Neuropsychologia, 1969, Vol. 7, pp. 259 to 266. Pergamon Press. Printed in England

THE PRIMATE FRONTAL CORTEX*

KARL H. PRIBRAM
Stanford University, Palo Alto, California, U.S.A.

(*Received* 18 *November* 1968)

Abstract—An experimentally based model of the functions of the primate frontal cortex is presented. This model concerns the interactions which occur among neural inhibitory processes. At the neuronal level self-inhibition of the Renshaw type is assumed involved as the substrate of internal inhibition. At the psychophysiological level self-inhibition leads to habituation which has been shown to be the construction of a neuronal model of the organism's experience. At the systems-neurophysiological level the construction of this neuronal model is found to be controlled by efferent brain processes which can bias the input processing mechanism in favor of either external or internal inhibition. The frontal cortex shifts the mechanism toward internal inhibition, i.e. habituation. At the neurobehavioral level such a shift accomplishes the suppression of interference and thus serves to give temporal organization to the psychological process much as linguistic parsing gives meaning to language.

DURING the past few years a great surge of inquiry has focussed on neural and behavioral inhibitory processes. I have for some time declared loudly against the utter confusion that so often exists when the results of these inquiries are loosely combined in a neurobehavioral analysis that makes apparent sense but is so superficial that a more careful reading shows the banality of the effort. I will now turn about and do just what I have been declaring against. My reason is simple. The recent surge of endeavour has brought the possibility of talking hard sense with regard to relationship between behavioral and neural inhibition. Given the possibility an attempted first step must be ventured even if it falls short of completely satisfying one's more rigorous standards. Else how can the next step be generated?

My focus for bringing together behavioral and neural inhibitory processes will be the primate frontal cortex. I originally prepared this manuscript for inclusion in a Festschrift dedicated to Peter Anokhin published in the Soviet Union but thus far not available to Western readers. It is included in this symposium in slightly modified form because of its appropriateness in that it ties together and places in perspective several of the other presentations.

As with so many neurophysiological analyses of behavior, a good starting point is the orienting reaction and its habituation. A series of experiments has demonstrated beyond doubt than an intact anterior frontal cortex of man and monkey is important to the proper functioning of the orienting reaction. LURIA and HOMSKAYA [1], LURIA *et al.* [2], KIMBLE *et al.* [3] and GRUENINGER *et al.* [4] have reported that frontal injury radically impairs the galvanic skin response which accompanies the orienting reaction.

*The work reported here was supported by NIMH Grant MH 12970 and NIMH Research Career Award MH 15214.

Further analyses of the orienting reaction and its habituation [5–7] have made it plausible to suggest that orienting is made up of at least two components: one is characterized by reactions such as ear flicks and some aspects of the EEG; the other, by the GSR and changes in heart rate, respiration, etc. These two components are differentially affected by brain lesions. Habituation to irregular occurrences and complex problem solving appears to depend to a large extent on the second of the components, the process signalled by the GSR and other autonomic nervous system indicators. Studies on man [8] have shown that such GSR activity occurs during the pre-solution phase of discrimination, comes to a peak during the rapid "one element learning" phase (indicated by the sudden spurt of the slope of the learning curve), and subsides once the discrimination has been learnt. For convenience, this component of orienting has been labelled the "registration" process. In the absence of such "registration," orienting consists of "alerting" to the presence of the stimulus event, and most likely also signals an active processing or sampling of the complexities of that event. Thus, in the absence of the registration mechanism, only those events which recur monotonously can become "memorized." But more of this after the model has been spelled out fully.

The next question that arises is how the frontal cortex ordinarily participates in the registration process. Many of the indicators of registration are visceral in origin and the work of Anokhin and his collaborators as well as many others has amply demonstrated the physiological connection between some parts of the frontal cortex and visceral function. Yet, the primary role of the frontal lobe in determining the psychological process can hardly be visceral as is indicated by the fact that in subhuman primates high order problem solving is drastically disturbed [9, 10] by frontal ablations and that in man a variety of intellectual defects can be recorded after frontal injury [1, 2, 11].

How are we to reconcile these discrepancies? A careful examination of the implications of SOKOLOV's [12] work on the meaning of the orienting reaction suggests an answer to this problem. SOKOLOV demonstrated that habituation of the orienting reaction is not due to a generalized increase in the threshold of the central nervous system to stimulation. Rather, by showing that dishabituation occurs whenever *any* dimension of the stimulus configuration is altered, he argued that a precise "neuronal model" of the organism's environment is built up in the central nervous system during habituation.

