lum parallels the expansion of the cerebral cortex, and that even more widespread hippocampal efferent connections with the cerebral cortex may exist.

In the rhesus monkey the cortical areas that receive direct hippocampal efferents in turn send efferents to nearby association areas which appear to be either "polysensory" or many synapses removed from primary sensory cortex. Thus the medial and orbital frontal cortices send efferents to dorsolateral prefrontal association cortex. Retrosplenial cortex sends efferents to the inferior parietal lobule, recently shown to be generalized association cortex (*17*). Both the prefrontal and parietal association areas in the monkey may correspond to similar regions in the human where damage produces severe deficits in attention (*17*). Similarly, the perirhinal cortex, the caudal parahippocampal area, and the amygdala send efferents to large parts of the frontal and temporal lobe association cortex, where experimental lesions in monkeys produce deficits in complex discrimination learning and social behavior. If the subiculum is, as we suggest, a final common pathway for hippocampal efferents to the cerebral cortex of the monkey, then it is quite possible that in both the rhesus monkey and man, the hippocampus is only one synapse removed from specific areas of the cerebral cortex and only two synapses removed from important areas of association cortex.

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## Premotor Cortical Ablations in Monkeys: Contralateral Changes in Visually Guided Reaching Behavior

Abstract. *In rhesus monkeys (*Macaca mulatta*), ablation of the premotor and supplementary motor areas and the adjoining rostral half of the precentral gyrus impairs the capacity of the contralateral arm to reach around a transparent obstacle to a visible food reward, and results in a tendency of this arm to reach straight to where the food is visible. This may reflect a disinhibition of brainstem pathways which steer the arm and hand straight to a visual target.*

In a previous study in rhesus monkeys (*1*), a unilateral posterior parietal leucotomy combined with a commissurotomy leaving the optic chiasm intact produced a defect in visually guided relatively independent movements of the contralateral hand and fingers (*1*). In addition, when food was held outside of the cage in front of these animals, they quickly learned to reach with the intact arm—that is, contralateral to the intact hemisphere, through a hole low in the cage front, while with the affected arm contralateral to the leucotomy they generally tried to reach straight for the food by squeezing the hand and arm through the spaces between the cage bars (*1*). Since the intrahemispheric occipital and posterior parietal fibers to the frontal lobe transected by the leucotomy terminate mainly in the arcuate gyrus, the premotor and supplementary motor areas, and the adjoining rostral part of the precentral gyrus (*2*), it was expected that the same defects as caused by the leucotomy would be produced by an ablation of these frontal areas. The present report demonstrates that in keeping with this expectation, ablation of these frontal areas impairs the capacity of the animals to reach around an obstacle with the contralateral arm in order to obtain a visible food reward, and results in a tendency of this arm to reach straight to where the food is visible.

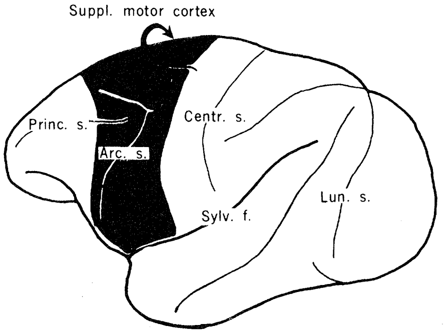

Fig. 1. Extent of the "premotor" cortical ablation, based on sketches made during surgery. Abbrevations: *Suppl. motor cortex*, supplementary motor cortex; *Princ. s.*, principal sulcus; *Arc. s.*, arcuate sulcus; *Centr. s.*, central sulcus; *Sylv. f.*, sylvian fissure; and *Lun. s.*, lunate sulcus.

The visually guided reaching behavior with the arm, as well as the visually guided relatively independent movements of the hand and fingers (*3*), were studied in three rhesus monkeys (*Macaca mulatta*). In these monkeys a unilateral "premotor" ablation was made involving the arcuate gyrus, the premotor and supplementary motor areas, and the adjoining rostral part of the precentral gyrus (Fig. 1); more than 6 months later a commissurotomy was performed without sectioning the optic chiasm.

