity. After the 45 minutes, animals were killed with an overdose of sodium pentobarbital and small electrolytic lesions were made at the electrode tip. The brains were then removed and processed for autoradiography as described by Sokoloff and colleagues (*9*). The developed autoradiographs were then examined visually and structures showing increased radioactivity were identified in cresyl violet–stained sections.

The most extensive pattern of increased glucose utilization was obtained when AD's were initiated in the ventral hippocampal formation by electrodes directly activating subicular cortex (five animals) (Fig. 1, A to D). Within the ventral hippocampal formation, markedly increased metabolic activity was found bilaterally throughout the hippocampus proper and dentate gyrus and ipsilaterally throughout the subicular cortex (Fig. 1A). Significant but less intense DG uptake was also seen bilaterally throughout the dorsal hippocampal formation (Fig. 1B).

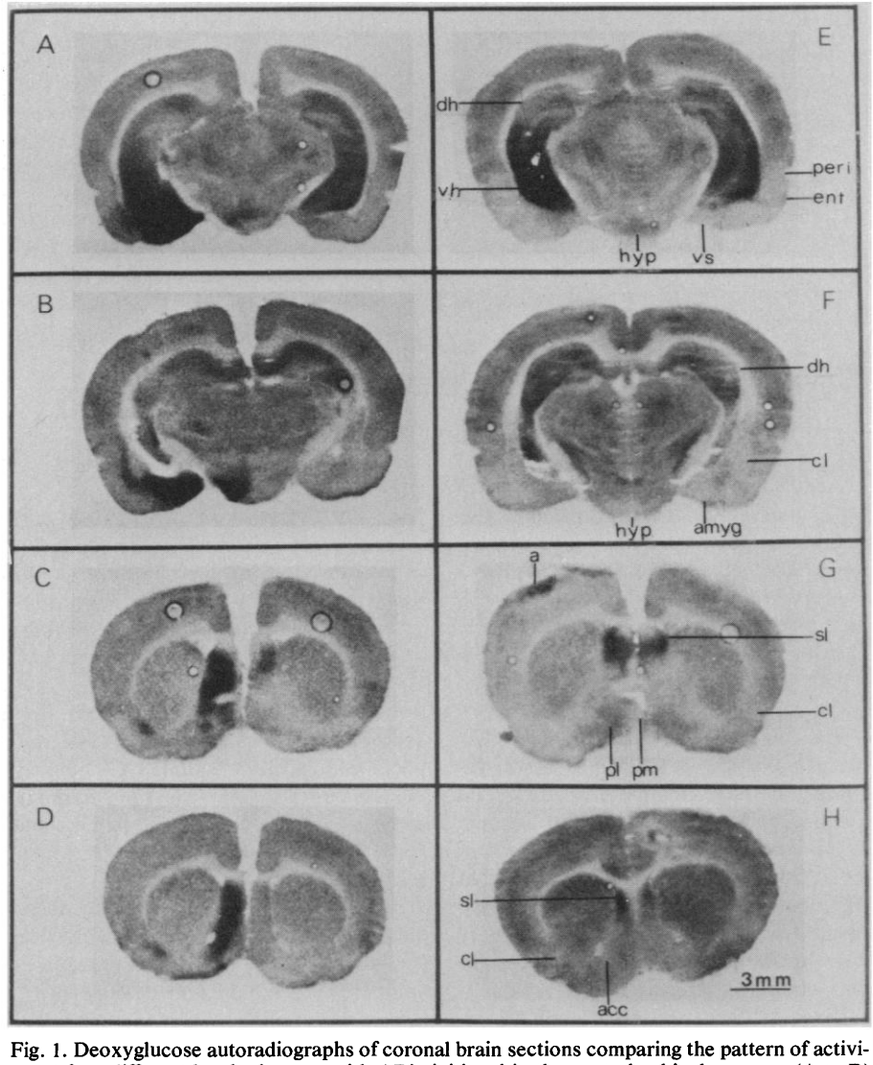

Fig. 1. Deoxyglucose autoradiographs of coronal brain sections comparing the pattern of activity, at four different levels, in a rat with AD's initiated in the ventral subicular cortex (A to D) and in a rat with AD's initiated in the ventral hippocampus (E to H). Note the bilateral increases in activity throughout the ventral hippocampus (*vh*) (A and E) and the dorsal hippocampus (*dh*) (B and F). Only direct activation of the ventral subicular cortex resulted in increased activity in the ventral subicular (*vs*) and entorhinal (*ent*) cortex, and the deep layers of the perirhinal (*peri*) cortex (A). Additional structures affected by ventral subicular activation were the ipsilateral amygdala (*amyg*) (B), claustrum (*cl*) (B to D), hypothalamus (*hyp*) (A and B), medial (*pm*) and lateral (*pl*) preoptic nuclei (C), nucleus accumbens (*acc*) (D), and the entire extent of the lateral septum (*sl*) (C and D). Outside the hippocampal formation, only the dorsal aspect of the lateral septum showed increased activity bilaterally in both groups of animals (C, D, G, and H). Note the lesion at the electrode tip in (E). The increased density at (*a*) is an artifact due to a fold in the cortex.

Outside the hippocampal formation glucose utilization was markedly increased ipsilaterally throughout the entorhinal cortex and deep layers of the perirhinal cortex (Fig. 1A). Similar increases were also found in the ipsilateral amygdala (Fig. 1B), specifically the cortical, central, medial, and basal nuclei, as well as the confluence zone, a region of transition between the cortical nucleus and the ventral subiculum. Increased glucose consumption was also found in the ipsilateral claustrum (Fig. 1, B to D).