But one of the most consistent and constant "environments" to which the brain is subject is, of course, the input from the organism's own body including the viscera. Thus there must be built up in the brain, through a process identical or very similar to habituation, a neuronal model of the organism's bodily functions. These show, of course, considerable regularity in recurrence and so the model based upon them should be more stable than the neuronal model of the ever-shifting external environment.

The suggestion that arises from these considerations is that the process of "registration" may depend on the maintenance of such a stable base. Any novel event, in order to become "registered" must find some organization into which it can register—otherwise the event will be only fleetingly experienced and not integrated into the life of the organism. Paradoxically, in the absence of such a stable organizational base, flexibility of behavior is precluded: behavior would become either stimulus bound or perseverative, depending on the complexity of the stimulus [9]. There is, of course, ample behavioral evidence that after frontal cortex ablation both man and monkey show these very tendencies toward inflexibility [9].

A stable basic organization is one requirement for registration; another is a mechanism for the control of input. Without such control, external events would continuously preempt the functions of the brain– stimulus binding in the extreme would result.

Here again evidence is available that the frontal cortex can exert an influence on input processing. In a series of experiments SPINELLI and myself [13] demonstrated that recovery cycles in the visual system, and even visual receptive field organization could be altered by electrical stimulation of the frontal cortex. Effects were obtained as far peripherally as the optic tract (Fig. 1).

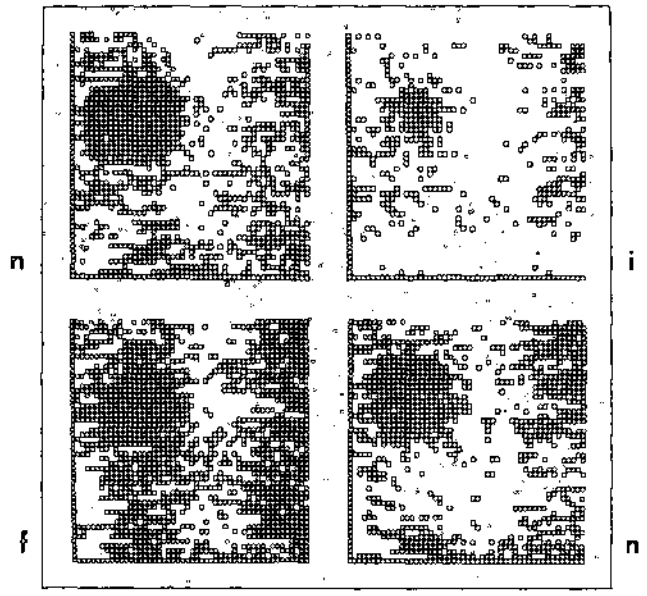


FIG. 1. Receptive field maps from a lateral geniculate unit. n, top left: control; i: mapped while inferotemporal cortex was being stimulated; f: mapped during frontal cortex stimulation; n, bottom right: final control. A third control was taken between the i and the f maps and was not included because it was not significantly different from the first and the last. Note that inferotemporal stimulation decreases the size of the "on" center; frontal cortex stimulation, while not really changing the circular part of the receptive field, brings out another region below it. The level of activity shown is 3 standard deviations above the normal background for this unit.

Further, we were able to suggest that the effect on recovery cycles (which was to speed recovery) could be interpreted to mean that information processing in the visual system is slowed due to the enhanced redundancy produced in the organization of the visual channel. Slowing of information processing is tantamount to slowing the reaction to novelty, thus spacing the occasions for orienting. This spacing is, of course, necessary if sufficient time for "registration" is to elapse before the "Neuronal Model" is again disequilibrated by another novel occurrence.

These and similar experiments on orienting and habituation and on input control led to the development of a model of the orienting reaction and its habituation. The most likely site of efferent control in the input systems is the inhibitory process. Two types of inhibition are clearly distinguishable: inhibition of its neighbors by the activity of a neuron; and self inhibition produced by the neuron's own activity. Inhibition of neighbors,

or lateral inhibition, is the basis of the phenomenon of enhanced contrast in the visual system (e.g. the formation of Mach bands) and shows most of the characteristics of external inhibition defined by Pavlov. Thus there is good reason to suppose that the specificities of the orienting process, so dependent on contrast enhancement, are a function of external inhibition, i.e. the inhibition of the neighbors of a stimulated neuron.

