Chapter 5

BRAIN AND BEHAVIOR: HIERARCHY OF FEEDBACK SYSTEMS AND CONTROL OF INPUT

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I. ABSTRACT

The cornerstone of this chapter is W. Powers' definition of behavior: behavior is the control of the sensory input of the organism. By definition, behavior is conceived as a process by which the organization inside the organism controls the input of the organism; the brain is thereby conceived as an integrated whole of negative feedback systems controlling this input. In this chapter I have attempted to elaborate the usefulness of this concept for getting insight into basic functions of distinct neuronal substrates in programming behavior. For that purpose the relational and dynamic features of different levels of cerebral organization of behavior (hierarchies) are examined. I discuss how input signals derived from interoceptive, proprioceptive, and exteroceptive stimuli are transformed into abstract, invariant functions, the degree of abstraction of these stimuli increasing at each higher order level within the hierarchy. I also discuss how behavioral commands result from behavioral program signals, the degree of freedom in programming behavior decreasing at each lower order level in the hierarchy. The usefulness of Powers' concept is illustrated by investigating how information that is sent to the neostriatum is transformed on its way downstream in the hierarchy.

The resulting data reveal several characteristic features of the cerebral organization of behavior: (1) the enormous degree of freedom in

programming a single behavioral state via totally distinct neuronal substrates, (2) the principal lack of the cerebral representation of behavior at levels superior to the lowest order level in the hierarchy, and (3) the potency to activate successively higher order levels during ontogeny, maturation, and situations in which a disturbance at a particular level within the brain cannot be counteracted by input signals. In general, Powers' concept is found to link J. C. Fentress' concept of "hierarchical patterning of behavior." a successful attempt to unify knowledge about ethology in its broadest sense, with P. Teitelbaum's concept of "hierarchically organized systems inside the brain," a successful attempt to unify knowledge about separate response systems inside the central nervous system.

I believe that Powers' concept provides a real bridge between different branches of science in which investigators are searching for "rules of order" in species-specific behavior, including its causal, ontogenetic, phylogenetic, evolutionary, and functional aspects.

II. INTRODUCTION

Neuroethology, in its broadest sense, is the search for "rules of order" in the cerebral organization of behavior. Such a research program requires a clear-cut delineation of the frame of reference. Until a short time ago, it was not recognized that the currently employed frame of reference actually consisted of two distinct frames: one in which behavior is considered to be a single entity and one in which the brain is considered to be a single entity. As discussed elsewhere (Cools, 1981a), such an ambiguity produces sterile, invalid, and irrelevant questions about the cerebral organization of behavior. In view of this, I have proposed another frame of reference, in which brain processes and behavioral phenomena form part of a single entity; the mutual relationship between brain, organism, and environment is thereby conceived as an integrated whole. The cornerstone of this approach is W. Powers' definition of behavior: behavior is the control of the input of the organism. By definition, behavior is conceived as a process by which the organization inside the organism controls the input of the organism; the brain is thereby conceived as a hierarchy of negative feedback systems controlling this input (Powers, 1973a,b). It is this concept that has allowed us to delineate two new types of research strategies in brain and behavior research (Cools, 1981a):

1. "Input/output function" strategy. Following this strategy, knowledge of the input/output function of a particular brain region at the

cellular level is used to understand behavioral changes following manipulations with that brain region, because both input and output of the target unit under study ultimately contain crucial information about the way in which the organism maintains its dynamic relation with the environment. In practice this approach implies (a) delineating the brain region under study within the frame of reference in which the chosen target unit is a single entity; (b) defining the function of this target unit in terms of input/output relationships with the help of electrophysiological studies, for instance; and (c) analyzing behavioral changes triggered by selective manipulations with the target unit in terms of their being consequences of changes in the latter function. Use of this strategy has revealed that the noradrenergic cells within the locus coeruleus, for instance, determine the degree of distractibility by virtue of their ability to change the signal/noise ratio according to the relevance of the incoming stimuli; as a consequence, they increase the impact of relevant stimuli and decrease that of irrelevant stimuli (Van Dongen, 1980). From that point of view it became possible to understand the particular role of central, noradrenergic processes in aggressive behavior, not because they form part of a so-called "aggressive substrate" within the brain, but because they play a circumscribed role in the cerebral organization of behavior as such (Cools, 1981a).

2. "Consequence" strategy. In this strategy the behavioral changes following a selective manipulation with a particular brain region are considered as consequences of one common underlying mechanism, i.e., mechanisms that are not themselves observable do account, by virtue of their properties, for observable behavior. In practice this approach implies (a) delineating the borders of the brain region under study within the frame of reference in which the chosen target unit is a single entity; (b) defining the common features in behavior displayed by organisms in which the activity of the chosen target unit is selectively modified; and (c) analyzing the input/output function of the brain region under study in terms of the latter common features. Use of this strategy has revealed that the dopaminergic and cholinergic processes within the neostriatum determine the degree of flexibility with which the organism copes with its environment by virtue of their ability to change the ordering and sequencing of units at hierarchically distinct levels of cerebrally organized behavior; as a consequence, the organism has access to information relevant for directing the syntax under study (Cools, 1973, 1981a; Cools and Van den Bercken, 1977; Van den Bercken and Cools, 1979). From that point of view it became possible to understand the differential ability of a single dopaminergic agent to modify aggressive behavior in different experimental situations (Cools, 1981a).

In this chapter I attempt to elaborate more fully the usefulness of Powers' concept by examining the relational and dynamic features of different levels of cerebral organization of behavior (hierarchies). The basic terminology relevant to Powers' concept is introduced in Section III. In Section IV the given definitions are used to delineate the basic principles directing behavior; for the sake of generality, at this point they are left unspecified in terms of particular brain structures. Next, I attempt to illustrate how one can delineate "rules of order" in the cerebral organization of behavior. Both studies on behavioral changes that are elicited by techniques altering the activity of circumscribed brain entities (lesion, chemical and electrical stimulation) and studies on behavioral changes that spontaneously occur during development, maturation, and recovery from central nervous system lesions are discussed in this context in Section V. In Sections VI–IX the usefulness of Powers' concept is illustrated by investigating how information arriving at the neostriatum is transformed on its way downstream in the hierarchy. In Section VI it is shown how one can specify the hierarchical level to which a particular brain entity belongs; for that purpose the nigrostriatal dopaminergic fibers are chosen. In the same section it is shown how one can specify the function of such a brain entity in terms of one of the following signals: signals carrying information derived from interoceptive, proprioceptive, and exteroceptive stimuli (input signals); signals carrying information about the "desired state" of the hierarchical system (reference signals); signals carrying information about the difference between input and reference signals (error signals); and signals carrying information about the behavioral program to be executed (output signals). The given examples show that the neostriatum, which is innervated by the nigrostriatal dopaminergic fibers allows that organism to program arbitrarily the ordering and sequencing of behavioral states. Sections VII and VIII show how a behavioral program that is carried downstream in the hierarchy by output signals of the chosen brain entity is transformed on its way downstream. In Section VII the function of the substrantia nigra, pars reticulata—one of the main output stations of the neostriatum—is discussed. It is shown that this brain structure, which receives information from the neostriatum via striatonigral GABA-ergic fibers, reduces the degree of freedom in programming behavior by adding information about the ordering and sequencing of behavioral states with the help of input signals derived from proprioceptive stimuli. Section VIII discusses the function of the colliculus superior, especially its deeper layers—one of the main output stations of the substantia nigra, pars reticulata. It is shown that this brain structure, which receives information from the substantia nigra via nigrocollicular GABA-ergic fibers, once more reduces the degree of free-

dom in programming behavior by adding information about the ordering and sequencing of behavioral states with the help of input signals derived from exteroceptive stimuli. The overall impact of the transformation of the information flow going upstream and downstream in the hierarchy is discussed in Sections IX and X.

III. POWERS' CONCEPT: A GLOBAL VIEW ON THE CEREBRAL ORGANIZATION OF BEHAVIOR

Although the definition of behavior given in the preceding section (Powers, 1973a,b) is actually a modern-day version of the classic "Subjekt-Umwelt" theory of Jakob von Uexküll (1934), Powers added a new dimension. What is new in Powers' concept is the recognition that the outer shell of the organization inside the organism is the only one that directly interacts with the physical environment of the organism via a set of input devices such as sensory receptors for pressure, light, vibration, chemical qualities, etc., on the one hand, and via a set of output devices such as muscles and glands on the other hand. Systems that are hierarchically superior yet as close as possible to these lowest order or first-order systems receive their input from them. The output of these hierarchically superior, *second-order* systems can only influence the physical environment via the first-order systems by constructing (reference) signals for the latter systems (Fig. 1). In this way the brain is postulated to consist of a large number of hierarchically organized higher order systems (Fig. 2).

To appreciate the implications of such a hierarchical organization, consider the patterning of locomotion in cats. Although "generators" for locomotion have been localized in the spinal cord (Grillner, 1975, 1976; Grillner and Zangger, 1979; Miller and Scott, 1977), i.e., the lowest order systems for emitting signals to the trunk and limbs, experimentally induced interventions with signals leaving higher order systems and reaching the spinal cord also alter the patterning of locomotion (Grillner and Shik, 1973; Mori *et al.*, 1977, 1978; Orlowvskii, 1969; Shimamura *et al.*, 1982). These data do not throw doubt upon the "localization" of locomotor "generators" within the spinal cord. According to Powers' concept, they simply imply that supraspinal brain regions direct the functioning of the spinal regions involved, but not the resulting behavior (Feldman and Latash, 1982; Rothwell *et al.*, 1982). We will see, in Sections V–VIII, that supraspinal structures indeed determine the degree of free-

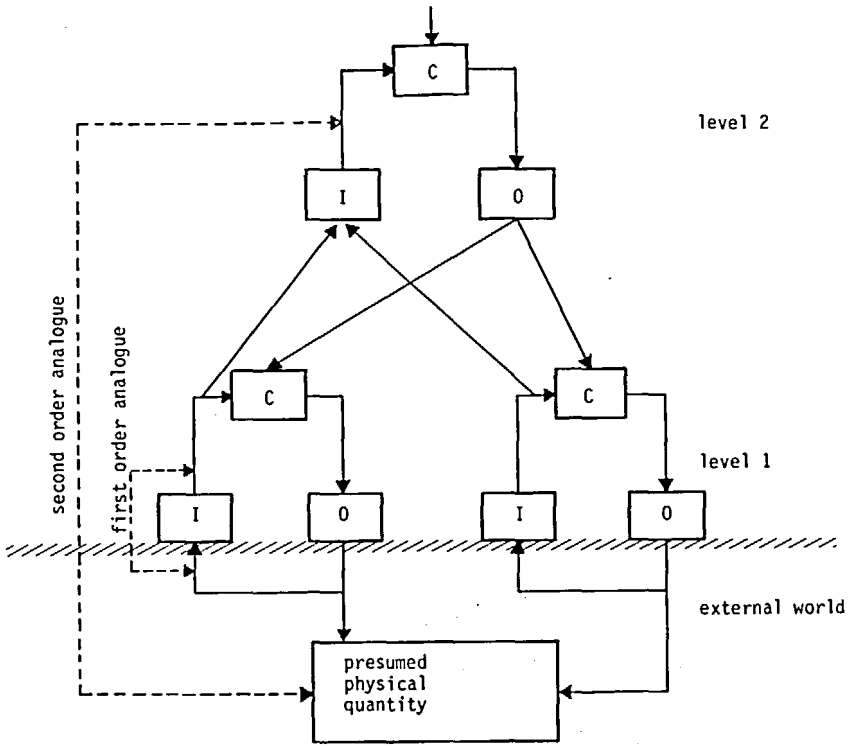

Fig. 1. Hierarchy of two first-order control systems and one second-order system. I, input function, receiving input signals derived from exteroceptive, proprioceptive, and interoceptive stimuli; the input signals at level 2, i.e., second-order system, are analogues of the input signals of the lowest order, i.e., first-order, system. C, comparator function, comparing input signals and reference signals, i.e., output signals of higher order systems, and producing error signals. O, output function, transforming error signals into output signals. Output signals sent to lower order systems are behavioral program signals, whereas output signals sent to output devices (glands and muscles) are behavioral commands. [From Cools and Van den Bercken (1977).]

dom of the spinal cord in programming the behavior under discussion (Edgerton *et al.*, 1976).