In basal diencephalic structures activity increased markedly throughout the ipsilateral hypothalamus, preoptic region, and basal forebrain. In the hypothalamus (Fig. 1, A and B), structures showing intense increases included the anterior, ventromedial, dorsal, lateral, posterior, and premammillary nuclei. In the preoptic region (Fig. 1C) both the medial and lateral preoptic nuclei showed marked increases in activity. Intense DG uptake in the basal forebrain (Fig. 1, C and D) included the nucleus accumbens, nucleus of the diagonal band, nucleus of the lateral olfactory tract, bed nucleus of the stria terminalis, as well as the entire extent of the lateral septum.

When AD's were initiated in the dorsal hippocampal formation (four animals), increased glucose utilization in basal diencephalic structures was far less extensive. Within the hippocampal formation, the hippocampus proper, dentate gyrus, and dorsal subiculum showed marked increases in activity bilaterally with only variable increases in the ventral subicular cortex. Marked increases were also found bilaterally in perirhinal cortex. In the basal diencephalon increases were consistently found bilaterally only in the dorsal aspect of the lateral septum. Modest increases in DG uptake in the nucleus accumbens, basal nucleus of the amygdala, and entorhinal cortex were found only in animals showing augmented activity in ventral subicular cortex.

Figure 1, E through H, illustrates the

results from a third group (six animals) in which AD's were elicited in the ventral hippocampus proper without direct activation of the ventral subicular cortex. Markedly increased activity was found bilaterally throughout the ventral hippocampus (Fig. 1E) and, to a lesser extent, the dorsal hippocampal formation (Fig. 1F). Variable increases found in the ventral subicular cortex were associated with increased DG uptake in the nucleus accumbens, entorhinal cortex, and basal, medial, and cortical amygdaloid nuclei, as well as the confluence zone. The pattern of increased metabolism seen in the lateral septum was similar to that found in the dorsal hippocampal group but showed increased activity extending more ventrally in the ipsilateral lateral septum (Fig. 1, G and H).

When the ventral hippocampus proper was stimulated below the threshold for eliciting an AD (two animals) (*11*), a more localized pattern of increased activity was found in the ipsilateral hippocampal formation, limited to parts of the ventral hippocampus proper and posterior subiculum. Outside the hippocampal formation, increased activity was seen only in the dorsal margin of the lateral septum. The more frequently stimulated animal (*11*) showed a similar although lighter pattern of increased activity contralaterally in homologous structures.

Control rats implanted with electrodes (eight animals) showed increased activity only immediately adjacent to the electrode shaft.

This study demonstrates that the site of AD initiation within the hippocampal formation determines the pattern of increased activity seen in the temporal lobe and basal diencephalon. The close correlation between the propagation of AD's initiated in the dorsal and ventral hippocampus, shown by the DG technique, and known hippocampal projections (*4*) supports the concept that hippocampal AD's spread along the same efferent pathways used by less intense physiological activity.

Of particular interest is the finding of a far more extensive ventral subicular influence on hypothalamic structures than would be expected from the findings of axonal transport studies which show ventral subicular projections via the fornix confined primarily to the ventromedial region and mammillary nuclei of the hypothalamus (*5*, *6*). This suggests that some of the increased activity seen in the hypothalamus might arise from other projections.

It has been shown in our laboratory that the ventral hippocampal formation influences the hypothalamus primarily via nonfornix pathways (*8*). One possibility suggested by our findings is that the ventral subicular cortex influences the hypothalamus via the amygdala. The amygdala has been found by Krettek and Price (*12*) to project to anterior, lateral, and ventral premammillary regions of the hypothalamus, structures all showing increased metabolic activity. In the primate we found a high percentage of units in the basomedial nucleus of the amygdala responding with short latencies to ventral hippocampal formation stimulation (*13*). In addition, a direct projection from the ventral subiculum to the basomedial nucleus of the amygdala was demonstrated by Rosene and Van Hoesen (*6*). Increased activity in the claustrum associated with ventral subicular AD's may point to an as yet undescribed projection, either via the amygdala or perhaps directly from the ventral subicular cortex.

The DG technique has been shown to be highly effective in mapping the differential spread of temporal lobe AD activity initiated in different parts of the hippocampal formation. This system could be used to determine new hippocampal projections, such as the nonfornix pathway or pathways to the hypothalamus (*8*). It could also be employed to study kindling as well as the actions of drugs used in the treatment of epilepsy. These models might provide additional insight into the nature and treatment of this disease.

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References and Notes

1. As used in this report, the term hippocampal formation includes the dentate gyrus, the hippocampus proper (fields CA1 to CA4 of Ammon's horn), and the subicular cortex (prosubiculum, subiculum, presubiculum, and parasubiculum). Hippocampus alone refers to both the hippocampus proper and the dentate gyrus.
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Brain Grafts Reduce Motor Abnormalities Produced by Destruction of Nigrostriatal Dopamine System

Abstract. *In order to determine if brain tissue grafts can provide functional input to recipient central nervous system tissue, fetal rat dopamine-containing neurons were implanted adjacent to the caudate nucleus of adult recipients whose endogenous dopaminergic input had been destroyed. The grafts showed good survival and axonal outgrowth. Motor abnormalities, which had been induced by the destruction of the endogenous dopaminergic input to the caudate, were significantly reduced after grafting of the fetal brain tissue. These data suggest that such implants may be potentially useful in reversing deficits after circumscribed destruction of brain tissue.*

Many neurological disorders are associated with degeneration of discrete populations of neuronal elements. Parkinson's disease, for example, manifested primarily by abnormalities of movement and posture (*1*), is characterized by neuronal loss and gliosis in the dopamine-containing zona compacta of the substantia nigra (SN) (*2*). The syndrome is also characterized by decreased concentrations of dopamine (DA) and its principal metabolite, homovanillic acid

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