There is equally good reason to identify self-inhibition (e.g. of the Renshaw type) with Pavlov's internal inhibitory process since the properties described are so similar. Again the suggestion may be ventured that the process of habituation is a primordial manifestation of the mechanism of internal, i.e. self-inhibition.

One other inference can be drawn from these juxtapositions: external and internal inhibition are opposing processes. An active cell is actively inhibiting its neighbors; as self-inhibition begins to reduce the cell's activity, so also the inhibition of its neighbors is diminished. The mechanisms of lateral and self-inhibition are therefore bucked against one another in a negative feedback couplet (Fig. 2).

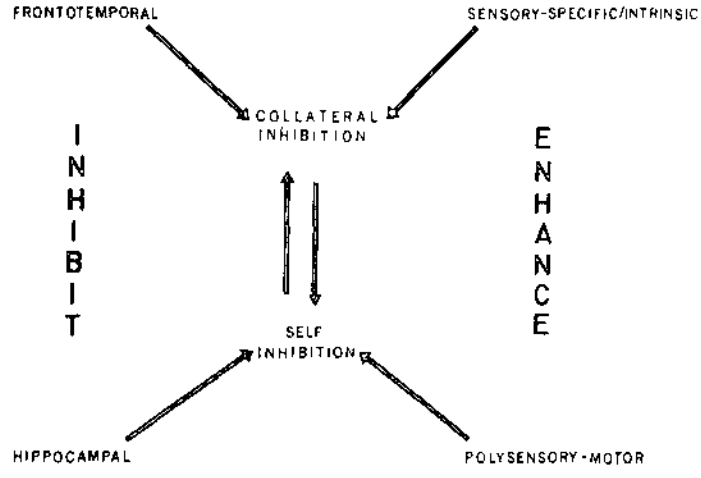
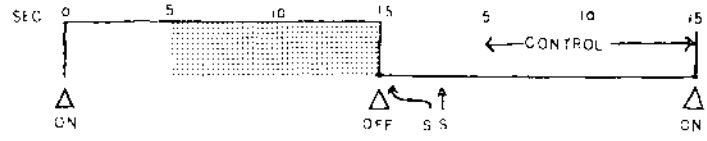


FIG. 2. Diagram of the model of cortical control over afferent inhibitory processes.

Our proposal was that efferent control over input processing occurs by changing the bias on this couplet thus changing the relative dominance of lateral vs. self-inhibition. At the same time, of course, the relationship between orienting and habituation is altered. The absence of the "registration" components of orienting after frontal lesions is thus interpreted as indicating a shift toward external inhibition in the input processing mechanisms: contrast is enhanced, novelty is not assimilated (see for instance the behavioral evidence in [14]) and the organism is stimulus bound. This interpretation is, of course, in harmony with the neurophysiological evidence which resulted in the model, the shortening of the recovery cycle (a shift toward internal inhibition) following frontal *stimulation*. The interpretation receives added support from other experiments which have demonstrated a powerful inhibitory system to originate from frontal cortex [15, 16].

To return now to the proposal that the frontal cortex is crucially involved in Anokhin's "acceptor of the outcomes of action." The outcomes of action are in behavioral psychology called reinforcers [17]. The process of reinforcement, whether initiated by reinforcers or by unconditional stimuli in the classical Pavlovian situation demands the functioning of some sort of temporal mechanism. A recently completed study by BAGSHAW [6] in my

laboratory has shown that the same lesion which interferes with the "registration" as defined in the orienting situation, also interferes with the classical conditioning process. Further, BAGSHAW demonstrated that the failure is due to the inability of the lesioned subjects to make progressively more anticipatory reactions to the unconditional stimulus (Fig. 3). It is as if the normal animals began some sort of "rehearsal" prior to the onset of the unconditional cue and that this "rehearsal" began sooner and sooner until it coincided and even considerably anticipated the onset of the conditional stimulus. Thus the temporal extension of the reaction to stimulation is critically involved in the orienting situation the extension follows, in the conditioning situation the extension precedes, the stimulus. Registration and reinforcement both depend on an adequate temporal extension of the effects of stimulation (see also [8]). This extension is conceived to be made possible, as has been detailed above, by the mechanism of internal, i.e. neuronal self-inhibition.