Thus, Powers created a conceptual model for nervous system operation by conceiving the brain as an integrated whole of hierarchically ordered feedback systems controlling the input signals of the organism. In principle the cerebral organization of behavior shares all properties inherent to any hierarchical system model. Thus, correct functioning of higher order levels and wrong functioning of lower order levels or *vice versa* can occur simultaneously. Furthermore, both activation of systems

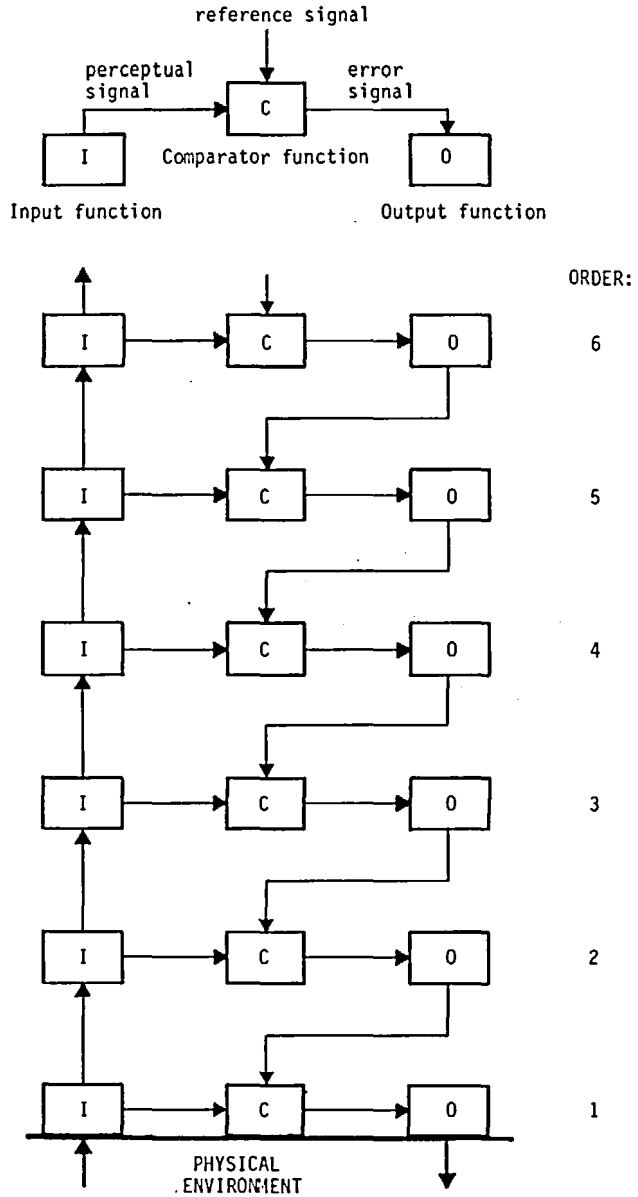

Fig. 2. Behavioral control system hierarchy; a simplified model. [From Cools and Van den Bercken (1977).]

at successively lower order levels and activation of systems at successively higher order levels are available to counteract disturbances at one or another level in the hierarchy. From this point of view, Powers' model provides a real bridge between Fentress' detailed concept of "hierarchical patterning of behavior," a successful attempt to unify knowledge about ethology in its broadest sense (Fentress, 1983), and Teitelbaum's detailed concept of "hierarchically organized systems inside the brain," a successful attempt to unify knowledge about separate response systems inside the nervous system (Teitelbaum *et al.*, 1983). Although I have to leave the discussion of the consistency between Powers' model and the other concepts in the hands of the reader—who is strongly advised to consider the excellent contributions of all three authors cited above—the key points of Powers' model, which will be discussed in the next sections, are certainly helpful in this respect (Carver and Scheier, 1982).

A. Delineation of Basic Terminology: Key Points of Powers' Concept

By definition, the organization inside the organism (brain) is an integrated whole of feedback control systems, which one can examine using principles and definitions of information theory, computer theory, servomechanism theory, and especially cybernetics. Thus, the organism receives input representing information on its current state, i.e., *input signals*, compares it with input representing information on the "desired" state, i.e., *reference signals*, produces *error signals* representing the difference between current and "desired" state, and, as a result, processes *output signals* directing behavior (Fig. 2). In principle, each hierarchical level deals with input, reference, error, and output signals. The input signals, derived from input signals of lower order systems (see below), carry information about the actual behavioral state; the reference signals, derived from output signals of higher order systems (see below), carry information about the behavioral state to be reached; the error signals, the weighted sum of input and reference signals, carry information about the magnitude of the discrepancy between the current and "desired" state; and the output signals, the reference signals for lower order systems (see below), carry information about what is to be done in order to reduce the error signals.

To illustrate this point, consider a situation in which a rat is bitten by a congener. Let us consider the bitten rat. Its current state is determined by the act of the partner: the bite. Its "desired" state is also evident: not receiving another bite. Accordingly, the bitten rat produces signals whose intent is to reduce the difference between the current and

the "desired" states by resulting in behavior that alters its input signals in such a way that the resulting error becomes zero. As soon as the bitten rat engages in behavior that prevents its partner from continuing to bite, the bitten rat has reached its reference condition. In practice, the rat will select a whole series of behavior patterns, varying from lateral threat to freezing, and ultimately will go one with the most successful one.

This example illustrates why Powers' concept also has direct consequences for classifying behavior. When classifying behavior according to common functional consequences, it is evident that lateral threat and freezing belong to different classes, i.e., offensive and defensive behavior, respectively. According to Powers' concept, however, these activities should be lumped together because both forms of behavior serve the same function: terminating the "undesired" state of the animal under discussion. In other words, Powers' concept implies that behavior should be analyzed in terms of formal aspects of its organization if one wants to delineate the properties of neuronal substrates controlling it. Thus, considering behavior in terms of common features instead of differences forms the cornerstone of the search for the function of a particular neuronal substrate.

B. Cerebral Organization of Input Signals

By definition, input signals to the outer shell or lowest order systems emanate from the physical environment (exteroceptive stimuli), interior of the body (interoceptive stimuli), and muscles, tendons, joints (proprioceptive stimuli). In contrast, all input signals of higher order control systems are analogues of quantities derived from input signals of lower order systems. Accordingly, the degree of abstraction of observable quantities of the physical effects increases at each higher order level in the hierarchy. These considerations provide the foundation for getting from "distal" to "proximal" stimuli.

In the example of the bitten rat, tactile, pressure, and, possibly, pain stimuli resulting from the bite are signals reaching the lowest order systems. When the organism engages in behavior attempting to reduce the resulting discrepancy between input and reference signals at this lowest order level, we are dealing with "reflexes." Since input signals reaching this outer shell of the organization inside the organism are also transformed into input signals of higher order systems, the organism ultimately has at its disposal the weighted sum of all input signals, i.e., signals received by the highest order systems. As the latter signals are just derived from "distal" stimuli, the resulting "proximal" input signals are still an-

alogues of attributes of the organism's "world" and accordingly represent the integrated whole of all aspects of this world at the highest order level. Since such signals are abstract, invariant functions constructed by the lower order systems themselves, they cannot be observed in any one of the physical effects. Still, knowledge about input signals becomes available on the condition that one knows the reference signals of the system under study, for input signals are compared with reference signals, and, accordingly, belong to the same class of signals. We will illustrate this in Section V–VII.

Given this insight, one can see how Powers' concept also has direct consequences for concepts such as "voluntary control." Let us consider two extremes: "operant behavior" and "adjusting the diameter of the pupil in response to changes in the amount of light on the retina." We are accustomed to thinking of two fully distinct phenomena: the former is defined as an attribute of the organism and is classified as adaptive behavior according to the adaptive consequences it serves (voluntary control), whereas the latter is defined as an attribute of the visual system and is classified as "reflex" behavior according to the causal factors on which it depends (involuntary control). According to Powers' concept, these behaviors are not that different. What is relevant is the recognition that there is a difference with respect to the degree of abstraction of observable quantities of the physical effects. When dealing with "operant behavior" the degree of abstraction is far more complex than in the case of the pupil response. Accordingly, input signals controlling "operant behavior" are far more difficult to understand than those controlling the pupil response: "voluntary control" or even "spontaneity" simply implies a greater lack of insight into their input signals, but certainly not an absence of such signals. There is only a quantitative, not a qualitative, difference between "voluntary control" and "involuntary control." This is exactly what Teitelbaum and his colleagues have recognized during the past decades. Their studies demonstrate how one can determine stimuli controlling motivated behavior [for review see Teitelbaum *et al.* (1983)].

C. Cerebral Organization of Reference Signals

By definition, the reference condition in a feedback control system is the controlled quantity of the system. The nature of this controlled quantity can be discovered by analyzing the responses of the system, for such responses are always characterized by a tendency to reduce the error in order to move toward a zero-error condition calling for no effort. In conceiving behavior as a process by which an integrated whole of hier-

archically ordered feedback systems, i.e., the brain, controls its input, it follows that the reference condition of the lowest order systems is determined by output signals of higher order systems. By the same token it follows that output signals of hierarchically higher order systems are reference signals for hierarchically lower order systems. Only the lowest order output signals are directly transformed by some output function into behavior. In this way one gets from "programs" to "behavior," with the restriction that *program* is defined as a nested set of rules reducing the degree of freedom in programming behavior. Since only the lowest order output signals direct *behavioral states*, i.e., actual consequences of a particular interaction between input signals and internal organization inside the organism, I propose to label these signals *behavioral commands*, in contrast to the reference signals reaching this and higher order systems, which I propose to label *behavioral program signals*.

Returning to the example of the localization of locomotor "generators" within the spinal cord, it will be evident that supraspinal structures direct the reference signals of these "generators." Absence of such reference signals in decerebrated cats, for instance, produces a zero-error condition calling for no shifts in behavioral states: such cats are indeed unable to walk or even to stand. When the cat is suspended in a waistband and its limbs are put on a treadmill, it immediately starts to trot or gallop, depending on the speed of the belt of the treadmill (Grillner, 1975, 1976). In fact, the researcher has now produced changes in the input signals of the lowest order systems, i.e., signals representing changes in tactile, pressure signals, and so on. Comparison of these signals with the reference condition—which is zero, due to the decerebration—results in an error signal, which in turn processes an output signal, the latter signal directs behavioral commands producing behavioral states attempting to reduce this error to the zero condition (Edgerton *et al.*, 1976).

D. Cerebral Organization of Output Signals

When one is dealing with a hierarchy of feedback control systems, it is clear that information available for directing behavioral commands is minimal at the highest order level: it simply contains reference signals for lower order systems. This implies that output signals of these latter systems remain indefinite as long as their incoming reference signals, i.e., output signals of higher order systems, are not yet compared with their corresponding input signals. In a hierarchy controlling behavior, it is evident that the information going downstream carries more and more details about the behavioral state to be executed. In other words, the information

available for directing behavioral commands increases at each lower order level in the hierarchy and reaches its maximum value at the lowest order level in the hierarchy. The reverse holds true for the degree of freedom in programming behavior. The degree of freedom in programming behavior is maximal at the highest order systems, is reduced at each lower order level, and ultimately disappears at the lowest order level in the hierarchy. This has a great impact for ongoing behavioral programs: the information going downstream can be continuously updated according to changes occurring in input signals of levels that are not yet set by their incoming reference signals. In the given example of the "generators" for locomotor patterning this implies that the output signals leaving the reticular formation and directly reaching the spinal cord will have a lesser degree of freedom in programming and adjusting motor patterning than those output signals that leave the cortex and indirectly reach the spinal cord via a great number of intercalated brain structures, such as the neostriatum. We discuss this aspect in more detail in Section V.

IV. BEHAVIORAL CONSEQUENCES OF CHANGES IN THE CEREBRAL ORGANIZATION

Now that the general outline has been established for a model of cerebral organization of behavior it becomes possible to refine our insight into the function of a particular level by using more explicitly formulated principles. What could the behavioral consequences be of a system being disturbed? In general, spontaneously occurring or experimentally induced changes in a particular part of the brain always affect one or another level in the hierarchy. In principle such changes can be due to an actual intervention with input, reference, error, or output signals of the affected system. Since such an intervention can ultimately produce two extremes, i.e., the magnitude of the signals becomes zero or the magnitude of the signals becomes maximal, it is evident that explaining a behavioral change in terms of feedback control systems is an extremely difficult task, especially when the hierarchy itself has a nonlinear, overlapping structure. Solving such a problem requires a dynamic system approach. Although our present state of knowledge does not yet allow us to develop exact system equations, Powers' concept offers two relevant starting points:

1. Behavior—the consequence of the interaction between input signals and organization inside the organism—controls the organism's input. This definition allows us to derive the most relevant parameters for a

dynamic system approach from behavior itself, especially its programming features.

2. Brain is a (nonlinear, overlapping) hierarchy of negative feedback control systems. This definition allows us to conceive of behavior as responses that normally reduce, but not increase, the error between input and reference signals.

For the sake of generality, at this point I leave unspecified the system level under discussion and denote it merely as level *n*. Later I use the principles discussed in this section.

A. Initiation, Maintenance, and Termination of Behavioral Programs

Normally comparison of input and reference signals of system *n* results in error signals: there is a difference between the actual and "desired" states. As long as this difference at each instant of time is smaller than the difference at the preceding time, the output signals go on producing detailed reference signals for lower order systems, i.e., behavioral program signals that going downstream in the hierarchy, are ultimately transformed into behavioral commands. The consequence at the behavioral level is the execution of behavioral programs resulting in the initiation, maintenance, and termination of behavioral states. The resulting behavior, in turn, affects the input signals of system *n*. As soon as system *n*, comparing input and reference signals, detects no difference, the reference condition has been reached and will be reset for initiating the next behavioral program. Although the reference condition itself is not directly observable, analysis of the behavioral states, which, by definition, reduce the gap between input and reference signals, will do. As soon as the reference condition is reached, the relationship that a moment before constituted an error becomes the no-error condition; given a sudden change of the reference condition, the relationship that a moment before constituted the zero-error condition becomes the error condition.

Considering the example of the bitten rat, analysis of the mutual interaction between victim and aggressor following a bite will ultimately reveal the nature of the reference condition of the victim. As soon as the behavior of the victim is no longer directed by, but at most adjusted to, its partner, the victim has apparently reset its reference condition. Accordingly, all behavioral states being displayed should be analyzed in terms of one common feature, i.e., reducing the difference between input and reference signals. It will be clear that the reference condition will vary from victim to victim. A subdominant rat, for instance, may just try

to keep a certain distance between it and its partner, in contrast to a fully submissive rat, which may not rest until it becomes unobservable.

As long as resetting remains absent because of a particular intervention system, n will maintain its zero-error condition, which, by definition, calls for no effort: there will be a characteristic loss of behavior programmed by system n. In other words, the resulting loss of degree of freedom in programming behavioral states can be used to delineate the characteristic function of system n.