Two to three weeks after the "premotor" ablation, the reaching behavior was tested as follows. The cage front was replaced by a transparent plastic plate with a hole in the middle. From trial to trial slices of apple were stuck on the outside of this plate in different places around the hole. After the affected arm (that is, the one contralateral to the ablation) was taped to the animal's body, the animal quickly learned to retrieve the apple with its intact arm and hand by reaching through the hole. When the intact arm was restrained, the animal behaved differently and in the majority of the trials did not reach through the hole with the affected arm but brought the hand straight to the place where the apple was visible through the plastic. Only after considerable practice did the animal reach through the hole with this arm and retrieve the apple, and then usually only when the apple was stuck to the plastic plate on the side of the restrained arm, in which case the animal could extend its arm straight across the midline through the hole to the apple.

To demonstrate that the behavior did not result from the animal's inability to execute the required movements of the affected arm, we used a plastic floor plate (Fig. 2) instead of a front plate. This allowed the animal to approach the hole from any desired direction and thus freed it from the necessity to perform movements which may have been difficult to make. In this test situation the apple was kept in the same place, that is, in the center on the undersurface of the floor plate, while the position of the hole was changed from trial to trial. This was achieved by using two plastic plates. The upper one formed the floor of the cage and carried a circle of eight holes, while the second one carried one black-rimmed hole and was attached to the undersurface of the first one such that it could be rotated to match its black-rimmed hole with one of the holes in the floor plate.

As part of the study of the visual guidance of relatively independent hand and finger movements, the animals with the "premotor" ablations had in the meantime undergone a commissurotomy without sectioning of the optic chiasm. As a consequence, the animals were tested on the floor plate only after the commissurotomy. On this plate the animals showed the same difference in their control of the two arms as they did on the front plate. The performance of the animals was scored from 16 to 23 months after the ablations (that is, from 6 to 12 months after the commissurotomy) in two consecutive sessions of 20 trials (ten trials for each arm). In all three animals, in at least nine out of the ten trials, the affected arm brought the hand directly to the place where the apple was visible through the plastic, whereas in at least eight out of the ten trials the intact arm guided the hand directly through the hole. The abnormal reaching behavior appeared to apply only to the affected arm and did not seem to be a function of the position of the black-rimmed hole in the animal's visual field because the animal's intact arm virtually always guided the hand directly through the hole, no matter where the hole was located in relation to the animal.

The animal's behavior seemed to reflect an overriding tendency of the affected arm to guide the hand straight to where the apple was visible. When the apple was presented within the black-rimmed hole, the monkey with its affected arm and hand reached directly into the hole to retrieve the apple. Moreover, when the apple was stuck to the underside of the plastic, the animal sometimes guided the affected arm and hand toward the hole but then frequently brought the hand back to the place where the apple was visible through the plastic.