TRIALS	GRP	5-10 SEC ON	10-15 SEC ON	5-10 SEC OFF	10-15 SEC OFF
FIRST 40	NORM	3.7	7.0**	3.9	7.0
	AMX	3.7	5.3	3.9	5.3
SECOND 40	NORM	5.7**	9.8*	6.2	4.5
	AMX	2.7	4.3	2.5	4.3
ALL 80	NORM	9.3	14.6*	9.3	7.0
	AMX	6.6	8.2	7.3	5.3

* = $p < .05$

** = $p < .05$

MEAN NO. GSRS IN PERIODS PRECEDING SHOCK

(ANTICIPATORY RESPONSES)

FIG. 3. Mean number of GSRs occurring in 10 sec period of light on just preceding light offset in the first and second 40 trials.

There remains a crucial question. Is the temporal extension provided by the mechanism of internal inhibition a general, overall lengthening or is temporal organization imposed by the process? Neurophysiological evidence has as yet little to say on this topic. SOKOLOV's psychophysiological evidence on the high specificity of habituation suggests, however, that there is indeed a temporally organized process involved.

Neurobehavioral evidence supports this view. I have just completed [19] an experiment which demonstrates this point beyond reasonable doubt. The experiment took origin in the classical paradigm which showed that the anterior frontal cortex is involved in the short-term memory mechanism: the delayed alternation task. In this, the monkey is asked on each trial to find a peanut hidden alternately in the right, then the left of two identical cups. Trials are separated by the interposition of an opaque screen between the

subject and the cups. Monkeys with frontal ablations routinely fail this task [20] and this was found to be the case in the present experiment. Now, however, an additional manipulation was performed. Between each pair of R L presentations a 15 sec delay was inserted so that the task now given looked like this: R–L - - - - R–L - - - - R–L - - - - R L. Almost immediately after this "parsing" was done, the monkeys without frontal cortex solved the problem.

This result makes it unlikely that some sort of memory decay is hastened by the frontal lesion (Fig. 4) since the monkeys were able to perform excellently despite the 15-sec delay separating the trial pair. A 15-sec delay does not improve delayed alternation when placed between each trial, thus it is likely that the temporal organization produced by making trial pairs is critical. When this organization comes from the environment, the anterior frontal cortex appears unnecessary; in the absence of such external structure the frontal lobes become important (see also [21, 22]).

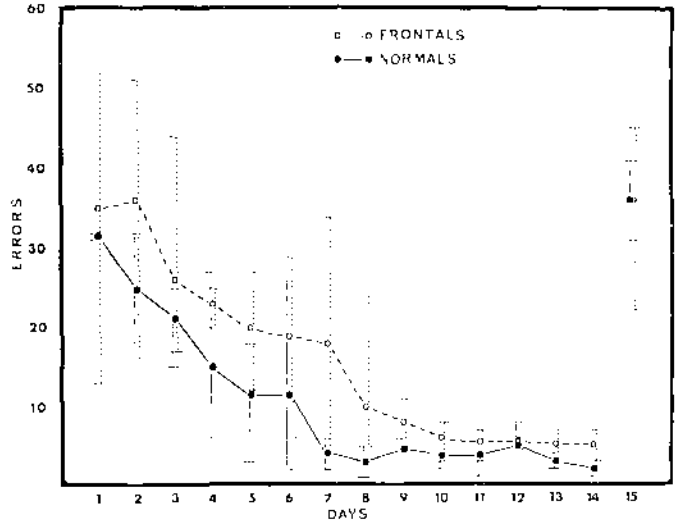


FIG. 4. Graph of the average number of errors made by the monkeys with ablations of the frontal cortex and their controls. Bars indicate *actual* range of errors made. Day 15 records the number of errors made on return to the classical 5 sec alternation task.

Thus the internal inhibitory process can be seen to be the basis for the organization of the temporal structure of behavior—the programs or Plans that regulate the psychological process. The nature of this sort of regulation is perhaps best illustrated by an example of Warren McCulloch's:

INMUDEELSARE
INCLAYNONEARE
INPINETARIS
INOAKNONEIS

The matrix of letters makes no sense at all until properly parsed, divided into words and sentences:

IN MUD EELS ARE
IN CLAY NONE ARE
IN PINE TAR IS
IN OAK NONE IS

This illustration brings to mind LURIA's patients with frontal lesions who are unable properly to parse their behavior according to the verbal instructions given them [1]. There is, of course, a lack of temporal correspondence between the verbal and behavioral code; there is ample evidence that the grammar of behavior and the grammar of language are different. It is likely, in view of the alternation experiment performed on monkeys, that the patients with frontal lesions cannot effect a transfer from one (the verbal) code to the other (the behavioral). This explanation is supported by other evidence that these same patients experience difficulty even when two different behavioral codes are involved [2].