The remaining degree of freedom in programming behavior reflects the plasticity of unaffected systems in the brain. Limiting ourselves to the plasticity inherent to hierarchical structures, there are at least two factors underlying such a degree of freedom. First, systems superior to system n are still able to produce reference signals for systems inferior to system n in a nonlinear hierarchy. In that case the current reference signals that normally are sent to system n now bypass system n and consequently directly reach systems inferior to it, allowing the organism to direct behavioral programs that may produce input signals reducing the error condition of systems superior or inferior to system n. Second, systems inferior to system n are still able to produce correct output signals in an overlapping (and necessarily branching) hierarchy. In that case the remaining reference signals sent to systems inferior to system n, i.e., all output signals of systems superior to them apart from those of system n itself, determine the reference condition of systems inferior to system n, allowing the organism to use the latter systems for producing correctly functioning output signals. Considering the neuroanatomical connections, i.e., the prerequisites for transmission of signals within the brain, it is quite likely that the brain indeed operates as a nonlinear, overlapping hierarchy allowing the occurrence of the above-mentioned plasticity. We will see, in Sections VI and VII, that these phenomena indeed occur.

B. Repetition of a Particular Behavioral Program

In addition to circumstances in which the difference between input and reference signals is reduced to zero or remains zero, there are also circumstances in which this difference becomes fixed. In that case system n goes on producing fixed output signals, i.e., sending fixed reference signals to lower order systems, and, accordingly, producing behavioral states that deliver fixed input signals to system n. The consequence at the behavioral level is the repeated execution of a single behavioral program, resulting in repetition of the same behavior.

Organisms having a nonlinear, overlapping hierarchy can only alter this state when the reference signals sent to system *n* are reset; such a resetting only occurs on the condition that input signals of systems superior to system *n* are altered. Since systems inferior to system *n* go on receiving their reference signals from system *n*, these inferior systems remain functioning in a correct manner. Consequently, such organisms are not able to interrupt the ongoing behavioral program by resetting the reference signals of systems inferior to system *n* with the help of signals bypassing system *n*.

In normal animals such a situation often occurs. For the case of the behavior of the bitten rat, for instance, such a state is present during the execution of behavioral programs responsible for freezing. According to Powers' concept, the ongoing repetition of this program implies that the resulting behavior state does not alter the input signals of the system directing this program. In that case the input signals reaching the system responsible for freezing can only be "spin offs" of input signals of systems superior to that system. Given the notion that freezing is rather successful in terms of terminating the biting behavior, the program responsible for freezing is probably directed by input signals derived from stimuli deriving from the partner. Since the ultimate reference condition for any rat will be the maximally realizable degree of freedom in programming its own behavior, it is likely that the system directing the program for freezing in response to the partner's behavior is indeed superimposed on other systems. Since such superimposed systems will vary their output signals according to changes in their corresponding input signals, the reference signals of the system responsible for freezing are reset as soon as such changes occur, resulting in the termination of freezing. Consequently, analysis of the behavior that immediately precedes the disappearace of freezing can provide information on the relevant input signals of the systems sending reference signals to the system responsible for freezing.

C. Abrupt Interruption of Behavioral Programs

Finally, there are circumstances in which the difference between input and reference signals increases, but does not decrease. When this occurs the magnitude of the error and output signals also increases. Consequently, the ongoing behavioral program is interrupted, starts over, finishes hastily, and so on. In a hierarchy of feedback control systems such a disturbance at the level of system *n* will affect all systems at successively lower order levels. Again, organisms having a nonlinear, overlapping hierarchy can only alter such a state when the magnitude of

reference signals sent to system *n* alters as a consequence of changes in the magnitude of input signals of systems superior to system *n*.

Such a state can indeed occur under particular circumstances. For the case of the behavior of a rat being bitten by an aggressor in a small enclosure, such a state is present during the time preceding the freezing. During that period the victim goes on executing shorter and shorter behavioral sequences, which show a decreasing degree of complexity as time progresses: ultimately the rat may just display chaotic sequences of isolated motor elements as manifested in shivering. Apart from one behavioral program, i.e., the one responsible for freezing, all remaining programs share one common characteristic feature: they result in changes in posture and/or movements that *per se* increase the "undesired" behavior, i.e., receiving another bite. According to Powers' concept, the rat's behavior produces consequences that deliver input signals that increase, but do not decrease, the error condition of the system responsible for the "desired" state. Since the resulting output signals are reference signals for lower order systems, the magnitude of reference signals received by systems downstream in the hierarchy increases, but does not decrease. From this point of view the successive appearance of behavioral elements with a decreasing degree of complexity simply reflects the successive activation of lower order systems in the hierarchy. I discuss this in more detail in Section VI. Since such rats may ultimately start to freeze, the "chaotic" shifts of behavioral programs of lower order systems in the hierarchy are ultimately successful in providing input signals for systems superior to the system responsible for freezing: only systems superior to the latter one are able to fix the reference signals of that system, a *conditio sine qua non* for the maintenance of freezing behavior. In other words, the animal produces changes at successively lower order levels, i.e., chaotic sequences of behavioral elements with a decreasing degree of complexity, until one of the resulting behavioral consequences produces input signals that affect systems superior to the system responsible for freezing. Consequently, analysis of the successively appearing behavioral states can provide information on the hierarchical structure of the cerebral organization of behavior.

V. DELINEATION OF RULES OF ORDER IN THE CEREBRAL ORGANIZATION OF BEHAVIOR

Now that we know something about the function of a single level within a nonlinear, overlapping hierarchy of negative feedback control

systems, we can put the formulated principles into practice. Since the behavioral consequences of disturbed systems form the basis of the search for "rules of order" in a hierarchy of feedback control systems, one has to select techniques that are as specific and selective as possible with respect to the disturbance produced. In brain and behavior research several techniques are used to alter the functioning of demarcated regions or processes within the brain, each of them having its own characteristic advantages and disadvantages: electrical stimulation (Ranck, 1975), lesioning (Schoenfeld and Hamilton, 1977), and chemical stimulation (Myers, 1974). In my opinion, a short-term chemical intervention is the most powerful technique, provided (1) one uses the intracerebral technique, (2) selects the agent on the basis of its pharmacological specificity and selectivity with respect to the postsynaptic receptors involved, and (3) includes adequate control studies in that respect (drug specificity, concentration, volume, pH, and solvent (Cools, 1981c). The latter condition allows us to intervene selectively with cells, but not passing fibers, glial cells, or blood vessels, to perform intraindividual studies, because of the reversibility of the experimentally induced effects, to interfere specifically with information carried by previously selected neurons, and to compare effects due to prevention of the transmission of particular information with effects due to facilitation of the transmission of that information. Because of these advantages, we have used the chemical intervention technique to delineate the function of circumscribed brain processes in programming behavior (see Section VI), a goal that cannot be reached with the help of the other techniques.

On the other hand, the lesion technique is a very powerful tool in searching for rules of order in the cerebral organization of behavior. Teitelbaum and his colleagues have beautifully illustrated how the lesion technique can provide information on the input signals directing isolated systems in animals with lesioned brain structures [for a review see Teitelbaum *et al.* (1983)]. For instance, large lateral hypothalamus lesions have been found to result in the isolation of lower order systems directing the behavioral program responsible for support. Detailed search for input signals affecting this so-called "postural support subsystem" has revealed that vestibular, kinesthetic, tactile, gastric, and thermal stimuli are relevant in this respect. Only some stimuli, such as pressure and cold, are input signals of the lowest order systems, whereas the remaining ones are known to affect higher order systems. In other words, the so-called "postural support subsystem" consists of at least one or more systems superior to the lowest order systems. Teitelbaum *et al.* (1983) have been able to delineate at least five of such subsystems, systems responsible for locomotion, postural support, head-scanning, orienting, and mouthing,

respectively. In addition, the lesion technique allows us to obtain information on the order in which hierarchical systems superior to the isolated ones become successively activated and reintegrated. It is known that lesioned animals initially show one or another type of invariant behavior. During recovery, however, the degree of variability at the behavioral level slowly returns. According to Powers' concept, lack of degree of freedom in programming particular behavioral states, an effect initially seen after a lesion, implies that there are no higher order systems controlling the reference signals of the system responsible for programming the invariant behavioral state. As soon as systems superior to the system responsible for the display of invariant behavior become operative, the reference signals of that system become variable and consequently produce variability at the behavioral level. Since the degree of abstraction of observable quantities of the physical effects increases at each higher order level in the hierarchy, animals recovering from a lesion not only show an increasing degree of variability in their behavior, but also become susceptible to more and more complex input signals. Again, Teitelbaum and his colleagues (1983) have obtained very nice data in this respect by studying animals recovering from lateral hypothalamus lesions; for details, the reader is referred to their articles [for review see Teitelbaum *et al.* (1983)].

An analogous activation and integration of lower order systems into higher order systems occurs during ontogeny and maturation, a phenomenon recognized by Kortlandt (1955) and later elaborated by Plooy (1980), Fentress (1983), and Teitelbaum *et al.* (1983). Plooy's (1980) study, "The behavioral development of free-living chimpanzee babies and infants," is of great interest in this context. It nicely illustrates how even ontogenetic studies on open-field behavior of chimpanzees provide a demonstration of how lower order systems become successively integrated during development and maturation into systems that are hierarchically superior. This study also illustrates how the use of Powers' concept helps us to analyze the nature of reference signals controlling the systems that successively appear in the process of development and maturation; for details the reader is referred to Plooy's (1980) studies. Thus, both ontogenetic and lesion studies are very useful for searching for rules of order in the cerebral organization of behavior.

One of the main goals of neuroethology is to investigate which brain processes direct these rules of order. For that purpose the lesion technique is less useful because of its relative aspecificity with respect to the channels transmitting functionally distinct signals within a particular, spatiotemporally defined brain region: in addition to lesion-induced changes in passing fibers, glial cells, and blood vessels, the lesion affects all nerve cells and neurons independent of the signals carried by them. Given these

limitations, which also hold for electrical stimulation, it appears that chemical stimulation is the tool of choice for the purpose outlined above.

VI. DELINEATION OF BRAIN PROCESSES DIRECTING RULES OF ORDER IN THE CEREBRAL ORGANIZATION OF BEHAVIOR

In the search for brain entities directing rules of order in programming behavior the following questions occupy a central position:

1. To which hierarchical level does the selected brain entity belong?
2. Which afferents, efferents, and intrinsic neurons of the selected brain entity carry input, reference, error, and output signals?
3. Along which pathways are the output signals, i.e., reference signals for lower order systems, carried downstream in the hierarchy?
4. How is the information being carried by the output signals ultimately transformed into behavioral commands?

To illustrate how to attack these questions, we consider the nigrostriatal dopaminergic fibers terminating within the neostriatum (rats) or caudate nucleus (higher mammals). As mentioned, use of the "consequence" strategy has allowed us to delineate the function of this brain entity as follows. It determines the degree of flexibility with which the organism can cope with its environment by virtue of its ability to change the ordering and sequencing of behavioral programs at hierarchically distinct levels of the cerebral organization of behavior; as a consequence, the organism has access to information relevant for directing the syntax involved (Cools, 1981b; cf. Ridley *et al.*, 1981). This conclusion is based upon the finding that a spontaneously occurring or experimentally induced hypoactivity of this entity in rats, cats, monkeys, and even humans reduces the capacity to alter the ordering and sequencing under certain highly specified conditions (Cools, 1980; Cools *et al.*, 1983a,b, 1984; Jaspers *et al.*, 1983a–c; Van den Bercken and Cools, 1982); studies using animals with a chemically induced hyperactivity have offered analogous data.

Since all systems superior to the lowest order systems direct behavioral programs, interference with any level superior to the lowest ones will alter the ordering and sequencing of behavioral states: by definition, any program deals with ordering and sequencing. In other words, we need to specify "the degree of flexibility in coping with its environment." Thus, specifying the hierarchical level involved requires a more precise de-

scription of the actual loss of degree of freedom in programming behavior. For that purpose we have to describe the behavioral states, i.e., consequences of changes in the output signals of the unknown system, in relation to available input stimuli, i.e., putative input signals of the system under study. Concerning the putative input signals, one has to realize that they are derived from (1) exteroceptive, (2) proprioceptive, and (3) interoceptive stimuli. Below I illustrate how to define the nature of the hierarchical system affected by haloperidol, a drug that selectively prevents the transmission of information from the nigrostriatal dopaminergic fibers to their corresponding postsynaptic elements by blocking the postsynaptic dopamine receptors, and by apomorphine, a drug that selectively facilitates the transmission of the latter information by activating the postsynaptic dopamine receptors.

A. How to Specify the Hierarchical Level of a Brain Entity: An Illustration

To analyze alterations in the ordering and sequencing of behavioral states it is necessary to select a design allowing the animal to switch behavioral states under different, but specified, conditions with regard to the possible use of exteroceptive, proprioceptive, or interoceptive stimuli as sources for input signals. The so-called swimming test for rats creates such a situation [for details see Cools (1980)].

1. Swimming Test

Rats forced to swim in a basin from which there is no escape start to explore the basin by switching behavioral states. During the so-called exploration phase the rat displays such behavioral states as swimming to the side of the basin and exploring the side just above the surface of the water with snout and forelimbs, diving to the bottom of the basin and exploring all parts under water, crossing the center of the basin and treading water together with scanning the area above the surface of the water, and so on. All these behavioral states are apparently directed by input signals derived from exteroceptive stimuli that *per se* are invariant.

After a certain time interval a so-called life-saving phase starts. During that phase the rat switches to such behavioral states as swimming in circles, treading water in the center of the basin, using hindlimb kicks to propel it above the surface of the water, planing without success (i.e., hanging immobile followed by sinking to the bottom or half-way and then swimming to the surface), and so on. The rat repeats each behavioral

state a few times and then switches to another. In this case the behavioral states are at most adjusted to, but not directed by, input signals derived from exteroceptive sources. Thus, the behavioral states, not directed by input signals derived from exteroceptive and proprioceptive (see below) stimuli, are apparently directed by a different kind of input signals, the degree to which the input signals are derived from interoceptive stimuli remains to be investigated.

