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Neuropsychologia, 1964, Vol. 2, pp. 257 to 280. Pergamon Press Ltd. Printed in England

AN EXPERIMENTAL ANALYSIS OF THE BEHAVIORAL DISTURBANCE PRODUCED BY A LEFT FRONTAL ARACHNOIDAL ENDOTHELIOMA (MENINGIOMA)

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(*Received* 10 *July* 1964)

Abstract—A patient with a left frontal arachnoidal endothelioma was examined at the bedside. A series of simple tasks was administered. These showed:

(1) An inability to carry out compounded instructions whether these were given verbally or presented as a visual model.

(2) An inability to carry out "symbolic" instructions.

(3) These incapacities did not depend on any difficulty in apprehending the instructions *per se*.

(4) Error utilization appeared related to ease of disequilibration as tested by the orienting reaction.

These results are believed to be indicative of frontal lobe impairment despite the presence of more generalized brain damage which may serve to bring out in relief and carricature the essence of a disturbance produced by the local lesion.

1. INTRODUCTION

THE functions of man's anterior frontal cortex have remained a persistent enigma despite a century and a half of study. Yet progress is discernible and during the past few years several lines of investigation have converged sufficiently to allow new and specific questions to be posed.

Animal studies have shown two types of effect to follow frontal lobe removal. One type is a defect demonstrated in situations that demand problem solution when the cues to solution are no longer evident. This type is a tendency to shift behavior from the task at hand which had been variously attributed to (a) loss of recent memory [14], (b) hyper-reactivity [27], (c) increased distractibility [26], (d) failure to make a "prestarting synthesis" [1, 2, 3, 32, 33], and (e) disturbance of the process of internal inhibition [17, 18]. The second type of effect, noted not only in problem solving situations, but more generally as well, is stereotype in behavior with a tendency to repetition. This type has been descriptively labled "perseveration" [11, 28]. As recently shown [29] these two types of effects though opposite to one another, can, paradoxically, occur in the same subjects: whether a tendency to shift or perseveration is manifest depends on the situation and how closely the behavior is examined. Two suggestions have been made in an attempt to resolve the paradox. One proposes that behavior is arranged in hierarchical sets differing in degree of complexity and recency and that frontal resection "regresses" the subject to a lower or earlier state in that hierarchy [28]. The other proposal focuses more specifically on the process that is disturbed. The suggestion, which has been detailed elsewhere [29], is that frontal lobe resection limits the subject's ability to organize and reorganize his behavior when flexibility is demanded, and especially when external cues to support such organization are wanting. The mechanism for such a process is conceived as an impermanent confluence of neural excitation into patterns which act as effective guides on the neural traffic that begets behavior. The model for such patterns is the production of temporary dominant foci as in the experiments of UKNTOMSKI [35] and of RUSINOV [31].

The clinic has produced another set of observation. V. M. BEKHTEREV [4] expressed the observed changes produced in patients with destruction of the anterior frontal parts of the brain as follows: "They do not evaluate the results of their actions, they do not establish a definite relationship between imprints of external impressions and the results of past experience and . . . do not consciously direct movements and actions to the end of personal advantage." He suggested therefore that the frontal lobes functioned as "psychoregulatory" organs.

Similar observations have repeatedly been made since, e.g. by FEUTCHWANGER [7], KLEIST [16], BRICKNER [5], HALSTEAD [10] and DENNY-BROWN [6].

Only recently have *experiments* been performed that go beyond the limits of such descriptions. These experiments began with the study of those stages through which development of man's voluntary behavior passes. The investigations, initiated by L. S. VYGOTSKII [36, 37] and continued by A. N. LEONTIEV [19], A. V. ZAPORZHETS [38] and P. IA. GAL'PERIN [8], showed that in the development of the child, individual actions become directed by instructions, first in the form of speech from an external source, and later, as the child's inner speech develops, in part by his own verbalizations, until in the last stages of ontogenesis complex actions are programmed wholly by such verbally organized systems which then partake of the characteristics usually called "voluntary behavior" by neurologists. Several basic steps in the development of such voluntary behavior, organized under the regulatory influence of speech, were studied in a special series of experiments [see A. R. LURIA 20, 21, 22].

This analysis of the formation of voluntary activity in children permitted a new approach to the frontal lobe problem [23, 24, 25]. The destruction of the frontal lobes has relatively little effect on the course of simple and well-consolidated motor stereotypes. Yet, the patient with frontal lobe destruction is often unable to fulfill instructions, is unable to inhibit impulsive reactions or to hold back the tendency towards fixed repetition of movement. The crux of the problem may be that verbal instructions given by others or internally, as intentions, fail to establish firm dominating neural systems—a conception independently arrived at, yet remarkably similar to that derived from animal studies. The conception is that as a result of this failure, complex sequences of acts are fragmented, and impulsive or perseverative reactions substitued. This happens because the process by which the consequences of action ordinarily become effective, through signalling achievement or error, appears disrupted. And in fact, the signalling property of all stimuli—the ability to evoke an orienting reaction—may be drastically disturbed [12, 13].

These two major experimental endeavors have spelled out specific ways of posing the problem of frontal lobe function: questions can now be asked to ascertain whether there is indeed a convergence of views, or whether the similarities between statements is only superficial. We felt that, ideally, representatives of the human and the animal workshops should, shoulder to shoulder, study the same subject matter. Through the gracious cooperation of the Soviet Ministry of Health and the United States Department of Health, Education, and Welfare, a collaborative effort was made possible. This report details the results of observations made during September 1962 at the bedside of a patient admitted (to the Burdenko Institute of Neurosurgery, Academy of Medical Sciences, U.S.S.R.) with a verified arachnoidal endothelioma (meningioma) pressing down on the anterior portion of both frontal lobes. The results were checked on other patients who had had bilateral resections of the anterior portions of their frontal lobes, and, by way of controls, on a series of subjects with lesions in or resections of other parts of the cerebral hemispheres.

2. GENERAL OBSERVATIONS AND COURSE OF THE PATIENT'S ILLNESS

Patient Zav. (N34358), a 43 year old office worker, entered the Burdenko Institute of Neurosurgery in the beginning of September 1962 with a suspected tumour of the left frontal lobe.