In conclusion I shall summarize the model presented here. At the neuronal level the process is presumed to be based on self-inhibition of the Renshaw type or some similar negative feedback mechanism. This mechanism is purported to be the substrate of internal inhibition as defined by Pavlov. At the psychophysiological level self-inhibition leads to habituation which has been shown to be the construction of a neuronal model of the organism's experience. At the systems-neurophysiological level the construction of this neuronal model is found to be controlled by efferent brain processes which can bias the input processing mechanism in favor of either external or internal inhibition. The frontal cortex shifts the mechanism toward internal inhibition, i.e. habituation. At the neurobehavioral level such a shift accomplishes the suppression of interference and thus the temporal extension of the effect of repetitious or biologically significant stimulus configurations. This temporal extension is both pro- and retroactive, i.e. helps to register the stimulus configuration and allows the organism to rehearse stimulus consequences prior to their recurrence. Finally, the temporal extension is not a uniform or general one. Rather, it is programmed and serves to give temporal organization to the psychological process much as linguistic parsing gives meaning to language.

In short, the frontal cortex participates, according to this model, in providing a set of neural programs, programs which structure experience and provide a grammar for behavior.

REFERENCES

1. LURIA, A. R. and HOMSKAYA, E. D. Disturbance in the regulation role of speech with frontal lobe lesions. In *The Frontal Granular Cortex and Behavior*, J. M. WARREN and K. AKERT (Editors), pp. 353–371. McGraw-Hill, New York, 1964.
2. LURIA, A. R., PRIBRAM, K. H. and HOMSKAYA, E. D. An experimental analysis of the behavioral disturbance produced by a left frontal arachnoidal endothelioma (meningioma). *Neuropsychologia* **2**, 257–280, 1964.
3. KIMBLE, D. P., BAGSHAW, M. H. and PRIBRAM, K. H. The GSR of monkeys during orienting and habituation after selective partial ablations of the cingulate and frontal cortex. *Neuropsychologia* **3**, 121–128, 1965.
4. GREUNINGER, W., KIMBLE, D. P., GREUNINGER, J. and LEVINE, S. GSR and corticosteroid response in monkeys with frontal ablations. *Neuropsychologia* **3**, 205–216, 1965.
5. BAGSHAW, M. H. and BENZIES, S. Multiple measures of the orienting reaction and their dissociation after amygdalectomy in monkeys. *Expl Neurol* **20**, 175–187, 1968.
6. BAGSHAW, M. H. and COPPOCK, H. W. GSR conditioning deficit in amygdalectomized monkeys. *Expl Neurol* **20**, 188–196, 1968.
7. BAGSHAW, M. H. and PRIBRAM, J. D. The effect of amygdalectomy on shock threshold of the monkey. *Expl Neurol* **20**, 197–202, 1968.
8. KINTSCH, W. Habituation of the GSR component of the orienting reflex during paired-associate learning before and after learning has taken place. *J. Math. Psychol.* **2**, 330–341, 1965.
9. PRIBRAM, K. H., AHUMADA, A., HARTOG, J. and ROOS, L. A progress report on the neurological processes disturbed by frontal lesions in primates. In *The Frontal Granular Cortex and Behavior*, J. M. WARREN and K. AKERT (Editors), pp. 165–187. Academic Press, New York, 1966.
10. SHUSTIN, N. A. *Physiology of the Frontal Lobes*. Moscow, 1959.
11. LURIA, A. R., HOMSKAYA, E. D., BLINKOV, S. M. and CRITCHLEY, M. Impaired selectivity of mental processes in association with a lesion of the frontal lobe. *Neuropsychologia* **5**, 105–117, 1968.