As time progresses the rat goes on switching its behavior from one state to another until it is able to keep its head well above the surface of the water. Most often the rat, having a spherical shape, possibly due to filled lungs, is planing with its forelimbs held immobile in front of it. From that moment on the rat goes on maintaining the final state and as a result survives. Thus, detecting a successful behavioral state implies the end of the process of switching. During the whole process of switching the behavioral states themselves are directed by input signals derived from proprioceptive stimuli that vary according to the postures adopted. When the invariant exteroceptive stimuli are changed by dropping a rope into the center of the basin during the display of a successful strategy, the rat sooner or later detects the rope and, after touching it a few times, escapes by climbing onto it. Now again the resulting behavioral state is directed by input signals derived from exteroceptive stimuli. When the rat is retested, it rapidly switches to the previously performed successful strategy, indicating that one-trial learning occurs in this design (A. R. Cools, unpublished data). After such a one-trial experience, input signals derived from exteroceptive stimuli are apparently able to direct the whole chain of required behavioral events, a phenomenon absent in the initial trial. In other words, the exteroceptive stimuli have now become conditioned stimuli, i.e., exteroceptive stimuli triggering a whole behavioral program. Accordingly, the resulting behavioral states are now directed by input signals derived from conditioned stimuli.

2. *Rats with Hypofunctioning or Hyperfunctioning Dopaminergic Activity within the Neostriatum*

With the help of the swimming test it was possible to show that a haloperidol-induced hypofunctioning dopaminergic activity within the neostriatum of rats only reduces the capacity of ordering and sequencing of behavioral states when the animal is unable to use input signals derived from proprioceptive, exteroceptive, or conditioned stimuli for directing the behavioral states to be executed (Cools, 1980, and unpublished data). Thus, such rats still execute (1) normal postural adjustments with the help of proprioceptive stimuli, (2) correct switchings during the exploration

phase with the help of exteroceptive stimuli, (3) climbing onto the rope with the help of exteroceptive stimuli, and (4) correct switching to planing with success in a second trial with the help of conditioned stimuli. In contrast, such rats are unable to switch behavioral states during the life-saving phase: they are not able to switch to behavioral states without using exteroceptive or proprioceptive stimuli. Experiments with rats with an apomorphine-induced hyperfunctioning dopaminergic activity within the neostriatum have confirmed that the striatal dopaminergic activity indeed determines the degree of ordering and the sequencing of behavioral states that are not directed by input signals derived from exteroceptive, proprioceptive, or conditioned stimuli (Cools, 1980).

In other words, these experiments allow the investigator to specify the nature of the hierarchical system affected. The nigrostriatal dopaminergic fibers belong to a system that orders and sequences behavioral programs without input signals derived from exteroceptive, proprioceptive, and conditioned stimuli. I propose to define the function of this system as *arbitrarily programming the ordering and sequencing of behavioral states*, labeling the underlying capacity a *shifting aptitude*. To prevent misunderstanding, recall that all signals directing behavioral programs, including those controlling the system under discussion, are ultimately derived from physical effects. Thus, organisms with an operative neostriatum have only a relatively higher degree of freedom in ordering and sequencing behavioral programs than organisms with an inoperative neostriatum: they are still using analogues of attributes of stimuli to direct the programming of their behavior, although the degree of abstraction of physical effects in animals with an operative neostriatum is greater than that of animals with an inoperative neostriatum.

B. How to Specify Signals Carried by a Brain Entity: An Illustration

Having delineated the nature of a hierarchical system, now we can analyze the output signals of this system, since the system-specific loss of degree of freedom in programming behavior is ultimately the consequence of a disturbed output condition of that system. Thus, experimentally induced disturbances that suppress the capacity of arbitrarily programming the ordering and sequencing of behavioral states indicate that the output signals of the affected system normally carry information allowing the animal to use this capacity. Given this knowledge, it becomes possible to specify the target site of the chemical intervention in terms of input, reference, error, and output signals. For that purpose it is necessary to select a design allowing the animal to alter its reference condition

during a test. As illustrated below, such a design enables the investigator to predict which signals are affected by the chemical intervention. The so-called treadmill test for cats creates such a situation: in this design the animal alters its zero-reference condition to a reference condition with a fixed magnitude larger than zero (Cools *et al.*, 1983a,b; Jaspers *et al.*, 1983a–c; Heim *et al.*, 1983).

Before discussing this design, it is useful to recall that there are in principle the following sources for directing behavioral states: (1) exteroceptive stimuli, which are emitted by the physical environment of the organism and detected by sensory receptors for pressure, light, vibration, chemical quantities, etc.; behavioral states directed by such stimuli are labeled as exteroceptively directed; (2) proprioceptive stimuli, which are emitted by muscles, tendon, organs, and joints; they are detected by sensory receptors for the position of limbs and body, length of striped muscles, etc.; behavioral states directed by these stimuli are labeled as proprioceptively directed; (3) interoceptive stimuli, which are emitted by the interior of the body and detected by sensory receptors for contraction of the stomach, etc.; behavioral states directed by these stimuli are labeled as interoceptively directed; and (4) coordinating mechanisms within the brain. Behavioral states directed by the latter mechanisms should be labeled as non-stimulus-directed; in practice, however, they are labeled as non-exteroceptively directed, given "the benefit of the doubt." In the case of conditioning we must include here conditioned stimuli, i.e., stimuli that direct a particular chain of behavioral states as a consequence of a learning process; in that case we label such a chain of behavioral states exteroceptively triggered when exteroceptive stimuli are conditioned, proprioceptively triggered when proprioceptive stimuli are conditoned, and interoceptively triggered when interoceptive stimuli are conditioned. In the following sections this terminology will be used to characterize the distinct behavioral states.

1. Treadmill Test

Cats walking on a treadmill have the freedom to alter their behavior by approaching a panel at the front of the treadmill, pushing their head through a small opening in this panel, and collecting food pellets by bending their head toward a hidden food-dispenser; there are no auditory, visual, or olfactory stimuli signalling the presence of food behind the panel. Normally, cats trained to walk on the treadmill and deprived of food for a minimum period of 24 hr display one or more of the following behaviors:

1. The cat simply maintains the ongoing motor patterning, i.e., trotting somewhere in the middle of the treadmill. According to the servomechanism theory, such a cat has a zero-reference condition for food-collecting behavior: it does not show any attempt in this direction.

2. The cat switches to exteroceptively directed behavioral states, continuously matching the stimuli inherent to the treadmill; the states allowing the cat to collect food are directed by input signals derived from exteroceptive stimuli. For example, the cat starts to fix visually a particular part of the opening in the front panel and proceeds upon approaching this opening to increase its speed or alter its gait, thereby continuously fixating the chosen target; as soon as the cat sees the pellet through the opening, it shifts its gaze from the opening toward the food, which is now fixed until the pellet is collected. In other words, such a cat suddenly changes its original zero-reference condition for food-collecting behavior: it starts exhibiting fruitful attempts in this direction by performing a series of behavioral acts, each of which is directed by a particular exteroceptive stimulus.

3. The cat switches to non-exteroceptively directed behavioral states allowing it to collect food: it switches without using observable exteroceptive stimuli to direct its behavioral acts. For example, the cat fixes neither visually nor tactually any part of the treadmill: it simply shifts from staying in the middle of the belt toward approaching the front of the panel by increasing its speed or altering its gait without having the opportunity to see, smell, or touch the food at the moment of this shift and without using any other stimulus inherent to the apparatus. In other words, such a cat also changes its original zero-reference condition for food-collecting behavior: it starts exhibiting fruitful attempts in this direction by performing a series of behavioral acts, of which at least the first ones are certainly not directed by exteroceptive stimuli.

4. The cat switches to exteroceptively triggered behavioral states allowing it to collect food: it is using exteroceptive stimuli to direct the whole chain of required behavioral events, a phenomenon that only occurs in cats tested often in this design. In practice this implies that the cat uses one of the available exteroceptive stimuli as a conditioned stimulus for the performance of the whole sequence. For example, a cat starts to execute the sequence of approaching the front panel, bending its head through the opening, and collecting the food as soon as the belt starts moving; in that case the altered speed triggers the whole sequence. In other words, such a cat also changes its original zero-reference condition for food-collecting behavior: it starts exhibiting fruitful attempts in this direction by performing an exteroceptively triggered chain of behavioral acts.

Before considering the actual shift of the reference condition from zero to larger than zero, it is useful to point out that this design, in common with the swimming test for rats, allows us to describe behavioral consequences in relation to input signals derived from available stimuli. First, the cats are permanently forced to adjust their postures during walking; thus, deficits due to a reduced capacity to use proprioceptive stimuli can be detected. Second, cats can display a mix of behaviors 2 and 3; thus, deficits due to a reduced capacity to use exteroceptive stimuli (behavior 2) and deficits due to a reduced capacity to switch to non-exteroceptively directed behavioral states (behavior 3) can be detected. Third, cats can show behavior 4; thus, deficits due to a reduced capacity to use conditioned stimuli can also be detected. Finally, only deprived cats are able to display the food-collecting behavior; thus, deficits due to a reduced ability to use stimuli inherent to deprivation can be detected.

What is relevant for specifying the actual target site of the chosen chemical intervention, haloperidol, is the recognition that cats that have not yet altered their ongoing motor patterning are marked by a zero-reference condition, matched with a zero-input condition, concerning the food-collecting behavior: in that case the cats are displaying behavior 1. Since all cats apart from the conditioned ones only display this behavior at the beginning of the trial, the cats are always marked by a zero-reference condition, matched with a zero-input condition, for food-collecting behavior at the beginning of the experiment. This implies that the magnitude of the output signals of the system controlling food-collecting behavior is also zero at that time. Since the output signals of this system have to be considered as reference signals for hierarchically inferior systems allowing the cat to collect food, it is evident that the latter systems are also marked by a zero-reference condition, matched with a zero-input condition, as long as the food-collecting behavior does not occur. In other words, the system controlling switching to non-exteroceptively directed behavioral states is also marked by a zero-input, zero-reference, zero-error, and zero-output condition at the beginning of each experiment; the same holds true for the system responsible for switching to exteroceptively directed behavioral states. Indeed, the cat does not show any attempt to switch to non-exteroceptively directed or exteroceptively directed behavioral states at the beginning of the experiment.

As time progresses, cats suddenly start to alter their ongoing motor patterning by executing the above-mentioned behaviors 2, 3, or 4. At that moment the zero-reference condition is apparently changed to a new reference condition. Given the fact that there is only one particular ordering allowing the cats to collect food, the new reference signals are locked in. The latter signals remain fixed until the cats exhibit behavioral conse-

quences producing input signals that match the new reference condition. Since the exteroceptive stimuli remain invariant during the whole experiment, only input signals derived from other sources can introduce the mentioned shifts. Given the fact that only deprived cats show the food-collecting behavior, changes in the degrees of deprivation may be relevant in this respect. In any event, cats that collect a single food pellet terminate their food-collecting behavior and reinitiate trotting. The latter implies that the zero-reference condition for food-collecting behavior is again reached and remains zero as long as the cats go on repeating their program for trotting or galloping.

2. *Cats with Hypofunctioning or Hyperfunctioning Dopaminergic Activity within the Caudate Nucleus*

Just as for rats with an experimentally induced hypofunctioning dopaminergic activity within the neostriatum, cats with analogous deficits due to intracaudate injections of haloperidol show a reduced capacity to program arbitrarily the ordering and sequencing of behavioral states, allowing us to generalize our earlier conclusion about the rat neostriatum to the feline caudate nucleus. In fact, assessment of the above-mentioned design has been shown that haloperidol-treated cats either are fully unable to display switching to non-exteroceptively directed behavior (behavior 3) or are significantly less able to display this behavior; in contrast, they are still able to display behaviors 1, 2, and 4 (Cools *et al.*, 1983a,b; Jaspers *et al.*, 1983a). In other words, they show a strong deficit concerning their ability to switch *arbitrarily* the ordering and sequencing of behavioral states. Since the system-specific loss of degree of freedom in programming behavior is ultimately the consequence of a disturbed output condition of that system, the chosen chemical intervention, bilateral intracaudate injections of haloperidol, has accordingly produced this disturbance. Thus, such cats are at least marked by a disturbed output condition of the system responsible for switching to non-exteroceptively directed behavioral states. From the theoretical point of view such a phenomenon can be the consequence of four different effects of haloperidol:

1. The cat that wants to start eating and accordingly alters its original zero-reference condition in this respect remains unable to switch to non-exteroceptively directed behavioral states because haloperidol might fix the original zero-output condition of the system responsible for switching to non-exteroceptively directed behavioral states. Thus, haloperidol is assumed to reduce directly the magnitude of the *output* signals of this system. Accordingly, haloperidol also prevents this magnitude from

changing from the zero-output condition when the zero-output condition is reached. Given the fact that the output condition of the system responsible for switching to non-exteroceptively directed behavioral states is zero at the beginning of the experiment (see the description of the treadmill test), it will remain zero as long as haloperidol is operative: neither changes in input signals nor changes in reference signals of this system can alter such a fixed output condition.

2. The cat that wants to start eating and accordingly alters its original zero-reference condition in this respect remains unable to switch to non-exteroceptively directed behavioral states because haloperidol might fix the original zero-error condition of the system responsible for switching to non-exteroceptively directed behavioral states. Thus, haloperidol is assumed to produce indirectly a zero-output condition of that system as a consequence of its ability to reduce the magnitude of its *error* signals. Accordingly, haloperidol also prevents this magnitude from changing when the zero-error condition is reached. Given the fact that the error condition of the system responsible for switching to non-exteroceptively directed behavioral states is zero at the beginning of the experiment (see the description of the treadmill test), it will remain zero as long as haloperidol is operative.