In November 1961 she began to complain of headaches and nausea, sometimes accompanied by vomiting. She became forgetful, although her behavior did not yet begin to change. From August 1962 her condition grew worse; a right-sided hemiparesis with heightened tonus appeared.

Neurological examination showed that the patient was aware of her surroundings and responded quickly and accurately to questions about her orientation in place and time. During a testing session (one hour) she did, however, show a progressive weariness and overall difficulty in cooperating fully. (This difficulty was taken into account by altering the order in which tasks were presented during the several sessions.)

There was moderate papilledema bilaterally, probably of fairly long standing, since some degeneration of ventral part of the papillae was observed. Localizing signs pointed to the left frontal lobe—a left anosmia, a moderate right hemiparesis, and spasticity with hyperactive stretch reflexes was present both in the right upper and lower extremities. The hemiparesis was accompanied by an up going big toe elicited as a Babinski sign, some forced grasping and incoordination in the finger to nose test (right). However, the incoordination was sporadic and was best observed when the patient was fatigued. At such times, the spasticity and Babinski sign could also occasionally be obtained on the left side, albeit only slightly when compared to the right side. On the electroencephalogram, pathological slow waves appeared, especially in the left frontal regions of the brain. An arteriogram was performed—a large mass, possibly an arachnoendothelioma (meningioma) in the anterior portion of the left frontal lobe, was visualized.

On the 2nd of October, 1962, an operation was performed on the patient (by Professor B. G. Egorov) which revealed a large extra-cerebral tumor in the left frontal region joined by firm brain membrane going into the depths of the left frontal lobe by way of the falx and pressing on the corpus callosum. A ligature was placed around the tumor which was gently retracted and removal begun with the aid of suction and cautery. Considerable bleeding accompanied the operation. Despite blood transfusions, blood pressure fell alarmingly, so only that part of the tumor was removed which was adjacent to the falx. The patient died of heart failure about 24 hours after the operation.

Histological examination (Professor S. M. Blinkov and B. B. Arkhangel'skii) presented the following picture: In the left frontal lobe, a chamber of fresh hemorrhagic softening 6.5 by 2.5 cm was found. The superior and middle frontal gyrus of the frontal lobe showed moderate depression, forming an oval outline, presumbably that of the removed portions of the tumor. At the medial edge, the remains of the partially removed tumor reaches the fissure palii; however the remains did not adhere to the falx. The forward edge of the tumor was 4.5 cm from the frontal pole. The limbic gyrus was free and pushed forward. The lower gyrus was free. On the base of the brain both gyri recti were deformed.

The prechiasmal cistern was pushed caudally. Both hippocampal gyri, especially the left, were pushed medially, cut by a deep furrow with traces of pressure at the edge of the tentorium cerebelli. On frontal sectioning of the brain, the tumor was seen to form a depression up to 2.5 cm deep in the cerebral matter. The tumor remnant was situated in the pre-motor zone in the region of the upper frontal and, in part, of the mid-frontal gyri, and extended through the massa intermedia. Its diameter was 7 cm anterior-posterior and 4 cm transversely and about 2.8 cm dorsoventrally.

The whole left hemisphere, especially the anterior part, was markedly edematous. The edema spread as far as the occipital lobe, where on transverse section, the left hemisphere measured 7 cm and the right 6 cm in diameter. The cingulate gyrus was pushed over to the right. The corpus callosum was twisted. The volume of the centrum semiovale of the left frontal lobe was increased, the left half of the corpus callosum pushed aside ventrally, compressing the head of the left caudate nucleus. The septum pallucidum, deviated to the right of the midline, compressed the lumen of the anterior horn of the right lateral ventricle, its posterior horn being dilated. Figure 1 shows photographs of the sections of the brain.

3. VERBAL BEHAVIOR OF THE PATIENT

Superficially the patient's speech seemed intact. There was no indication of a disturbance of articulation or of defective grammatical construction. However on closer examination, she did show considerable echolalia and perseveration. Excerpts from conversations may illustrate the character of her speech.*

Demonstration 1

Hello, dear, Hello dear. *Where do you work*? Where do you work? . . . I work . . . 43-75 (an attempt to name the number of the hospital in which the patient worked). *What is your occupation*? What is your occupation? . . . 43 . . . 75 . . . *What kind of education do you have*? Seventh class (true). *And then*? And then . . . and then . . . 12th class . . . second class . . . 12 and 2 . . . (she is trying to say "second course of the technical institute", but the answer is confused with the stereotype "10th class of school"). *Do you have a daughter*? Yes . . . And what else? Two sisters and two daughters (In fact she has a sister and a daughter). *How many daughters do you have*? One daughter and one son. *What is your daughter's name*? Ludmilla. *And your son's*? Ruslan. *Who was here yesterday*? No one was here . . . And so forth?

The patient's dialogues shows gross echolalia and perseveration; "spontaneous" speech and monlogue were completely absent. She did not independently ask any questions or express any desires. Yet she showed complete retention of the ability to repeat words and considerable ability in naming objects.

The patient repeated separate words and phrases without difficulty, and only when *series of words or phrases* were given did she begin to exhibit perseveration. She correctly identified individual objects shown to her, but perseverated when attempting to identify two or more objects in sequence.

* In this, as in the following protocols, the investigator's question is italicized, the patient's answers are in normal type.

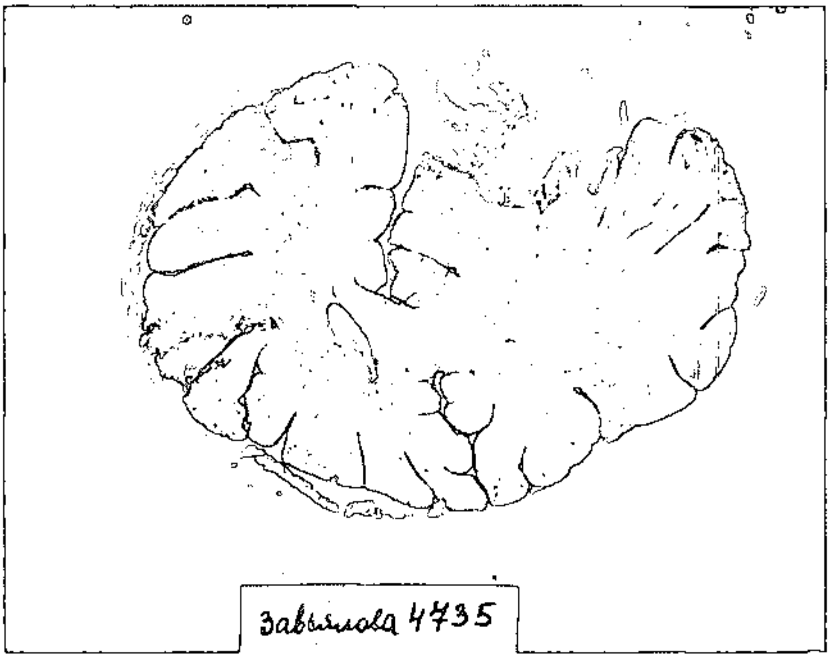


FIG. 1. Cross section through the frontal lobe of the brain of the patient examined in this study.