12. SOKOLOV, E. N. Neuronal models and the orienting reflex. In *The Central Nervous System and Behavior*, M. A. B. BRAZIER (Editor), pp. 187–276. Josiah Macy, Jr. Foundation, New York, 1960.
13. SPINELLI, D. N. and PRIBRAM, K. H. Changes in visual recovery function and unit activity produced by frontal cortex stimulation. *Electroenceph. clin. Neurophysiol.* **22**, 143–149 1967.
14. PRIBRAM, K. H. The intrinsic systems of the forebrain. In *Handbook of Physiology, Neurophysiology, Vol. II.*, J. FIELD and H. W. MAGOUN (Editors), pp. 1323–1344. American Physiological Society, Washington, 1960.
15. CLEMENTE, C. D., GREEN, J. D. and DE GROOT, J. Studies on behavior following rhinencephalic lesions in adult cats. *Anat. Rec. Ann. Ass. Anat.* **127**, 279, 1957.
16. LINDSLEY, D. P. In *The Organization of Recall*, D. P. KIMBLE (Editor). New York Academy of Sciences Interdisciplinary Communications Program, New York, 1967.
17. PRIBRAM, K. H. Reinforcement revisited: a structural view. In *Nebraska Symposium on Motivation*, M. JONES (Editor), pp. 113–159. Lincoln, University of Nebraska Press, 1965.
18. PRIBRAM, K. H. Some dimensions of remembering: steps toward a neuropsychological model of memory. In *Macromolecules and Behavior*, J. GAITO (Editor), pp. 165–187. Academic Press, New York, 1966.
19. PRIBRAM, K. H. and TUBBS, W. E. Short term memory, parsing and the primate frontal cortex. *Science* **156**, 1765–1767, 1967.
20. PRIBRAM, K. H. A neuropsychological analysis of cerebral function: an informal progress report of an experimental program. *Can. Psycholst* **72**, 324–367, 1966.
21. KIMBLE, D. P. and PRIBRAM, K. H. Hippocampectomy and behavior sequences. *Science* **139**, 824–825, 1963.
22. PINTO-HAMUY, T. and LINCK, P. The effect of frontal lesions on the performance of sequential tasks by monkeys. *Expl. Neurol* **12**, 96–107, 1965.

Résumé—On présente un modèle à base expérimentale des fonctions du cortex frontal des primates. Ce modèle s'occupe des interactions qui surviennent parmi les processus inhibiteurs nerveux. Au niveau neuronique, on admet que l'auto-inhibition du type Renshaw représente le substrat de l'inhibition interne. Au niveau psycho-physiologique, l'auto-inhibition conduit à l'habituation dont on a montré qu'elle était la base d'un modèle neuronique de l'experience de l'organisme. Au niveau physiologique des systèmes, il a été trouvé que la construction de ce modèle neuronique était contrôlé par les processus cérébraux efférents qui peuvent dériver les mécanismes qui traitent les entrées dans le sens soit de l'inhibition externe, soit de l'inhibition interne. Le cortex frontal déplace ces mécanismes vers l'inhibition interne, c'est-à-dire vers l'habituation. Au niveau neuro-comportemental, un tel déplacement réalise la suppression de l'interférence et ainsi permet de fournir leur organisation temporelle aux processus psychologiques de la même façon que la répartition linguistique donne la signification au langage.

Zusammenfassung—Es wird ein experimentell begründetes Modell der Funktionen der frontalen Hirnrinde bei Primaten vorgelegt. Dieses Modell befaßt sich mit den Wechselwirkungen, die zwischen neuralen Hemmungsprozessenv orkommen. Es wird angenommen, daß auf der neuronalen Ebene die Selbsthemmung nach dem Renshaw-Typ das Substrat der inneren Hemmung darstellt. Auf der psychophysiologischen Ebene führt Selbsthemmung zur Gewöhnung, von der gezeigt werden konnte, daß sie das Gerüst eines neuronalen Modells für die Erfahrungen des Organismus darstellt. Auf der neurophysiologischen Ebene des Systems wurde gefunden, daß das Gerüst dieses neuronalen Modells durch efferente Hirnprozesse kontrolliert wird, die den Mechanismus der Input-Prozesse zugunsten einer äußeren oder inneren Hemmung beeinflussen. Der frontale Cortex verschiebt den Mechanismus in Richtung auf die innere Hemmung, d.h. auf die Gewöhnung. Auf der Verhaltensebene vollendet solch eine Verschiebung die Unterdrückung von Interferenzen und führt auf diese Weise zu einer zeitlichen Organisation des psychologischen Prozesses in der Weise wie die linguistische Zergliederung Bedeutung für die Sprache hat.

electrodes

A17 L3 DV 0 — +7 caudate

response throughout tract to frontal — some IT — big frontal R at +2 → +6

A11-12 medial to putamen
caudate & gave amygdala +

brain stem ~ A4
apparently very rostal mesencephalon
seems to go right smack through ML + "RF"
catches SN at about DV -4

—

very weak R from SN both to caudate + "putamen" (the same as weaker than all other Rs in that tract)