3. The cat that wants to start eating remains unable to switch to non-exteroceptively directed behavioral states because haloperidol might fix the original zero-reference condition of the system responsible for switching to non-exteroceptively directed behavioral states. Thus, haloperidol is assumed to produce indirectly a zero-output condition of this system as a consequence of its ability to reduce the magnitude of its *reference* signals. Accordingly, haloperidol also prevents this magnitude from changing when the zero-reference condition is reached. Given the fact that the reference condition of the system responsible for switching to non-exteroceptively directed behavioral states is zero at the beginning of the experiment (see the description of the treadmill test), it will remain zero as long as haloperidol is operative. Since the zero-output condition that is present at the beginning of the experiment accounts for invariant input signals of the system responsible for switching to non-exteroceptively directed behavioral states, the zero-input condition of this system remains matched with its zero-reference condition. Accordingly, the resulting error and output conditions also remain zero as long as haloperidol is operative.

4. The cat that wants to start eating and accordingly alters its original zero-reference condition in this respect remains unable to switch to non-exteroceptively directed behavioral states because haloperidol might fix the original zero-input condition of the system responsible for switch-

ing to non-exteroceptively directed behavioral states. Thus, haloperidol is assumed to produce indirectly a disturbed output condition as a consequence of its ability to reduce the magnitude of the *input* signals of this system. Accordingly, haloperidol also prevents this magnitude from changing when the zero-input condition is reached. Given the fact that the input condition of the system responsible for switching to non-exteroceptively directed behavioral states is zero at the beginning of the experiment (see the description of the treadmill test), it will remain zero as long as haloperidol is operative. As soon as the zero-reference condition is replaced by a reference condition with a fixed value (see the treadmill test), the magnitudes of its error and output signals also become fixed. Given the experimentally induced zero-input condition of this system, the output signals are not able to affect the input signals and accordingly to reduce the resulting error and output signals as long as haloperidol is operative. This implies the presence of a fixed and consequently disturbed output condition: in that case the cat should suddenly increase its speed or alter its gait without using any stimulus inherent to the apparatus or food and subsequently interrupt this behavior before having reached the front panel, start over, finish hastily, and so on.

Given these four possibilities, we need additional information for specifying the actual target site of the chosen chemical intervention. In principle, two methods are available: also analyzing positive behavioral consequences of the chosen treatment, and analyzing the behavioral consequences elicited by a treatment altering the transmission in a direction that is diametrically opposite to that elicited by the former treatment.

When considering in more detail the behavioral consequences of haloperidol, two effects become apparent (Cools *et al.*, 1983a; Jaspers *et al.*, 1983a–c). First, some haloperidol-treated cats show no attempt to switch arbitrarily to non-exteroceptively directed behavioral states, whereas other haloperidol-treated cats show a significantly reduced capacity to switch in that sense. These phenomena, especially the former one, simply show that a zero-output condition is maintained throughout the whole experiment, allowing us to eliminate possibility 4. This conclusion fits in with the finding that none of the haloperidol-treated cats show behavior characteristic for the presence of output signals with a fixed value (see above) (Cools *et al.*, 1983a,b; Jaspers, 1983a). Second, haloperidol-treated cats switch to either exteroceptively directed or exteroceptively triggered behavioral states; they collect at least as many food pellets as solvent-treated cats do. In other words, the zero-reference condition for food-collecting behavior does change: systems controlling the exteroceptively directed or exteroceptively triggered behavioral states for food-collecting

behavior have apparently received correct reference signals in this respect. Such a phenomenon can only occur on the condition that systems sending reference signals to the striatal system are also sending their reference signals to other systems, bypassing the striatal system. Both sets of data show that altering the magnitude of output signals of systems superior to the striatal system does not have any consequence for the zero-output condition of the striatial system in haloperidol-treated cats. As mentioned above, it remains zero throughout the experiment.

By analyzing additionally the behavioral consequences elicited by a drug that promotes, rather than suppresses the transmission of information from nigrostriatal dopaminergic fibers to their corresponding postsynaptic elements, i.e., apomorphine, it becomes possible to specify the actual target site of haloperidol in terms of input, reference, error, and output signals. Cats that were treated with relatively high doses of apomorphine show a reduced number of attempts to switch to both non-exteroceptively directed and exteroceptively directed behavioral states; some cats do not even show any attempt to collect food (Cools *et al.*, 1983a,b; Jaspers *et al.*, 1983a–c). These phenomena, especially the latter ones, simply show that neither the error signals nor the output signals increase their magnitude. Had there been an increase the apomorphine-treated cats would have permanently shown unsuccessful attempts to switch arbitrarily to non-exteroceptively directed behavioral states. Given the fact that apomorphine is known to affect the transmission of information in a direction which is diametrically opposite to that in haloperidol-treated cats, it becomes possible to eliminate possibilities 1 and 2: it is impossible to reconcile apomorphine's inability to increase the magnitude of signals with haloperidol's ability to decrease the magnitude of the same signals. In other words, only possibility 3 is left: haloperidol indirectly produces a zero-output condition as a consequence of its ability to reduce the magnitude of the reference signals and, accordingly, to prevent the magnitude from changing when the zero-reference condition is reached. Given this notion it is evident that apomorphine increases the magnitude of these signals. In control cats the correct execution of programming arbitrarily the ordering and sequencing of non-exteroceptively directed behavioral states is a direct consequence of reducing the error between input signals and a fixed magnitude of reference signals (see explanation of treadmill test). Thus, an intervention that increases the magnitude of the reference signals will never result in a zero-reference condition; as mentioned, this is exactly what happens in some cats treated with relatively high doses of apomorphine. Such cats never use the freedom to program arbitrarily the ordering and sequencing of non-exteroceptively directed behavioral states.

Taking all the above-mentioned findings together, haloperidol, which inhibits the transmission of information from nigrostriatal dopaminergic fibers to their corresponding postysynaptic elements by blocking postsynaptic dopamine receptors, has been found to reduce the magnitude of the reference signals to zero and, accordingly, to prevent it from changing from the zero-reference condition when the latter condition is reached. In contrast, apomorphine, which promotes the transmission from the nigrostriatal dopaminergic fibers to their corresponding postsynaptic elements by activating postsynaptic dopamine receptors, has been found to increase the magnitude of the reference signals until maximum value is reached.

C. Neostriatum: System for Programming Arbitrarily the Ordering and Sequencing of Behavioral States

As mentioned, cats or rats that are marked by a haloperidol-induced zero-output condition of the striatal system are still able to switch to exteroceptively directed, exteroceptively triggered, or proprioceptively directed behavioral states, allowing them to reach the ultimately desired state (cats: collecting food; rats: surviving). Thus, such animals are still able to switch arbitrarily from one type of ordering and sequencing to another type, although they lack the capacity to program arbitrarily the ordering and sequencing itself. In other words, the reference signals sent to the striatal system are also sent to systems controlling programs responsible for switching arbitrarily to exteroceptively directed, exteroceptively triggered, and proprioceptively directed behavioral states; later we will see that the latter systems are, in fact, inferior to the striatal system (see Sections VII and VIII).

From this point of view it becomes evident that the reference signals under discussion carry the code for *arbitrarily programming behavior* without prescribing the required ordering and sequencing. Accordingly, the striatal system actually transforms this code into a new code, i.e., *arbitrarily programming the ordering and sequencing of behavioral states*. Consequently, the striatal system reduces the degree of freedom in programming behavior by adding information about the required ordering and sequencing of behavioral programs without the help of exteroceptive or proprioceptive stimuli. In this way the striatum contributes to the process of the necessary transformation of behavioral program signals into behavioral commands, i.e., signals directing behavioral states.

In summary, the chosen approach allows us to specify the function of a single neuronal fiber system in terms of input, reference, error, and

output signals of a particular system within the hierarchy of negative feedback systems controlling behavior. Once acquainted with the code carried by the output signals of a particular hierarchical system, it becomes possible to investigate how this information is carried downstream in the hierarchy, and how it is ultimately transformed into behavioral commands. Tracing the efferents of the hierarchical system under study is the method of choice for delineating systems that are inferior but as close as possible to it. Since output signals of higher order systems are reference signals of lower order systems, knowledge about the former output signals provides an excellent starting point for outlining the details of the function of lower order systems. Although it is not yet possible to map the whole process of transformation of behavioral programs into behavioral commands, we will consider two steps downstream in the hierarchy by following the information leaving the striatum. Before discussing these aspects (see Sections VII and VIII), it is relevant to consider the behavioral consequences of a striatal system that produces wrong output signals; such an analysis will help us understand the characteristic features of hierarchical systems inferior to the striatal system.

D. Behavioral Consequences of Increasing the Magnitude of Reference Signals of the Striatal System: Apomorphine

As mentioned above, apomorphine, which promotes the transmission of information from nigrostriatal dopaminergic fibers to their corresponding postsynaptic elements by activating postsynaptic dopamine receptors, increases the magnitude of reference signals of the striatal system until their maximum value is reached. Accordingly, animals so treated go on altering their output signals, which *per se* are correct. Since the latter signals are reference signals of hierarchical lower order systems, the whole flow of information going downstream in the hierarchy shows analogous fluctuations as long as the resulting behavioral consequences do not deliver input signals to systems superior to the striatal system. Such cats go on interrupting programs directed by systems inferior to the striatal system. In a hierarchy of negative feedback control systems the highest order system has the slowest response, and the lower in the hierarchy the output of these systems is affected, the less time it takes before the disturbance becomes manifest. Thus, behavioral consequences characteristic of disturbances of higher order systems will be successively replaced by behavioral consequences characteristic of disturbances of lower order systems. Consequently, the latter effects will ultimately dominate. This is exactly what happens in a number of cats treated with relatively

high doses of apomorphine (Cools *et al.*, 1983a; R. Jaspers *et al.*, unpublished data). Initially they show a reduced ability to program arbitrarily the ordering and sequencing of non-exteroceptively directed behavioral states. Then they show a reduced ability to program arbitrarily the ordering and sequencing with the help of exteroceptive stimuli. Ultimately they are no longer able to program their behavior in any respect: they have even lost their capacity to avoid falling down when their body touches the back panel of the treadmill.

Analogous effects are observed in rats displaying so-called apomorphine or amphetamine stereotypy. As outlined by Lyon and Robbins (1975) and later by Iversen (1977), the following events occur when the doses increase and consequently the magnitude of the reference signals of the striatial system increases: (1) complex behavioral chains or behaviors requiring longer pauses are the first to be eliminated as the dose–response effect increases (e.g., sleep, feeding, certain types of social behavior), (2) behaviors capable of repetition without long pauses then dominate the behavioral pattern and their rate increases as the drug effect increases (e.g., locomotion, rearing), (3) shorter and shorter response sequences (e.g., licking, biting, moving forepaws) come to dominate the overt behavioral pattern, until finally only tremor is possible, and (4) in the final stages all overt activity ceases because the nervous system is in such a rapidly changing repetition pattern that no activity of consequence can be completed (Iversen, 1977). In this context it is interesting to note that morphine given to cats produces similar effects, but now in the reversed order (Cools and Van den Bercken, 1977). Following a systemic injection of morphine the following events are successively displayed: (1) irregular contractions in various muscle groups (e.g., ears, tongue, neck, toes), (2) continuous attempts to sniff and lick (without being successful), (3) continuous changes in bodily positions, (4) execution of uncontrolled movements (e.g., head, body, limbs), (5) continuous attempts to walk, climb, and groom, and (6) chaotic sequences of attempts to groom, walk, explore, etc. (Cools and Van den Bercken, 1977).

The apomorphine-induced effects only occur as long as the resulting behavioral consequences do not deliver input signals to systems superior to the striatal system. In that case the superior systems will alter their output signals and consequently reset the magnitude of the reference signals sent to the striatal system. This is exactly what happens in the swimming test during the so-called life-saving period (Cools, 1980). During that period rats are forced to program arbitrarily the ordering and sequencing of behavioral states in order to survive. Given the finding that control rats start to produce a particular ordering that is repeated for some time and then replaced by a new ordering that is also repeated for some time,

and so on, the rats are apparently able to reduce the difference between the input and reference signals of the striatal system and subsequently to reset the magnitude of the reference signals at that level. Thus, systems superior to the striatal system are able to alter their own output signals and accordingly the reference signals of the striatal system. Since there are, in practice, several ways to survive, e.g., swimming in circles, planing, or treading water, the system assessing the degree of mismatch between input signals and the zero-reference condition for survival does not fix the magnitude of the reference signals of the striatal system. As long as the rat's behavioral consequences worsen the degree of survival, the magnitude of the reference signals of the striatal system will increase until the maximum degree of freedom in programming arbitrarily the ordering and sequencing of non-exteroceptively directed behavioral states is reached: rats do not survive unless the magnitude of the reference signals of the striatal system reaches its maximum value. Thus, the rats go on increasing the magnitude of these reference signals until the resulting behavioral consequences are able to alter the input signals of systems superior to the striatal system. From that moment on the output signals of these hierarchical superior systems and consequently the reference signals of the striatal system may become fixed, implying that the program responsible for the ongoing behavior will be repeated. It will be evident that this occurs as soon as the rat starts to follow a successful strategy in terms of survival. From this point of view it becomes understandable why striatally administered apomorphine, which facilitates the process of reaching the maximum value of the reference signals of the striatal system (see Section VIB), actually improves the capacity of rats to survive in the swimming test (Cools, 1980). The above example nicely illustrates how spontaneously occurring or experimentally induced fluctuations in the information going downstream in the hierarchy can be terminated: only input signals that reach systems superior to the one that is primarily affected are effective in this respect (cf. the earlier example of terminating the freezing behavior; see Section IVB).