*Demonstration 2: Repetition of isolated words and phrases**

house	*needle*	*finger*	*hand*	. . . and so on
+	+	+	+	

Today the weather is good.	*At the edge of the forest, the hunter shot a wolf*
+	+

(2a) *Repetition of word series*

house-forest	*cat-table*	*cat-forest-house*	*cat-house-forest*
+	+	+	(1) cat-forest-house (2) cat-forest-house (3) cat-forest-house

(2b) *Identification of isolated objects*

watch	*scissors*	*fish*	*shoes*	*thermometer*
+	+	+	+	+

(2c) *Identification of pairs of objects*

fish-watch	*shoes-thermometer*	*fish-thermometer*
golden fish and watch	shoes and watch	watch . . . and . . . watch

Correct?
Yes, correct

Note that the patient uses only the simplest and best-learned speech forms. As soon as the patient's verbal behavior becomes more complex and includes series of consecutive verbal statements that demand transition from one designation to another, adequate speech behavior is replaced by perseveration thus disrupting the relationship between the answer and the question.

Investigation showed that simple logical structures are potentially retained by the patient; however, after correctly solving one logical problem the patient invariably slipped into some inert stereotype in the solution of a second.

Demonstration 3

The patient is asked to give a word with the opposite meaning to the one given her:

black	*high*	*Is that the opposite?*
white	white	but what . . .

high—and what will the opposite be?
The opposite is white

(pause)

night—and the opposite?
day

* The presented words or pictures are in the numerator, the reaction of the patient in the denominator.

full—and the opposite?	*long*	*healthy*
hungry	hungry	the opposite—hungry.

Retention of logical-grammatical structure does not insure firm execution of the necessary verbal *sequence*. In the transition from one sequence to another, repetition of a single sterotype is substituted for the answer.

4. VERBAL *vs.* NON-VERBAL REGULATION OF BEHAVIOR

The patient executed simple movements according to direct verbal instructions without difficulty: raising her hand, closing her eyes, pointing to her nose, etc. As long as verbal instructions were given at reasonably spaced intervals and as long as they demanded the execution of movements firmly established in previous experience, they presented no noticeable difficulties.

More difficulty was elicited when verbal instructions demanded the execution of a given number of identical movements with termination of the series after a prescribed number. An example of such instructions is the request to shake hands 3, or 6, or 10 times. As a rule the patient began to perform the necessary movements, but was unable to stop them in time. She either continued the actions beyond the demanded point, or substituted for them prolonged tonic gripping of the investigator's hand.

Demonstration 4

Shake hands 3 *times.*
The patient starts to
shake hands many times.

What are you supposed to do?
Shake hands 3 times.

Do it.
Shakes hands many times
in a row.

Shake hands twice.
Shakes hands 3 times.

No, only twice.
Patient begins to shake
hands many times in
succesion, then initiates
prolonged tonic gripping of
the experimenter's hand.

Say "one-two" and shake hands twice.

(1) Patient repeats "one-two" but makes no movement.
(2) Patient says "one-two" and begins to shake hands many times in succession, or initiates prolonged tonic gripping.

As can be seen from this demonstration, the patient, having started an action according to verbal instructions, is unable to stop even when the instruction is repeated, though she also repeats the instructions.

As often occurs in patients with tumors deep to the posterior part of the frontal lobe which impinge on motor cortex or its afferent and efferent tract, single motor automatisms (in this case, a tonic grip) once initiated cannot easily be stopped. However, in this patient the regulatory function of speech over movement seems to be profoundly disturbed as well, and even echolalic repetition of the command does not enable the patient to execute the instructions correctly. This was shown in the following manner:

Verbal instructions evoked greater difficulty than when visual models were used to demonstrate the desired response. The execution of rhythmical movements was asked for. The execution of all rhymical responses to verbal instructions seemed to be almost impossible. However such rhythmical movements were easily made in response to a visual model provided only one rhythm was demanded at a time; difficulties arose only in the transition from one rhythm to another whenever several rhythms were modeled in sequence before the patient was allowed to execute her responses. Without a corresponding visual model the patient invariably executed disorderly beats. The attempt to strengthen the verbal instruction did not help.

Demonstration 5: Execution of rhythms according to a visual model and to verbal instructions

(5a) *According to a visual model:*

'' '' ''   ''' ''' '''   '' '' ''

'' '' ''   '' ''' '''''''   ''' ''''''

(5b) *According to verbal instructions:*

beat in twos   *beat in threes*

'' '''' '''' ''''   ''''''''''''''''''''''''

Say "one-two" "one-two" and beat the same way
"one-two" . . . "one-two" . . . (no movements)

Instructions repeated
Patient does not repeat and beats: '' ''' ''''''' '''''

Thus, the most striking defect is that in the verbal regulation of behavior. But note that when visual modeling is used, here too a deficit is demonstrable. This becomes even more apparent in the next section.

5. SIMPLE *vs.* COMPOUND INSTRUCTIONS

This group of experiments took up the major part of each session. They show that the patient was *completely unable to execute series consisting of different movements* when these were asked for by verbal instructions. When she was asked to put a finger forward and then make a fist or strike the table with her palm and form a ring with her fingers, etc. she executed only the first of the series, repeating it several times. And here also the repetition of the verbal instructions did not help her to execute the movements. The experiments again began by asking the simplest question first: Does the patient retain the ability to follow simple nonverbal instructions and under what conditions are they disturbed?

5.1 *Experiments demanding simple movements in response to simple instructions*

We asked the patient to reproduce movements *which were shown to her by the experimenter* (her movements were to be isomorphic with those of the experimenter).