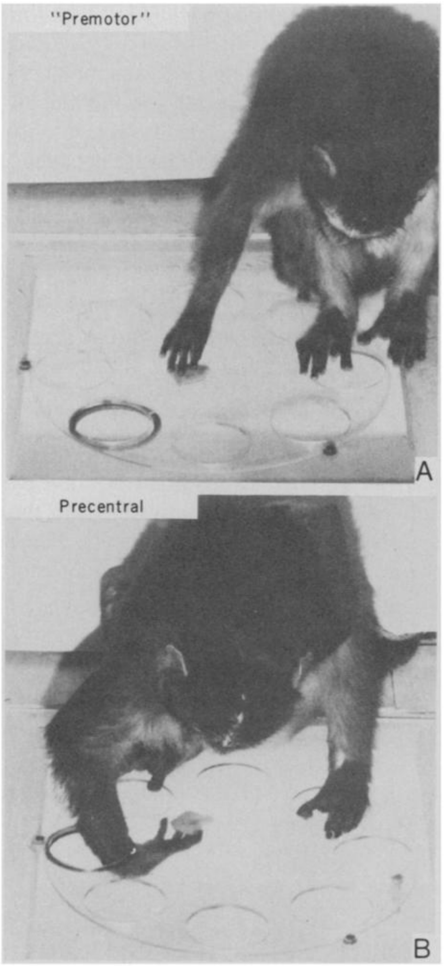

Fig. 2. (A) A monkey with a left "premotor" ablation reaching with the contralateral arm straight to the apple visible through the plastic floor plate of the test cage. (B) A monkey with a large ablation of the left precentral hand area reaching for the apple with the contralateral arm through the black-rimmed hole.

The floor plate test may not only test the animals' ability to reach for the apple but also their general ability to orient toward the apple or the black-rimmed hole. To test more specifically the animals' reaching behavior we used a small plastic plate (17 cm in diameter) with a black-rimmed hole (4.5 cm in diameter) located close to the edge of the plate. When a slice of apple was stuck in the center to the undersurface of the small plate, that is, only 4 cm away from the hole, all three animals used the affected arm in the same way as on the floor plate. The performance of the animals was scored in two sessions, each consisting of five trials for each arm, 19 to 21 months after the ablation (that is, 9 to 12 months after commissurotomy). In all animals in at least eight out of the ten trials the affected arm guided the hand directly to the place where the apple was visible; while in the same number of trials the intact arm guided the hand directly to the hole.

The abnormal reaching behavior apparently did not result from damage to the caudal part of the precentral gyrus, because another animal, in which a large lesion of the precentral hand area completely abolished the capacity to execute relatively independent finger movements of the contralateral hand, did not show abnormal reaching behavior with its affected arm either on the floor plate or on the small plate. From 19 to 22 months after the precentral lesion was made, this animal was scored in two consecutive sessions of 20 trials, ten for each hand. In nine out of ten trials the animal brought either hand directly through the hole (Fig. 2). However, when a "premotor" lesion was made on the other side, without a commissurotomy, the animal showed the abnormal reaching behavior with the arm contralateral to this ablation both on the floor plate and the small plate. This difference in the animal's use of the two arms was especially striking when neither arm was restrained and the animal reached with both hands simultaneously for the food on the small plate, placing the hand contralateral to the "premotor" ablation on the center of the plastic where the apple was visible, while bringing the hand contralateral to the precentral lesion through the hole to retrieve somewhat clumsily the apple from the undersurface of the plastic.

The abnormal reaching behavior is probably produced by a complete "premotor" ablation, since in two other animals in which the ablation either spared the arcuate gyrus or was restricted to it, and in which commissurotomy was not performed, the abnormal behavior, even when tested soon after the operation, was either mild or did not occur.

The monkeys' behavior with the affected arm may represent the visual counterpart of the somatosensory guided grasping and groping behavior (*4*) that can occur in monkey and man with contralateral premotor lesions. The behavior in some respects resembles the defect in delayed alternation response in which animals show an overriding tendency to reach to where food had previously been obtained. It also resembles Stepién's (*5*) "magnet reaction," in which animals presented with a conditioned stimulus at one place and a reward at another tend to go and to remain at the place where the conditioned stimulus is delivered. However, these behavioral defects are the result of bilateral lesions located more rostrally than our premotor ablation (*5, 6*).

The behavior of our animals might be due to the fact that the ablation, which presumably interferes with the cortical steering of axial and proximal movements (*7*), also results in a disinhibition of a subcortical region that directs the contralateral arm and hand straight to a visual target, in the same way as the superior colliculus, for example, may direct the gaze (*8*).