Against this background one may wonder why apomorphine-treated cats are not able to terminate the experimentally induced fluctuations in the information going downstream in the hierarchy. The reason for the absence of this phenomenon might be the magnitude of the apomorphine dose: only relatively high doses have been tested in the cat design, whereas much lower doses have been tested in the rat design. In a hierarchy of feedback control systems the lowest order system has the fastest response, and the higher in the hierarchy the output of these systems is affected, the more time it takes to send the information downstream in the hierarchy. Consequently, the degree to which disturbed

output signals of the striatal system are able to produce corresponding disturbances of systems at successively lower order levels is solely determined by the duration of the experimentally induced disturbance of the striatal output signals, i.e., a dose-dependent phenomenon.

As a final remark in this context, the above-mentioned explanation of the processes allowing the rat to survive during the life-saving period also illuminates why striatally administered haloperidol, which reduces the magnitude of the reference signals of the striatal system to zero and accordingly prevents it from changing when the zero-reference condition is reached (see Section VIB), prevents the rat from surviving (Cools, 1980). Given the haloperidol-induced zero-reference condition together with the invariant input signals derived from the ongoing behavior, the error and output signals remain fixed, resulting in the repetition of the ongoing behavioral program. This is exactly what happens in haloperidol-treated rats in the swimming test: they simply repeat the behavioral program responsible for the first, unsuccessful attempt to switch to non-exteroceptively directed behavioral states (Cools, 1980).

VII. HOW TO SPECIFY THE TRANSFORMATION OF BEHAVIORAL PROGRAM SIGNALS: ILLUSTRATION OF A SINGLE STEP DOWNSTREAM IN THE HIERARCHY

During recent years it has become evident that the substantia nigra, pars reticulata (SNR), which receives a monosynaptic GABA-ergic input from the striatum, is an important output station of the striatum [Cools *et al.* (1983c); for a review see Scheel-Krüger (1983)]. Given the availability of rather selective chemical tools to enhance this GABA-ergic activity with the help of muscimol, a direct GABA-ergic receptor agonist, and to attenuate it with the help of picrotoxin, a drug closing the chloride channels opened by GABA, this output station of the striatum can be studied provided that adequate control studies about the specificity and selectivity of the behavioral consequences elicited by these tools are included. Since the striatonigral GABA-ergic fibers are known to increase and decrease the nigral GABA release during activation and inhibition, respectively, of the nigrostriatal dopaminergic fibers [for a review see Scheel-Krüger (1983)], it seems reasonable to use picrotoxin in order to produce a zero-reference condition at the SNR level, for the striatonigral GABA-ergic fibers contain information carrying reference signals of the SNR. When such a zero-reference condition is produced, the animals will

show behavioral consequences marked by a characteristic loss of degree of freedom in programming their behavior.

A. Substantia Nigra, Pars Reticulata: Picrotoxin-Induced Effects

Cats receiving unilateral injections of picrotoxin into the SNR show highly characteristic deficits (Cools *et al.*, 1983c; Heim *et al.*, 1983; Sontag *et al.*, 1983; Wolfarth *et al.*, 1981). First, they freeze on the spot: i.e., they cannot use proprioceptive stimuli to adjust their body position. Second, they are unable to lift their hindlimbs when their forelimbs are put on a bar placed more than 2 m above the floor: i.e., they cannot use proprioceptive information from their hindlimbs to retract them. Finally, they are unable to put their auricle upright when its upper part is retroflexed: i.e., they cannot use proprioceptive stimuli from their auricle (W. Kolasiewicz, unpublished data). Although picrotoxin has additional behavioral consequences (Wolfarth *et al.*, 1981), these are aspecific for the brain structure under discussion because they remain present when the SNR is lesioned, are not dose-dependent, and/or cannot be inhibited by muscimol (Cools *et al.*, 1983a,b; Jaspers *et al.*, 1983d). The former effects, however, are SNR-specific because they are absent when the SNR is lesioned, are dose-dependent, and are inhibited by muscimol (Cools *et al.*, 1983a; Jaspers *et al.*, 1983d). The finding that the SNR-specific effects are bilateral despite of the unilateral injections is due to the fact that a GABA-ergic inhibition at one side of the brain is able to produce an analogous GABA-inhibition at the opposite side of the brain via crossed nigrothalamocaudatonigral fibers (Chesselet *et al.*, 1983).

It is evident that picrotoxin-treated cats are unable to switch to behavioral states directed by input signals that are ultimately constructed from proprioceptive stimuli; the degree of abstraction of these input signals, however, is not yet clear. Thus, a reduced GABA-ergic activity within the SNR prevents the organism from programming the ordering and sequencing of behavioral states with the help of input signals derived from proprioceptive stimuli. Considering the positive behavioral consequences of the chosen chemical intervention, it appears that such cats show improved capacity to switch arbitrarily to exteroceptively directed behavioral states. For instance, cats trained to walk on a treadmill equipped with obstacles—small cross-laths of about 10 mm height on the belt—normally attempt to avoid touching these obstacles. In this test picrotoxin-treated cats, which freeze as long as the belt stands still, not only start trotting as soon as the belt moves, but also make significantly

fewer errors, i.e., touch the obstacles, than solvent-treated cats. I discuss this effect in Section VIII (Heim *et al.*, 1983; Sontag *et al.*, 1983).

Although picrotoxin is chosen to prevent the transmission of information carried by striatonigral GABA-ergic fibers, i.e., the reference signals of the nigral SNR system, there is no direct proof for this, because of the fact that the SNR is loaded with GABA synapses, only a part of which may belong to the striatonigral fibers. Accordingly, one needs additional information to specify whether the picrotoxin effects are indeed due to a direct intervention with these reference signals. As mentioned, such information can be collected in studies using a chemical intervention that produces pharmacological effects in a direction diametrically opposite that of the chosen treatment; muscimol is such an agent.

B. Substantia Nigra, Pars Reticulata: Muscimol-Induced Effects

Very recently muscimol has been found to produce a highly complex series of movements when unilaterally administered to the SNR. The effects discussed below are specific for the brain region under discussion, because they disappear when the SNR is lesioned, are dose-dependent, and are suppressed by picrotoxin (Cools *et al.*, 1983a; Jaspers *et al.*, 1983d). All movements are restricted to spatiotemporal alterations between two given points, each of them characterized by fixed coordinates in terms of a coordinate system with one or another part of the body as point of reference, i.e., a coordinate system with so-called *egocentric* coordinates (Figs. 3 and 4). In practice the fully symmetric posture serves as point of departure for the drug-induced movements, which are directed toward a point whose coordinates are fixed. This point of departure lies somewhere on the vertical axis of the egocentric coordinate system. The drug-induced movements are regularly interrupted by smooth movements directed toward the point of departure. Thus, muscimol elicits forced movements directed toward a point whose drug-induced coordinates show fixed deviations from the initial point on the axes of the egocentric coordinate system. Thus, the muscimol-treated cats continuously display movements bridging the gap between one naturally given point, the point of departure, and a point marked by drug-induced, fixed egocentric coordinates (Fig. 5).

As time progresses, the part of the body forming the center of the egocentric coordinate system, i.e., the point of reference for describing the coordinates of the position to be reached, moves from the ears to the eyes, to the midline of the head, and then into the cephalocaudal direction from the head, to the shoulders, to the tail. Thus, the muscimol-treated

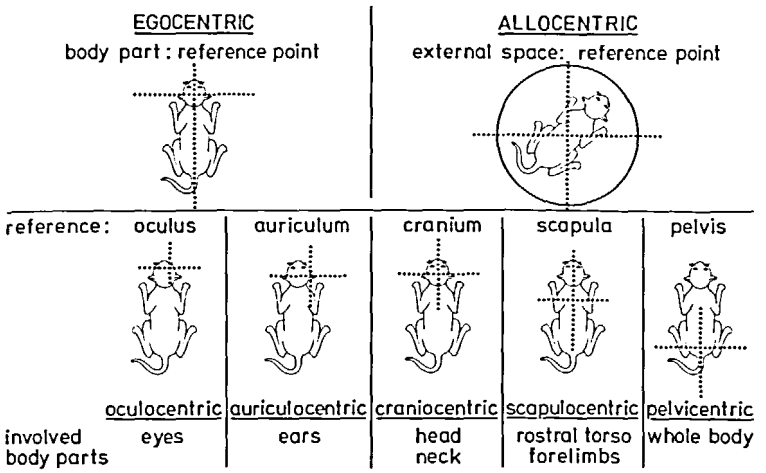

Fig. 3. Movement coordinate systems. In the upper left part the axes of the so-called egocentric coordinate system are given; the body (or a part) serves as the point of reference. In the lower part several egocentric coordinate subsystems are depicted; in these cases the system is classified according to the particular body part serving as the point of reference. In the upper right part the so-called allocentric coordinate system is illustrated; the frame of reference is prescribed by the immediate surroundings of the animal. The dotted lines are allocentric vectors deviating from the axes of the allocentric system; these axes are determined by the position taken by the organism in space. [Cools *et al.* (1983a); Jaspers *et al.* (1983d).]

cats initially move their ears, add eye movements, and progress to include head movements and movements involving head, neck, shoulders, and forelimbs, and ultimately terminate with movements involving all parts of the body. Apart from the ear and eye movements, which have not yet been evaluated in a quantitative way, all remaining movements are restricted to the spatial alterations described above (Fig. 5).

In other words, muscimol alters the nigral SNR system in such a manner that the animal permanently executes attempts to bridge the spatiotemporal gap between one naturally given point, i.e., the point of departure, and a point marked by drug-induced, fixed egocentric coordinates. This information has allowed us to draw two conclusions. First, the nigral system apparently carries a code enabling the organism to switch to behavioral states that are normally directed by input signals derived from proprioceptive stimuli, for proprioceptive stimuli are essential prerequisites for directing movements toward a point characterized by fixed egocentric coordinates. For the time being I propose to label this code a *proprioceptive code*, i.e., a code prescribing egocentric coordinates

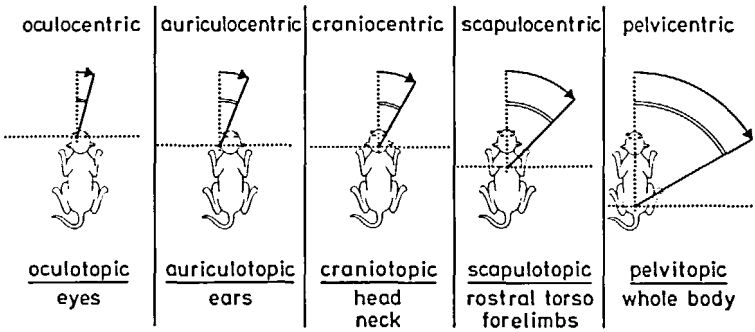

Fig. 4. Propriotopic movements (dynamic→static; not directed by external signals: no distraction; at most adjusted to external signals), i.e., movements directed toward a point whose egocentric coordinates are prescribed by a "propriotopic code," a code derived from proprioceptive stimuli. This code varies according to the given egocentric coordinate subsystem, from oculotopic to pelvitopic (cf. Fig. 3). [Cools *et al.* (1983a); Jaspers *et al.* (1983d).]

of behavioral states in terms of abstract, invariant functions that are normally constructed from proprioceptive stimuli. In muscimol-treated cats, however, proprioceptive stimuli are not offered, and accordingly the code is created by the treatment itself; I return to the latter notion later in this section. The second conclusion deals with the question of specifying the actual target site of the chosen GABA-ergic drugs in terms of input, reference, error, and output signals. As noted above, muscimol-treated cats make continuous attempts to bridge the gap between the given points but remain unsuccessful. In principle, such a behavior implies the presence of fixed output signals, which in turn may result from fixed magnitude of input, reference, error, or output signals (see Section IVB). Given the finding that muscimol-treated cats neither freeze nor let their hindlimbs hang when their forelimbs are put on a bar placed more than 2 m above the floor (Wolfarth *et al.*, 1981; Cools *et al.*, 1983c) it appears that such animals are perfectly able to switch to behavioral states with the help of propriotopic codes derived from proprioceptive stimuli. Thus, they are still able to record changes in input signals derived from proprioceptive stimuli and to reduce the magnitude of the resulting error and output signals. Given this notion, the muscimol-induced effects have to be ascribed to interference with the reference signals, an outcome predicted on the basis of the known striatonigral GABA-ergic input. It becomes

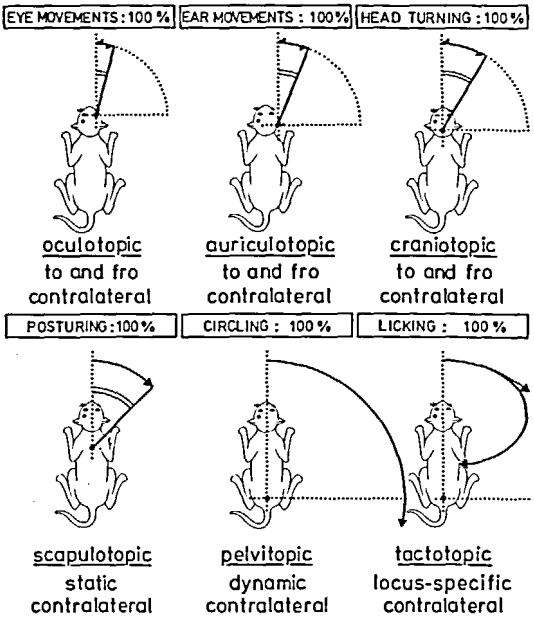

Fig. 5. Propriotopic movements elicited by unilateral nigral administration of muscimol (400 ng/1.0 μl) into the left substantia nigra, pars reticulata of cats (n = 20); these movements are observed in a familiar and static environment. [Cools *et al.* (1983a); Jaspers *et al.* (1983d).]

evident now that the muscimol-induced fixed output condition results from muscimol's ability to fix the magnitude of the reference signals of the nigral SNR system. Consequently, it creates a propriotopic code without using input signals derived from proprioceptive stimuli. This in turn implies that picrotoxin, which ultimately produces a zero-output condition of the nigral system (see above), actually produces a *zero-reference* condition at this level. Consequently, the reference signals of the nigral system are actually transmitted by GABA within the substantia nigra, pars reticulata, implying that the GABA-induced effects are due to intervention with the striatonigral GABA-ergic fibers.