Demonstration 6.

The patient is asked to reproduce simple movements shown to her by the experimenter (put out a finger make a fist and so forth). Each "model" is presented with an interval of 15–20 sec. The patient's hand each time is in the starting position. The patient performed the following tasks correctly:

	Stretch out 2nd finger.
	+
(15 sec)	*Make a fist.*
	+
(12 sec)	*Form a ring with the 1st and 2nd fingers.*
	+
(15 sec)	*Stretch out the 2nd finger*
	+
(and so forth)	

5.2 *Experiments demanding simple movements in response to compounded instructions*

Echopractic reproduction of movements did not give rise to any difficulties. However, if the presented forms quickly replaced each other the patient exhibited difficulty in making the transition from one movement to another; a single motor reaction acquired forced character; its inhibition and the transition to the next often became too difficult for her and she was able to correct the error only under the influence of special questions.

Demonstration 7

The same models are presented in a group. Each presentation is separated from the next by only 2–3 sec; under these conditions the patient does not return to the initial position between each of the movements and performance of the tasks begins to provoke difficulties.

	Form ring with 1st and 2nd fingers.
	+
(2 sec)	*Stretch forward 2nd and 3rd fingers.*
	The patient continues to form a ring.

This way?
Patient repeats the ring.
Isn't it this way?
Patient corrects herself and makes the correct response.

(pause 40 sec)	*Stretch forward 2nd and 5th fingers.*
	+
	Form a ring with 1st and 2nd fingers.
	Patient reproduces the preceding pose.

This way?
Patient stretches forward 2nd and 3rd fingers.

This way?
Patient responds correctly.

Thus, though the patient had repeated separate movements with ease and switched from one to another when each was evoked separately, she had marked difficulty when the transition from one movement to another had to be made without the interposition of the relevant instruction.

5.3 *Experiments demanding consecutive movements to an instruction given as a single unit*

The patient's difficulty became even more pronounced if she had to reproduce two consecutive movements (e.g. show your finger and make a fist, or straighten the fingers of your outstretched hand and form a ring) to an instruction given as a unit. In such cases the patient reproduced the first movement of the series but was usually unable to complete the second one.

Demonstration 8

The patient was asked to reproduce two consecutive movements on command.

Stretch forward the 2nd finger and make a fist.
The patient stretched out her 2nd finger and then repeated the same movement several times.

Clench your fist and then show your 1st and 2nd fingers.
The patient clenches her fist and moves it in the air several times, than helplessly resets her fingers.

Did you do it correctly?
Yes . . . (confused, ends experiment)

Similar difficulties show up when the patient is asked to repeat three consecutive movements.

Demonstration 8(*b*)

The patient is asked to form first and second fingers into a circle (R), strike the table with the edge of a brush (I), and place her palm flat on the table (–). She is unable to do this, executing only fragments of the demanded series or stereotypically repeating one of the movements.

R I –
R . . I . . (refusal)

R I –
R – . . . RR . . . I (refusal)

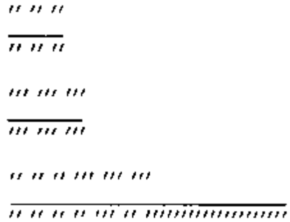
Thus, *although able to reproduce single movements with ease, the patient was unable to make the transition from one movement to another when the instructions were given as a unit.*

5.4. *Experiments to assay whether the difficulty lies in the visual mode* per se, *or in the complexity of the instruction*

This experiment requires reproduction of rhythmical beats. Again, the patient echopractically executes separate tasks with ease, but is unable to follow compound instructions.

Demonstration 9

The patient is asked to repeat with a pencil a series of rhythmical beats made by the experimenter on a piece of wood with his pencil.



The patient was unable to assess the correctness of her response or to correct her errors. Even when kinesthetic complexity of the motor task is reduced to a minimum and the instructions are given aurally, the patient shows this difficulty.

5.5. *Summary of experiments A–D*

(1) Echopractic execution of separately presented instructions separated by an interval gave the patient no difficulties.
(2) Execution of a series of quickly changing instructions begins to evoke difficulties despite the isomorphism of movement and instruction.
(3) Execution of a compound instruction requiring a sequence of movements was beyond the patient's ability.

Thus, the disturbance lies in the execution of actions in response to complex, serially organized instructions. The following experiments demonstrate this difficulty in yet another manner. They also permit analysis of the factors which influence the disturbance. We used the following methods to study this question: the subject was given checkers of two colors (black and white) and was asked to lay them out in a row of definite consecutive links. In order to avoid simple stereotypic alternations, the program usually included asymmetrical distribution of the colors (e.g. black and two whites). The program was presented either visually, the patient being asked to continue a started row, or verbally (e.g., "Lay out a row, 1 black and 2 whites"). In one case, the entire process was visually controlled; in the other, the laid-out row was concealed by a screen and the patient was required to execute the program without visual control from memory. In order to learn how firmly the program was retained and in order to strengthen the response to the program, the patient was asked to call aloud the desired consecutive colors.

The demonstration showed that execution of a serially programmed task either visually or verbally controlled was beyond the patient's ability. Usually a stereotyped alternation of groups of checkers was substituted or checkers of the same color were all grouped together.

Such deviation from the assigned instructions and the substitution of a simple response was shown with simultaneous complete retention of the instruction in the patient's verbal system. As with the other tasks, the process of relating her actions to the instruction was hampered. Recognition of errors was almost impossible.

An excerpt from the demonstration follows.

Demonstration 10

(1) The patient is given a started row (○○○) and is asked to continue it:

○○○

○○○○○○○○○○.

When asked whether she has executed the task correctly, the patient compares her row with the model and corrects it as follows:

○○○○○○○○○○○○.

Thus, the visually presented instruction elicits stereotyped repetition.

With the attempt to turn the patient's attention to the error, alternation of black and white checkers is substituted.

(2) The patient is shown a completed row of checkers. Then it is covered and the patient is asked to reproduce it from memory. The results are the same:

○○○○○○○○○○

○○○○○○○○○○○○.

(3) The patient is asked to lay out a row according to verbal instructions: "one black and two whites". The patient correctly repeats the instructions and lays out the following row:

○○○○○○○○○○○○○○○.