This postulated subcortical region probably contributes fibers to the ventromedial group of descending brainstem pathways (*9*), since accurate reaching movements of the arm to a visible object can be readily elicited in bilaterally pyramidotomized animals (*9*), but are largely abolished when in these animals the ventromedial brainstem pathways (*9*) are also transected. The cells of origin of these brainstem pathways receive many cortical connections directly from the ablated premotor areas and the rostral part of the precentral gyrus (*10*), as well as indirectly by way of the striatum and the substantia nigra (*11*). Elimination of some of these connections may be responsible for the disinhibition of the postulated subcortical region steering the arm directly to a visual target.

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## How Many Anticodons?

Abstract. *Much new information on codon composition is becoming available from the sequencing of molecules of DNA and RNA. The "wobble rules" for codon-anticodon pairing are applicable to this information. These rules provide for only 54 anticodons to pair with 61 codons, because the base A is not found in the first position of anticodons.*

Recent advances in molecular biology have enabled long sequences of nucleotides to be identified in DNA and RNA molecules (*1*). This new information enlarges the scope of molecular evolution, which formerly depended mainly on comparisons of the amino acid sequences of proteins. Such sequences reveal very little about the third bases of codons, but, with the new information on nucleotide sequences, these are now identified. As a result, Sanger *et al.* (*2*) found that there is a disproportionately high use of T (U) (*3*) in the third base position of the codons of $\phi$X174. Such information draws attention to the "wobble rules" of pairing (*4*) between the first bases of anticodons and the third bases of codons. Some amino acids have only pyrimidine-terminated codons. The only known anticodons for such amino acids start with G, for example, GAA for phenylalanine. The wobble rules do not exclude the possibility of AAA; the absence of A from the first position of all known anticodons is thought to result from the action of anticodon deaminase (*5*). This changes adenine to hypoxanthine, so that anticodons starting with I (inosine) occur in the case of amino acids with more than two codons, such as valine. The absence of an IAA anticodon for phenylalanine is explainable by concluding that this anticodon is eliminated by lethality, for it could "mis-pair" with UUA (leucine), and similarly pari passu for the other amino acids whose codons terminate only with a pyrimidine. It is therefore anticodon deaminase rather than [as stated elsewhere (*6*)] the wobble rules that explain "why there are not 61 transfer RNA's (tRNA's)." Amino acids with two purine-terminated codons can have two anticodons, such as lysine with anticodons UUU and CUU. However, in the case of, for example, valine, with four codons, there are three known anticodons (IAC, GAC, and UAC) and there is no reason why CAC may not exist. The wobble rules provide for redundancy in coding rather than for postulating a number of anticodons less than 61, but the redundancy does not extend to amino acids whose codons terminate only with a pyrimidine. The total number

Table 1. Amino acid anticodons, possible and identified (italic).

| | | | |
|---|---|---|---|
| *GAA* | Phe | *IGC* | Ala |
| *UAA* | Leu | GGC | Ala |
| *CAA* | Leu | *UGC* | Ala |
| IAG | Leu | CGC | Ala |
| *GAG* | Leu | *GUA* | Tyr |
| *UAG* | Leu | *GUG* | His |
| *CAG* | Leu | *UUG* | Gln |
| *IAU* | Ile | *CUG* | Gln |
| *GAU* | Ile | *GUU* | Asn |
| UAU | Ile | *UUU* | Lys |
| *CAU* | Met | *CUU* | Lys |
| *IAC* | Val | *GUC* | Asp |
| *GAC* | Val | *UUC* | Glu |
| *UAC* | Val | CUC | Glu |
| CAC | Val | *GCA* | Cys |
| *IGA* | Ser | *CCA* | Trp |
| GGA | Ser | *ICG* | Arg |
| *UGA* | Ser | GCG | Arg |
| *CGA* | Ser | UCG | Arg |
| IGG | Pro | CCG | Arg |
| GGG | Pro | *GCU* | Ser |
| *UGG* | Pro | *UCU* | Arg |
| CGG | Pro | GCU | Arg |
| *ICU* | Thr | ICC | Gly |
| *GGU* | Thr | *GCC* | Gly |
| UGU | Thr | *UCC* | Gly |
| CGU | Thr | *CCC* | Gly |