Before summarizing this discussion, it is relevant to recall that output signals of hierarchical superior systems direct programs of hierarchical inferior systems, and that behavioral consequences characteristic of disturbances of higher order systems are successively replaced by behavioral consequences characteristic of disturbances of lower order systems (see

Section VID). Given the fact that muscimol fixes the magnitude of the reference signals of the nigral system and accordingly produces fixed output signals under certain circumstances, the animals will produce behavioral deficits characteristic for fixed output signals of systems at successively lower order levels within the hierarchy. This is what appears to happen in muscimol-treated cats. As time progresses, the part of the body forming the center of the egocentric coordinate system, i.e., the point of reference for describing the coordinates of the position to be reached, moves from the ears, to the eyes, to the midline of the head and then into the cephalocaudal direction from the head, to the shoulders, to the tail. The finding that both the recovery from hypothalamic lesions and the ontogeny of movement patterning in rats are marked by analogous shifts with regard to the activation and reintegration of systems responsible for movements [Golani *et al.* (1981); for a review see Teitelbaum *et al.* (1983)] supports the above-mentioned idea that the successive shifts of the center of egocentric coordinate systems in muscimol-treated cats reflects the order in which systems inferior to the nigral system are successively affected.

Summarizing the above considerations, it appears that the nigral SNR system receives the striatal code for arbitrarily programming the ordering and sequencing of behavioral states, via the striatonigral GABA-ergic pathways. The nigral system itself apparently transforms this striatal code into a new code for arbitrarily programming the ordering of behavioral states with the help of input signals derived from proprioceptive stimuli. In other words, *the nigral SNR system reduces the degree of freedom in programming behavior by adding information about the propriotopic coding of behavioral states to be executed.* In this way the nigral SNR system forms the next step in the process of transforming behavioral program signals into behavioral commands. In order to underline the power of the chosen approach, we will follow this process one step further downstream in the hierarchy.

As a final remark, however, it is relevant to recall that there are several possibilities for counteracting disturbances occurring at a particular level within a nonlinear, overlapping hierarchy (see Section IVA). Given the fact that picrotoxin produces a zero-output condition of the nigral SNR system, it now becomes possible to understand why picrotoxin-treated cats actually show an improved capacity to switch to exteroceptively directed behavioral states when tested on a treadmill equipped with obstacles (Sontag *et al.*, 1983). This is due to the fact that systems inferior to the nigral SNR system are still able to produce correct output signals (see Section IVA).

VIII. HOW TO SPECIFY THE TRANSFORMATION OF BEHAVIORAL PROGRAM SIGNALS: ILLUSTRATION OF A SECOND STEP DOWNSTREAM IN THE HIERARCHY

Given the nigral SNR system as an output station of the striatum, we have to trace the efferents of this brain structure to delineate the hierarchical system inferior, but as close as possible to it. Since there is no doubt about the existence of a monosynaptic striatonigrocollicular pathway [for a review see Scheel-Krüger (1983)], we have to consider the colliculus superior (CS), especially its deeper layers (DL), as a station intercalated between the striatum and the lowest order system. Since the nigrocollicular fibers contain GABA as neurotransmitter, the drugs muscimol and picrotoxin are the tools of choice in order to produce changes in the function of the collicular DL system. Starting from the fact that the nigrocollicular fibers increase and decrease the collicular GABA release during inhibition and activation, respectively, of the striatonigral GABA-ergic fibers [for a review see Scheel-Krüger (1983)], we can expect intracollicularly administered muscimol to produce a zero-reference condition in view of the result that the nigrocollicular fibers contain information carrying the output signals of the nigral SNR system, i.e., the reference signals of the collicular DL system. Accordingly, muscimol-treated animals should show behavioral consequences marked by a characteristic loss of degree of freedom in programming their behavior.

A. Colliculus Superior, Deeper Layers: Muscimol-Induced Effects

Cats receiving unilateral injections of muscimol into the CS-DL show highly characteristic deficits (Cools *et al.*, 1983a; Jaspers *et al.*, 1983e). When such cats are put on a narrow bar of 2 cm width and 2 m length about 2 m above the floor, they are unable to bridge the gap between the point of departure, i.e., the beginning of the bar, and the end of the bar, where they can collect milk from a small cup, unless their movements are continuously directed by visual and/or tactile stimuli. In contrast to solvent-treated cats, which walk straight toward the end of the bar without any visual fixation or wrong placing responses, muscimol-treated CS-DL cats either do not move at all or move slowly forward, visually fixating the bar just 30–40 cm in front of their heads and producing a large number of misplacements, which are immediately corrected. On the other hand, such cats show no deficits when their forelimbs are put on this bar and their hindlimbs are hanging: they immediately switch to behavioral states directed by input signals derived from proprioceptive stimuli, as illus-

trated by the fact that they retract their hanging hindlimbs and climb up on the bar. The former, negative CS-DL effects are specific for the brain region under discussion because they are absent when the deeper layers of the colliculus superior are lesioned; furthermore, they are dose-dependent and antagonized by picrotoxin (Cools *et al.*, 1983b; Jaspers *et al.*, 1983e).

Although the muscimol-treated CS-DL cats are apparently able to switch to behavioral states that are directed by input signals ultimately constructed from proprioceptive and/or exteroceptive stimuli, they differ from normal cats in the sense that the exteroceptive information inherent to the object to be reached is insufficient for programming behavioral states allowing them to reach that object: they need additional, exteroceptive stimuli for executing the required program. Thus, intracollicularly administered muscimol produces a highly characteristic deficit, which may be the direct consequence of a zero-reference condition of the CS-DL system. In order to verify the latter suggestion, we need additional information from studies on effects of a chemical intervention that produces pharmacological effects in a diametrically opposite direction. As illustrated below, such studies also allow us to specify the actual deficit underlying the muscimol-induced behavioral consequences.

B. Colliculus Superior, Deeper Layers: Picrotoxin-Induced Effects

When picrotoxin instead of muscimol is administered into the deeper layers of the colliculus superior a complex series of movements appear (Cools *et al.*, 1983a; Jaspers *et al.*, 1983e). The effects described below are specific for the brain region under study because they disappear when the CS-DL is lesioned, are dose-dependent, and are suppressed by muscimol (Cools *et al.*, 1983; Jaspers *et al.*, 1983e). In contrast to movements elicited by nigral muscimol, the movements elicited by collicular picrotoxin are not restricted to spatiotemporal alterations between points with fixed egocentric coordinates. Instead, the movements elicited by collicular picrotoxin share another feature: these movements are restricted to spatiotemporal alterations between one point with fixed egocentric coordinates and one point whose egocentric coordinates drift away from the initial point on the vertical axis of the egocentric system according to a particular rule.

Before describing the picrotoxin-induced movements in CS-DL cats in more detail, it is important to realize that, in principle, movements may be directed either by exteroceptive information, i.e., exteroceptively directed movements, or by proprioceptive information, i.e., propriocep-

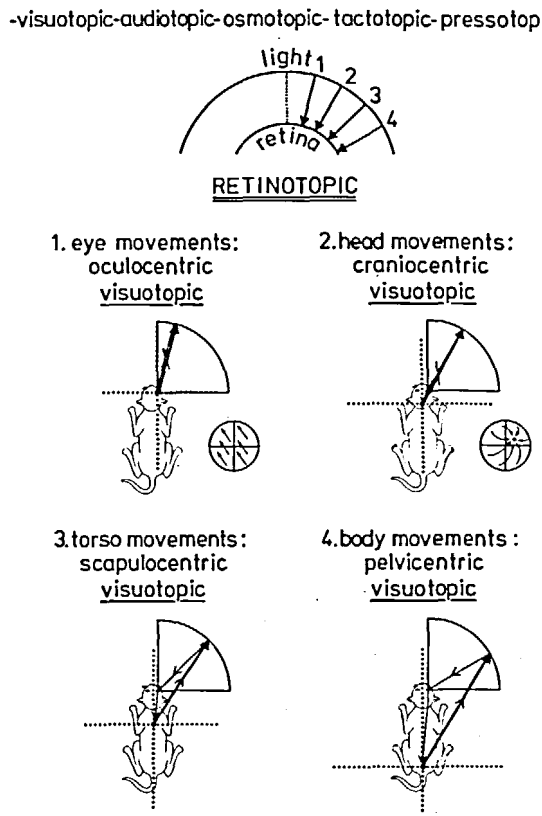

Fig. 6. Exterotopic movements (distraction possible), i.e., movements directed toward a spatial point whose egocentric coordinates are prescribed by an "exterotopic code," a code prescribing how allocentric coordinates of the spatial point have to be transformed into egocentric coordinates of movements to be executed in order to reach that point. The code itself is derived from exteroceptive stimuli and varies according to the given egocentric coordinate subsystem, from visuotopic to pressotopic. This figure shows four different codes, each of them derived from the light illuminating the retina in four different manners (1–4). [Cools *et al.* (1983a); Jaspers *et al.* (1983e).]

tively directed movements. In contrast to the proprioceptively directed movements, which can solely be described in terms of an egocentric coordinate system, i.e., a system with one or another part of the body as point of reference, the exteroceptively directed movements can be described either in terms of an egocentric coordinate system or in terms of a so called *allocentric* coordinate system, a system in which the immediate environment of the organism is the frame of reference (Figs. 3 and 6). The axes of the allocentric coordinate system are instantaneously deter-

mined by the position taken by the organism in space: the axes are identical to those of the egocentric system. As soon as the organism starts to approach a spatial point whose coordinates deviate from those of the original point, the allocentric coordinates of the spatial point have to be transformed into egocentric coordinates that define the direction of the required movements (Regan and Beverley, 1982). I propose to label the information controlling this process of transformation the *exterotopic code*, i.e., a code prescribing how allocentric coordinates of a spatial point have to be transformed into egocentric coordinates specifying the behavioral movements to be executed in order to reach the given spatial point (Fig. 6). It will be evident that the resulting egocentric coordinates of the spatial point will vary according to the degree of ongoing changes in the distance between the point of departure and the spatial point to be reached. In this respect the exteroceptively directed movements differ from the proprioceptively directed movements, which are directed at points with fixed egocentric coordinates (cf. Figs. 4 and 6).

Against this background it becomes possible to describe the picrotoxin-induced movements in CS-DL cats. Overall, the cats move to and from two points in space. The fully symmetric posture again serves as point of departure for the drug-induced movements, which are directed toward a spatial point whose coordinates are not fixed. In fact, the drug-induced movements are regularly terminated when the body has reached a position marked by fixed deviations from the axes of the egocentric coordinate system. Then these movements are replaced by movements that are either directed toward the point of departure or directed toward a spatial point whose coordinates are determined by doubling the initial degree of deviation from the original point on the axes of the egocentric coordinate system. Thus, picrotoxin elicits forced movements toward a spatial point whose drug-induced coordinates show variable deviations from the original point on the axes of the egocentric coordinate system. Thus the picrotoxin-treated cats continuously display movements bridging the gap between one naturally given point, i.e., the point of departure, and a point marked by drug-induced variable egocentric coordinates (Fig. 7). For instance, a picrotoxin-treated CS-DL cat anteroflexes its head 10 deg, keeps its position fixed for a while, and then either returns its head to the point of departure or anteroflexes its head another 10 deg. When it reaches the maximum degree of head bending, it starts to bend its torso into that direction according to the same process of doubling the original degree of deviation. Ultimately the whole body becomes involved in the movements; the cat displays a great variety of fully distinct movement patterns, from bending its head between its limbs, to bending its head along the outer part of one of its limbs, to jumping backwards and then

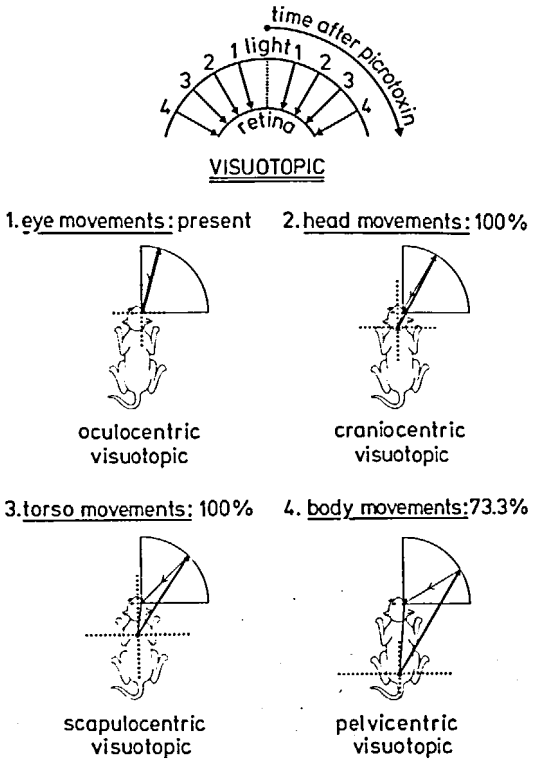

Fig. 7. Movements (exterotopic; distraction possible; dynamic) elicited by unilateral collicular administration of picrotoxin (200 ng/0.5 µl) into the colliculus superior, especially its deeper layers, of cats (n = 15). These movements are observed in a familiar and static environment. [Cools *et al.* (1983a); Jaspers *et al.* (1983e).]

bending its head. As time progresses the point of reference for describing the egocentric coordinates of the spatial point to be reached moves from the ears, to the eyes, to the midline of the head, and then into the cephalocaudal direction from the head, to the shoulders, to the tail. Thus, the picrotoxin-treated CS-DL cats initially move their ears, add eye movements, progress to include head movements and movements involving head, neck, shoulders, and forelimbs, and ultimately terminate with movements involving all parts of the body (Fig. 7). Apart from the ear and eye movements, which have not yet been evaluated in a quantitative manner, all movements are restricted to spatiotemporal alterations between one naturally given point, i.e., the point of departure, and a point whose egocentric coordinates are drifting away from the original point on the axes

of the egocentric coordinate system according to a fixed rule (Fig. 7). Since the latter features are characteristic of exteroceptively directed movements (see above), picrotoxin apparently alters the collicular DL system in such a manner that the animal permanently executes attempts to bridge the gap between its instantaneously generated point of departure and a point characterized by drug-induced allocentric coordinates, forcing the animal to activate the process of exterotopic coding.