The instructions are repeated. The patient lays out the following row:

○○○○○○○○○○○.

Thus, verbal instructions also lead to the substitution of a simpler sequence as did the visual model.

(4) In order to reinforce the influence of the verbal instructions the patient is asked at all times to repeat them aloud. The demonstration continues as follows: (Upper line, the patient's speech; lower line, the executed actions):

black	*white*	*white*	*black*	*white*	*white*	*black*	*white*	*white*
○	○	○	○	○	○	○	○	○.

The patient is asked whether she correctly executed the task. She answers that she "became confused". She is asked to repeat the task again. The results are the same as before with one exception. This time the patient correctly retaining the verbal instruction repeats the stereotyped alternation of pairs of different elements:

black white white black white white black white white


.

(5) In order to reinforce the instruction, a sign is put in front of the patient—black, white, white, black, white, white, and she is asked to look at it and lay out the required program, The patient looks at the model but continues to lay out a row independent of it:

black white white black white white black white white


.

(6) The same experiment is repeated, but this time the word "black" is written in black, the word "white" in white. This time the patient, copying the color of the word itself, does it correctly:

black white white black white white black white white


.

This demonstration indicates that *the execution of either visually or verbally presented instructions that demand the serial organization of behavior is unattainable for this patient with massive frontal lobe destruction* unless a great deal of isomorphism between instruction and execution exists. Even in those cases in which instructions are firmly retained, they do not regulate behavior.

6. "SYMBOLIC" INSTRUCTIONS

From the observations made in the last section, the question arises: can the patient execute even simple instructions when appropriate action requires preliminary *recoding* of the signal; in other words, if the signal bears no direct but only a "symbolic" relationship to the act, can the patient execute the appropriate response? The following tasks were designed to explore the degree to which the behavior of the patient with frontal lobe destruction can be guided by symbolic instructions.

The *first* is a demonstration in which the symbolic instruction consists of a familiar action well-established in previous experience. For example, "When you hear the bell, press the key".

The *second* consists of those demonstrations in which the symbolic instruction only partially loses its "isomorphicity" to the signal or, retaining it, prescribes the reverse meaning. An example of such a form is a demonstration in which the subject is asked to knock twice in response to one sound, or once in response to two sounds.

The *third* form consists of demonstrations in which the symbolic instruction is reinforced kinesthetically by employing repeated passive movement to carry out the appropriate action.

These demonstrations can be conducted either with a single alternative (when one signal is presented, one corresponding response is required) or with a *choice* of responses (when the subject is presented one of two signals to which it is possible to give one of two symbolic responses). Obviously, in this case the instructions are noticeably more complex, since they allow for alternative actions.

Our patient was unable to execute even simple symbolic verbal instructions. Correctly repeating the instructions, she did not follow the symbolic meaning of the signal, but matched her movements to its direct influence, i.e. made the movement "isomorphic" to the signal. Verbal reproduction by the patient of instructions did not lead to the requested movement.

Demonstration 11

The patient is given the instructions: "When I tap once, you tap twice". The patient correctly repeats the instructions:

$\frac{\prime}{\;}$ (10 sec) $\frac{\prime\ \prime}{\prime\prime\ \prime\prime}$ (10 sec)

What did you do?	*Was what you did correct?*
What did I do . . . I tapped once	Yes

Instructions are repeated:

$\frac{\prime}{\prime}$	*Did you do it right?*
	Yes
What did I ask you to do?	*And how did you tap?*
When you tap once, I tap twice	I tapped the correct number of times

Instructions are repeated:

$\frac{\prime}{\prime\prime}$ (10 sec) $\frac{\prime}{\prime\prime}$ (15 sec)

(pause with distracting conversation)

$\frac{\prime}{\prime}$ *Right?*
No

What should you have done?	*When I tap once, you tap – –*
I did it correctly.	Twice
Do it correctly $\frac{\prime}{\prime}$	*Correct?*
	Correct.

Similar results were obtained during demonstrations in which the patient was asked to tap once in response to two taps; here too the patient's reactions very quickly took on an isomorphic relationship to the signal instead of a symbolic one.

The results of these demonstrations are clear. For very short periods the patient was able to respond to the symbolic meaning of the verbal instructions, but any protracted exercise of this sort proved impossible. The attempt to reinforce the verbal instructions by having the patient repeat them did not lead to the desired results; repeating the instructions verbatim, the patient continued to respond "isomorphically" to the signal.
Characteristically, such a transition to "isomorphic" reactions was evoked by any kind of factor (exhaustion, pauses, distracting conversation, etc.). The process of relating the action to the symbolic instruction seemed to be barely achievable for the patient.

It should be noted that with long training during which *each* correct response is accompanied by reinforcement on the part of the experimenter, the patient succeeded in working out the correct symbolic reaction; however, any factor which complicated the execution of the given task (exhaustion, change of instruction, e.g. instructions "When you hear two taps, tap once", etc.) invariably led to substitution of echopractic or isomorphic responses for the correct response.

Similar results were obtained when the symbolic signal was a hand pose in response to which the patient had to make some different hand movement, unlike the model. An excerpt from such a demonstration follows.

Demonstration 12

The patient is asked to show a fist in response to a pointed finger. The patient hears the instructions and repeats them correctly. (Fist = ; Finger =).

Did you do it correctly? *What did I ask you to do?*

Yes Raise my finger

Instructions are repeated:

When I raise my finger, what will you raise?
I will raise my fist.

Correct? *What should you raise?*

Correct. My finger.

The instructions are repeated again. The patient repeats the verbal instructions correctly:

I will raise my finger, and you?
I will raise my fist.
(Simultaneously, raises finger.)

Is that a fist?
But . . . that . . .

Thus, in any situation in which an instruction is complicated in that its proper execution demands departure from direct reproduction, appropriate action is replaced by echopractic response. This disturbance of the regulatory influence of symbolic relationship is always in sharp contrast to the retained verbal formulation of the instruction.

In the last demonstration the patient, who should have made a response to the symbolic aspects of the signal, slipped into echopractic (or isomorphic) repetition of the signal. In the following demonstration only the verbal symbolic instructions is given, no visual or auditory model is presented to which an isomorphic response can be made. The execution of the action was completely blocked.

Demonstration 13

The patient is given the instructions: "When you see the cross, tap once". The patient repeats the instructions. The demonstration proceeds as follows:

+
Patient does nothing.

Instructions repeated:

What do you have to do when I show you the cross?
Tap once.

+
Patient does nothing.

Instructions repeated:

What do you have to do?	*Did you do it?*
Tap once	I tapped once.

When I show you the cross, what do you have to do?
Show the cross.

+
I must show the cross.

Further attempts to get symbolic responses from the patient in response to verbal instructions were equally unsuccesful.

This experiment is especially illustrative: receiving no visual support from the symbolic signal, the patient, while retaining the verbal instruction, reveals complete inability to execute the response and, as the experiment continues, substitutes other somewhat more isomorphic responses for the one demanded by the instructions.

All these demonstrations show that the ability of this patient with destruction of the frontal lobes to execute actions depends on the complexity of the instruction: *If the action is completely defined by isomorphic signals, the program is executed without difficulty; if appropriate action demands preliminary recoding of the instructions and is defined by a system of "symbolic" signals it becomes impossible to execute.*

This experiment shows how difficult it is for the patient with left frontal lobe destruction to organize actions in response to complex instructions. We shall conditionally call this method organization "from above". However, there is another way to organize such actions. *Prolonged training, combined with constant kinesthetic reinforcement of the motor response,* might accomplish appropriate execution of action.

This method will be called organization "from below". We now must ask the extent to which "direct" programming of motor skills from "below" is possible in this patient.

Demonstration 14

After attempts to provoke responses based on symbolic instructions (see Demonstration 11) were unsuccessful, we switched to working out the desired motor responses on the basis of kinesthetic reinforcement.

The patient, given the same verbal instructions, was presented with a drawing (cross) and each time her hand was made to passively produce a tap. After very short repetitions of such reinforcement, accompanied by verbal instructions, the patient began to tap when presented with the cross. However, the duration of the appropriate response was fragile. The effect was erased if another experiment was interpolated even for a short time. Another demonstration—in response to a raised finger the patient was asked to make a fist—failed completely; even after prolonged kinesthetic reinforcement, the necessary relationship was not formed and the patient, retaining the verbal instructions, continued to make movements "isomorphic" to the model. (In response to the finger, she showed her finger).

Until now we have been focusing on the difficulties which the patient encountered in attempting to respond to a single symbolic signal. She had even greater difficulty when asked to master a definite *system* of signals, choosing from two possible alternatives, one of which corresponded to the instructions.

Experiments involving such choices show with special clarity the disturbance characteristic of the patient. The demonstration indicated that the patient was able to master verbal instructions and retain the selective verbal relationships, but was unable to organize appropriate motor actions when these were demanded.

Demonstration 15

The patient is asked to raise her left hand on the command "one"; at the word "two", her right hand:

"One"
Patient is silent; (no movement).

What were you supposed to do?
At "one" to raise my left hand.

And on "two"?
My right hand.

Do it! *"Two"*
"Two" (raises left hand)

(10 sec) "*One*"
Silence (no movement)

(12 sec) "*One*"
"Left" (no movement)

(10 sec) "*One*"
Silence (no movement)

In order to reinforce the signal, the patient was asked to practice the instructions, on the signal "one" answering with the word "left", on the signal "two" answering with the word "right". The patient executed this task eight times without error. However, this correct verbal answer does not regulate her motor responses:

"*One*"
"Left" (raises left hand)

(8 sec) "*One*"
"Left"

(10 sec) "*Two*"
"Right" (raises left hand)

(10 sec) "*Two*"
Silence (no movement)

(10 sec) "*Two*"
"Right" (no movement)

(10 sec) "*One*"
"Left" (makes slight movement with left hand)

(12 sec) "*Two*"
Silence (makes slight movement with left hand)

(10 sec) "*One*"
"Left" (makes slight movement with left hand)

(12 sec) "*Two*"
"Right" (makes slight movement with left hand).

This experiment shows that even when adequately mastering the verbal responses to two symbolic signals, the patient is unable to organize the corresponding system of motor reactions; the verbal responses do not regulate the corresponding motor reaction—she continues stereotypic reproduction of movements independent of the adequate verbal response. Such dissociation of verbal and motor reactions is typical.

Let us make a resumé of the findings thus far obtained:

(1) The organization of simple movements "isomorphic" to a visual or verbal model or by well established previous experience is relatively easily acquired. Failure appears when attempts are made to organize motor responses to more complex instructions demanding sequential organization of action or an even more direct recoding of a signal.

(2) Verbal reinforcement is ineffective in guiding action; though the patient correctly repeats the verbal instructions, she continues to make echopractic or perseverative motor responses. Dissociation between well retained verbal instructions and inappropriate motor responses is typical.

(3) Kinesthetic reinforcement of actions is somewhat more effective. Though the patient is completely unable to organize her actions to symbolic instructions, she is some times able to do so when such actions are reinforced kinesthetically. However, such organizations are fragile in the face of distractions or other interruptions.

(4) The patient is unable to report clearly what her errors are, though she is able to report that an error has been made. More of this in the next section.

6. APPREHENSION OF INSTRUCTIONS AND THE EVALUATION OF ERRORS

In the experiments just described it became obvious that though our patient could on many occasions recognize that she made errors, she was often unable to correct them. This led us toward proposing at least two possible explanations of the defect observed. These were not incompatible, but differed in their emphasis. On the one hand, the disturbance could be due to defective appreciation of instructions *per se*. On the other, the disturbance might be in relating the outcomes of actions to the original instructions.

One disturbance that might well interfere with the patient's ability to apprehend instructions *per se* would be a limitation on the number of items which she could process at any time. Such a restriction of channel capacity would cripple understanding. The following demonstration makes it unlikely that our patient is impaired in this fashion.

Demonstration 16

On successive trials, an array of stimulus objects (pieces of paper with patterns written on them, e.g. + □ × ○) were placed in a row in front of the subject. Anywhere from two to twelve (the actual number selected at random) such stimuli were presented on each trial. The subject was asked to name each of the cues and then to choose the one that she had been previously instructed to keep in mind, e.g. the + on one trial, the × on the next trial and so forth.

First name each and then choose the plus:

□	Δ	×	○	+	≡	*Now choose the*
sq.	tr.	echs.	zero	plus	stripes	*right one*
						The plus

One variation of the task was to present the pieces of paper with the cues facing down and ask the patient to turn them over, one at a time, until she found the correct one.

The results of this experiment were straightforward and conclusive. The patient had no difficulty in identifying the correct cue according to instruction and her response did not vary as a function of the number of alternatives among which she had to choose.

Nor was there a difference between her performance when she had to search by merely looking at the stimulus papers and when she had to turn each paper over in order to locate the correct one. This task posed no special problem for the patient; she answered questions and performed with alacrity. Channel capacity and apprehension of instructions *per se* appears intact in this situation and the ability of the patient to verbally repeat instructions even while producing erroneous performances in other situations supports the generality of this finding.

Thus, it became likely that a major part of our patient's difficulty arose from a disturbance in the evaluation of the outcomes of her actions. Immediately the question arose: is this inability to use the outcome of actions limited only to the evaluation of relating the outcomes of *her own actions* to instructions or does it appear also in her evaluation of *the errors made by another person*. In evaluating her own actions, the observed defect could be the result of disturbance of kinesthetic signals coming from the effect of her own movements; in evaluation of the errors of others, it would be explained better by some general disturbance in the ability to relate two stages of any process (e.g. instruction with instruction, instruction with action).

To answer this question we conducted separate experiments which fell into two groups. In one, the subject was given instructions to carry out actions. The patient was asked whether or not she noticed her errors and to correct them. In the second, the same experiment was conducted in the presence of the subject with a "third person"; by previously arranged plan this person was to make errors at an assigned moment, and the patient was asked to note and correct them. We present the compared results.

Demonstration 17

(17a) *Evaluation of her own errors:* The patient is instructed to raise her finger in response to a fist (or the reverse) and is asked each time if she did it correctly.

As a rule, the patient substituted an echopractic movement for the symbolic reaction, simultaneously showing some inability to evaluate it as an error. As the protocol indicates, instead of relating the executed action to the conditions of the instructions, she usually compared her movement with the experimenter's movement and, if both were the same, answered "correct".

finger	*Is that correct?*	*What did I ask you to raise?*
finger	Correct	My finger

Instructions repeated

finger	*Is that correct?*	*What did I say? When I raise my finger, what will you show?*
		My fist

Instructions repeated

finger	*Is that correct?*
finger	Correct

Instructions repeated again. The patient is asked to repeat the instructions and simultaneously to make the corresponding movement:

finger	*Right?*
"and I—fist"	Patient is silent but makes no attempt
raises finger	to correct this error.

Thus, the patient cannot regulate her movements with the symbolic meaning given in the instructions. She substitutes movements "isomorphic" to the model. She usually evaluates it directly with respect to the model.

(17b) *Evaluation of the errors of others:* The same experiment is conducted in the patient's presence with "a third person". The patient is supposed to evaluate his errors. As the protocol indicates, the patient in this case makes somewhat more correct evaluations. However, they are also easily disturbed.

Third person's responses	*fist* fist	(10 sec)	*finger* fist	(10 sec)	*fist* fist
Patient's evaluation	*Right?* Right		*Correct?* Yes		*Correct?* Incorrect

The third person is asked to raise a fist in response to the word "one". The patient is supposed to evaluate the erroneous responses:

"*One*" fist	(10 sec)	"*One*" finger	(10 sec)
Correct? Yes		*Correct?* No, incorrect; he should do it like this: shows fist	
"*one*" fist			
Correct? No.		*What should he have done?* He should have shown his fist.	

The results of this experiment were inconclusive. The experiment was not repeated because the patient's condition took a turn for the worse indicating urgency for operative interference. However, the same experiment done with another patient with frontal lobe damage gave supportive evidence that the ability to evaluate his own errors is more severely impaired than the ability to evaluate the errors of others.*

8. THE ORIENTING REACTION

One possible approach to the study of disturbances of the registration of feedback produced by the outcomes of actions is an investigation of changes in indices of the patient's equilibration and disequilibration. Study of the autonomic (vascular and galvanic skin

* The results of these experiments conducted by one of us (A. R. LURIA) and V. V. LEBEDINSKII will be published separately.

response) components of the orienting reactions provide this opportunity and have the additional virtue that they may give evidence on the nature of the "signal" value carried by a "symbolic" instruction. Our patient presented a picture of gross disturbance of the plethysmogram and galvanic skin response component of the orienting reaction.

The background of the plethysmogram was areactive with poorly expressed waves of the III order and sharply intensified breathing waves. Clear vascular reactions were observed only in response to certain unconditioned stimuli (sigh, cough). All vascular reactions were absent in response to indifferent sounds of various intensity, sustained and intermittent. Only on certain experimental days, when the patient seemed more alert than usual, intensive sounds and electrocutaneous stimulation did produce small contraction of the vessels or short-lived disappearance of the breathing waves.

The background record of the galvanic skin response was also flat, showing only widely separated spontaneous oscillations of small amplitude. On some experimental days the *number* of such shallow spontaneous oscillations in the background of the GSR increased sharply. Either absent or weakly expressed were the slow changes of skin resistance (tonic form of the GSR). In response to unconditioned stimuli (sigh, cough), weak and inconsistent reactions were observed. The GSR was obtained when stimuli of great intensity were used. On the whole, the GSR component of the orienting reflex revealed greater reactivity than the vascular component.

Introduction of verbal instructions which gave signal meaning to indifferent sounds of moderated intensity ("Count the sounds" and "There will be a shock after the sound") had no influence either on the vascular or on the GSR components of the orienting reflex (Fig. 2.)

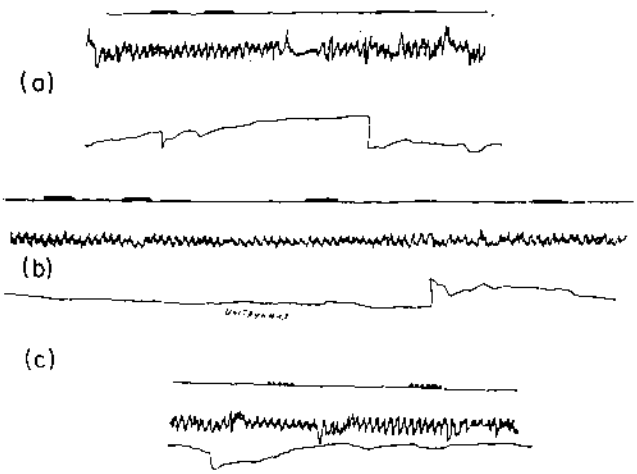


FIG. 2. Vegetative nervous system components of the orienting reaction showing the lack of activation by verbal instructions in the patient Zav:

(a) Vascular and galvanic skin components of the orienting reaction to sound alone. (Note variability and low amplitude of the response.)
(b) Same, after the introduction of the instruction: "towards the end of the sound there will be a prick". (Note absence of reaction.)
(c) Again, after the introduction of the instruction: "count the number of sounds". (Note that a reaction is again absent.)

The background of the plethysmogram did not undergo any changes, continuing to remain areactive with sharply expressed breathing waves. Vascular orienting reactions were absent both at the moment of count-the-sounds presentation and to sounds which signalled electrocutaneous reinforcement. Changes of the background set in only with presentation of the electrocutaneous stimuli themselves.

The background of the GSR, similarly, did not change, either in terms of spontaneous oscillations or increase of slow displacement (changes, improvements) of cutaneous resistence (tonic form of the GSR).

9. DISCUSSION

We have had the opportunity to study a patient with a left frontal arachnoidal endothelioma. Despite the infringement of the pathologic process on the left motor regions and on the right frontal lobe, some salient observations were made and these have been checked against those made in other patients in whom the distribution of pathology differed. It has been our experience that the more generalized brain damage brings out in relief and caricature the essence of a disturbance produced by a local lesion—a disturbance which may be covered by alternate modes of function which result in equivalent behavior when the remainder of the brain is intact (see also GOLDSTEIN). Needless to say however, caution must be exercised in the interpretation of evidence obtained when lesions are as massive as the one which led to the death of our patient.

The difficulties displayed by this patient fall into three categories: (a) A general fatiguability and lassitude, (b) Disturbances brought out by routine neurological examination, (c) Disturbance demonstrated by the test battery reported in detail here. These last can be summarized as follows:

(1) An inability to carry out compounded instructions whether these were given verbally or presented as a visual model: whenever the instruction called for a sequence of actions other than simple repetition of a rudimentary pattern, the patient failed despite her ability to repeat the instruction verbally.

(2) An inability to carry out "symbolic" instructions: Whenever the instruction conflicted with or was otherwise anisomorphic to the action required, and thus necessitated recoding for execution, the patient's performance showed marked impairment.

(3) These incapacities seem not to depend on any difficulty in apprehending the instructions *per se*: they may however, be related to an inability, shown by our patient, to evaluate errors, especially self produced errors.

(4) In turn, error utilization is possibly related to ease of disequilibration: Vascular and skin reactive components of the orienting reaction were found drastically disturbed.

Our experience at the bedside of this patient was thus amply rewarding. We found indeed that verbal regulation of behavior can be severely impaired by a frontal lesion. We also found that whenever flexibility was demanded in the execution of a task the patient's performance suffered. But we learned much more. We found that, just as in the animal studies, the patient could readily differentiate among clearly labelled alternatives. She understood well speech directed to her and she retained verbal formulations of a given task. Simple logical relationships were found uninfluenced by her cerebral damage. The defective performances were due to failures in organizing action on the basis of the verbal statements.

An additional fact emerged. Not only is verbal regulation of behavior impaired—instruction by means of visual models also proved sensitive to disruption. The defective verbal regulation is therefore only the most manifest impairment of a more general deficiency in the execution of any type of complex and symbolic instructions and intentions (internalized versions of such instructions).

Flexibility *per se* is also found to be only a part of the total picture of the disrupted relationship between instructions and their execution. Isomorphism between what is required and its requisition also appear important. Thus whenever recoding is necessary the frontal lesion makes itself felt.

Finally, the first steps of an analysis of the mechanism disturbed was accomplished. Error utilization is obviously interfered with. The mechanism of the orienting reaction, also drastically defective in our patient may well serve in normal subjects to signal that effective feedback from error (or any mismatch between input and expectation) is occurring [34].

In closing, we again want to note caution. This is a report on a single, more or less representative patient, whose brain damage though primarily of frontal lobe tissue did extend beyond the limits of the frontal eugranular isocortex. Nonetheless, we have been encouraged by our initial findings to pursue in both man and monkey this approach to the frontal lobe problem. Some further controlled obervations and experiments derived directly from those reported here are already completed and more are underway [9, 15, 30] in an effort to circumvent the limitations that go hand in hand with the challenge presented by the clinical opportunity.

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Résumé—Un malade atteint d'endotheliome arachnoidien du lobe frontal gauche fut examiné cliniquement au moyen d'une série d'épreuves simples. On constata ainsi:

(1) Une impossibilité d'exécuter des instructions complexes, que celles-ci soient données verbalement ou présentées visuellement.

(2) Une incapacité à exécuter des instructions "symboliques".

(3) Ces troubles ne dépendaient pas de difficultés dans l'appréhension des instructions en elles-mêmes.

(4) L'utilisation erronée apparaissait dépendre des possibilités de déséquilibration telles que testées par la réaction d'orientation.

On croit que ces résultats traduisent l'atteinte du lobe frontal malgré la présence d'un trouble cérébral plus généralisé qui peut aider à mettre en relief et à caricaturer l'essence d'un trouble produit par la lésion locale.

Zussammenfassung—Einem Patienten mit einem linksfrontalen Endotheliom wurde am Krankenbett eine Reihe von einfachen Testaufgaben gestellt. Die Ergebnisse waren folgende:

(1) Es bestand eine Unfähigkeit, komplexe Anweisungen auszuführen, ganz gleich, ob diese verbal gegeben oder optisch dargeboten wurden.

(2) Es zeigte sich ein Unvermögen, Aufgaben zu lösen, die "symbolischen" Charakter hatten.

(3) Die Mängel beruhten nicht auf einem fehlenden Aufgabenverständnis.

(4) Dass aus Fehlern kein Nutzen gezogen wurde, war der leichten Störbarkeit des seelischen Gleichgewichtes zuzuschreiben, was auch das Verhalten bei der Orientierung zeigte.

Die Befunde weisen auf eine spezifische Stirnhirnschädigung hin. Selbst bei gleichzeitig bestehender diffuser Hirnschädigung heben sich die charakteristischen Herdsymptome des Stirnhirns ab.