In other words, the collicular DL system carries information about the exterotopic coding of the movements to be executed. On the basis of the finding that picrotoxin-treated CS-DL cats with a bandage covering their eyes still execute the above movements (Cools *et al.*, 1983a; Jaspers *et al.*, 1983e), it would seem that exteroceptive stimuli cannot be used to generate this exterotopic code. Thus, the treatment itself has created this exterotopic code.

As noted above, picrotoxin-treated CS-DL cats continuously attempt to bridge the gap between the instantaneously generated point of departure and a spatial point prescribed by the exterotopic code. In principle such a behavioral consequence implies the presence of fixed output signals, which in turn may result from fixed values of input, reference, error, or output signals (see Section IVB). The finding that picrotoxin-treated CS-DL cats are fully capable of walking straight toward the end of the bar without any visual fixation and/or wrong placing responses (Cools *et al.*, 1983a; Jaspers *et al.*, 1983e), compared to the observation that muscimol-treated CS-DL cats show characteristic deficits (see above), indicates that the picrotoxin-treated CS-DL cats are perfectly able to switch to behavioral states with the help of exterotopic codes derived from exteroceptive stimuli. Thus, such cats are still able to record changes in input signals derived from exteroceptive stimuli and to reduce the magnitude of the resulting error and output signals. Given this notion, the picrotoxin effects have to be ascribed to the interference of picrotoxin with the reference signals, an outcome predicted on the basis of the known nigrocollicular GABA-ergic input. It now becomes evident that the picrotoxin-induced fixed output condition actually results from picrotoxin's ability to fix the magnitude of the reference signals of the collicular DL system. Consequently, picrotoxin creates an exterotopic code without using input signals derived from exteroceptive stimuli. Recalling the finding that muscimol-treated CS-DL cats cannot reach an object with the help of exteroceptive information inherent to that object, it also becomes evident that muscimol prevents the animals from using exterotopic codes. In view of this result, we reach the conclusion that muscimol produces a zero-reference condition at the collicular DL level. Consequently, the reference signals of the collicular DL system are transmitted by the GABA-ergic synapses

within this brain structure, implying that the GABA-induced effects are due to the interference with the nigrocollicular GABA-ergic fibers.

Summarizing, it has become evident that the collicular DL system receives the nigral SNR code for arbitrarily programming the ordering and sequencing of behavioral states with the help of input signals derived from proprioceptive stimuli, via the nigrocollicular GABA-ergic pathways. The collicular DL system itself transforms this nigral code into a new code for arbitrarily programming the ordering and sequencing of behavioral states with the help of input signals derived from exteroceptive stimuli. In other words, the collicular DL system reduces the degree of freedom in programming behavior by adding information about the exterotopic coding of the behavioral activities to be executed. In this manner the collicular DL system forms the next step in the process of transformation of behavioral programs into behavioral commands.

Before closing this discussion, two remarks should be made. First, the successive shifts in the center of the egocentric coordinate system of the spatial point to be reached by picrotoxin-treated CS-DL cats are identical to those seen in muscimol-treated SNR-cats. This underlines the validity of the earlier notion that these shifts reflect the order in which systems inferior to the affected systems are successively affected. From this point of view it appears likely that the reticular formation plays a crucial role in this respect (Sirkin *et al.*, 1980). Second, disturbances at a particular level in a nonlinear, overlapping hierarchy can be counteracted in several manners (see Section IVA). Given the fact that CS-DL muscimol produces a zero-output condition of the collicular DL system, it becomes possible to understand why muscimol-treated CS-DL cats are still able to switch to proprioceptively directed movements, i.e., movements requiring correct functioning output signals of the nigral SNR system, as we have seen in the previous section: this intact capacity in muscimol-treated CS-DL cats is simply due to the fact that the nigral SNR system, which is superior to the collicular DL system, is still able to send its output signals to systems inferior to the collicular DL system, bypassing the collicular DL system itself.

IX. TRANSFORMATION OF BEHAVIORAL PROGRAM SIGNALS INTO BEHAVIORAL COMMANDS

We have obtained some insight into the transformation of information arriving at the striatum and going downstream in the hierarchy via the nigral SNR system and the collicular DL system. Despite the very limited

degree of knowledge in this area, this allows us to point out some basic features of the cerebral organization of behavior: the enormous degree of freedom in programming a single behavioral state, and the principal lack of cerebral organization of behavioral states at levels superior to the lowest order level within the hierarchy of negative feedback control systems.

A. Dysfunctioning Striatal Programming Signals and Limited Degree of Behavioral Deficits

Let us consider the deficits seen in animals and man with an experimentally induced or spontaneously occurring hypofunctioning striatum in order to illustrate the enormous plasticity of the cerebral organization of behavior. As mentioned earlier, such organisms maintain a zero-reference condition of the striatal system despite the fact that the magnitude of the arriving reference signals may change. Due to this deficit, the organisms are unable to program arbitrarily the ordering and sequencing of behavioral states. Still, they are able to execute ultimately the correct behavioral states by switching arbitrarily to exteroceptively or proprioceptively directed behavioral states and/or exteroceptively triggered behavioral states, i.e., states directed by conditioned stimuli. Thus, their ability to arbitrarily program behavior is intact. As mentioned earlier, this is due to the fact that systems superior to the striatal system are able to bypass the striatum by sending their reference signals directly to other systems. Given the notion that the main afferents of the striatum have their origin in the cortex, it is reasonable to assume that the reference signals under discussion are derived from the cortex. From this point of view it is the cortex that contains the code for programming arbitrary behavior (Eccles, 1982; Roland *et al.*, 1980, 1982). Indeed, studies on man with lesions in the prefrontal lobes have shown that such patients have lost precisely this capacity (Nelson, 1976; cf. Cools *et al.*, 1984). Realizing that there are not only corticostriatal fibers, but also corticonigral, corticocollicular, corticoreticular, and corticospinal fibers (Kuypers, 1978), it is reasonable to assume that the latter fibers are also able to transmit the cortical code to the substantia nigra, pars reticulata; the colliculus superior, especially the deeper layers; the reticular formation; and even the spinal cord, thereby bypassing the striatum. In view of the previously mentioned data about the nigral SNR system (see Section VII) and the collicular DL system (see Section VIII) it now becomes understandable why animals with a hypofunctioning striatum are able to switch to proprioceptively directed behavioral states (nigral function) and/or extero-

ceptively directed behavioral states (collicular function). The fact that organisms with a hypofunctioning striatum can also switch to exteroceptively triggered behavioral states, i.e., states directed by conditioned stimuli, implies that there is in fact another possibile way to overcome spontaneously occurring or experimentally induced deficits in the striatum: sending input signals derived from exteroceptive or proprioceptive sources to systems superior to the striatum. Thus, organisms with deficits at a particular level within the hierarchy can still reach their goal: either they activate neuronal substrates sending input signals to systems superior or inferior to the affected system, changing the degree of abstraction of the input signals derived from exteroceptive, proprioceptive, and interoceptive sources, or they activate neuronal substrates sending output signals to systems inferior to the affected system, changing the degree of freedom in programming the particular behavioral state in question.

Given this result, it becomes evident that animals with corticostriatal lesions, for instance, can compensate the resulting deficit at the behavioral level by activating corticonigral, corticocollicular, corticoreticular, and/or corticospinal pathways. Thus, the process of recovery will last as long as the time required for optimizing this process. Such recovered animals, once having activated the corticospinal pathways, for instance, will not only have a lesser degree of freedom in programming their behavior, but also a lesser degree of freedom in updating their ongoing behavior: program signals sent directly to lower order systems cannot be altered by output signals of higher order systems (Eidelberg, 1981; Eidelberg *et al.*, 1981; Smith *et al.*, 1982). Accordingly, only lesions simultaneously affecting different pathways will produce gross behavioral deficits (Péchardre *et al.*, 1976).

Analogously, intact organisms will be able to activate selectively one of the available pathways for programming a particular behavioral state. It will be clear that a great variety of factors determine this process of selective activation. Apart from input signals generated instantaneously by the ongoing behavior of the organism and its surroundings, genetic disposition, ontogeny, development, maturation, and learning will be highly relevant in this respect. From this point of view it would be worthwhile to analyze intraspecies and interspecies differences in terms of activating different pathways for programming a single behavioral state.

The example nicely illustrates how a single behavioral state can be the consequence of totally different programs, reflecting the degree of plasticity within the brain. Since each program requires its own neuronal substrate for input, reference, error, and output signals, it is evident that a single behavioral state can be the consequence of activating totally different neuronal substrates (Fig. 8) (Desmedt and Godaux, 1981). In this

context, however, it should be recalled that the lowest order level within the hierarchy is the only one directing behavioral commands, i.e., signals lacking any degree of freedom in programming behavior. Accordingly, the execution of a particular behavioral state always requires a common neuronal substrate as far as its lowest order system is concerned.

B. Transformation of Striatal Program Signals into Behavioral Commands

Although the enormous degree of plasticity in the cerebral organization of behavior implies a great variety of different channels funneling information for the execution of a single behavior state, it is still possible that the structural organization of these channels varies from one behavioral state to another, implying that behavioral states are still cerebrally represented as distinct entities within the brain. Let us therefore consider the behavioral consequences of striatal interventions that differ with respect to the degree of pathology produced. For that purpose we simply need to analyze the behavioral consequences of increasing doses of haloperidol, a drug that reduces the magnitude of the reference signals of the striatal system to zero by virtue of its capacity to block the transmission of information from the nigrostriatal dopaminergic fibers to their corresponding postsynaptic receptors.

As mentioned in Section VIB, low doses of haloperidol simply prevent the organism from switching arbitrarily to non-exteroceptively directed behavioral states, because of the haloperidol-induced zero-reference condition of the striatal system.

Intermediate doses of haloperidol are known to produce artificial postures, labeled as catalepsy by some authors, as the consequence of a reduced capacity to switch to proprioceptively directed behavioral states (De Ryck *et al.*, 1980). This phenomenon is understandable in view of the fact that haloperidol can produce a *zero-output condition* of the striatal system as the result of its ability to produce a *zero-reference condition* of the striatal system. Since the output signals of the striatal system are in fact the reference signals of the nigral SNR system, haloperidol can also produce a zero-reference condition of the latter system (Fig. 8). As mentioned earlier, such a reduction, produced by nigral injections of picrotoxin, for instance (see Section VIIA) can prevent the organism from using propriotopic codes for directing behavioral states. The validity of this reasoning is underlined by the finding that haloperidol can indeed reduce the release of GABA from striatonigral GABA-ergic fibers [for a

review, see Scheel-Krüger (1983)], reducing the magnitude of the reference signals of the nigral SNR system.

Higher doses of haloperidol are known to produce animals that are bound to tactile and pressure stimuli (Schallert and Teitelbaum, 1981), the consequence of a reduced capacity to switch to exteroceptively directed behavioral states. This phenomenon is also understandable in view of the fact that haloperidol can ultimately produce a *zero-output condition* of the nigral SNR system as the result of its ability to produce a *zero-reference condition* of this system. Since the output signals of the nigral SNR system are in fact reference signals of the collicular DL system, haloperidol can indirectly produce a zero-reference condition of the collicular DL system (Fig. 8). As mentioned earlier (see Section VIIIA), such a reduction, produced by collicular injections of muscimol, for instance, can prevent the animals from using exterotopic codes for directing behavioral states. The validity of this reasoning is underlined by the finding that lowering the striatal dopamine activity can indeed increase the release of GABA from nigrocollicular GABA-ergic fibers [for a review see Scheel-Krüger (1983)], reducing the magnitude of the reference signals of the collicular DL system.

Still higher doses of haloperidol are known to produce pure motor deficits, as a consequence of a reduced capacity to produce correct motor commands at the level of the spinal cord. Again this phenomenon becomes understandable in view of the fact that the whole process of sending information downstream in the hierarchy is marked by reducing the magnitude of reference signals at successively lower order levels as long as the zero-reference condition at the striatal level is kept invariant (Fig. 8). The ultimate consequence of such a process will be a zero-output condition of the lowest order system, i.e., the spinal cord, producing pure motor disturbances.

What is relevant in considering the above effects is the recognition that a highly selective and specific interference with the magnitude of the reference signals of a single hierarchical system, i.e., the striatal system, produces a great variety of totally different behavioral states: the degree in which systems inferior to the striatal system are affected, but not the neuronal substrate itself, determines the actual nature of the resulting behavioral states (Table I). The latter conclusion is actually inherent to any hierarchy of negative feedback control systems: systems superior to the lowest order system direct programs but not responses (Polit and Bizzi, 1979; Terzuolo and Viviani, 1980). Thus, behavioral states are simply not cerebrally represented at levels superior to the lowest order system.

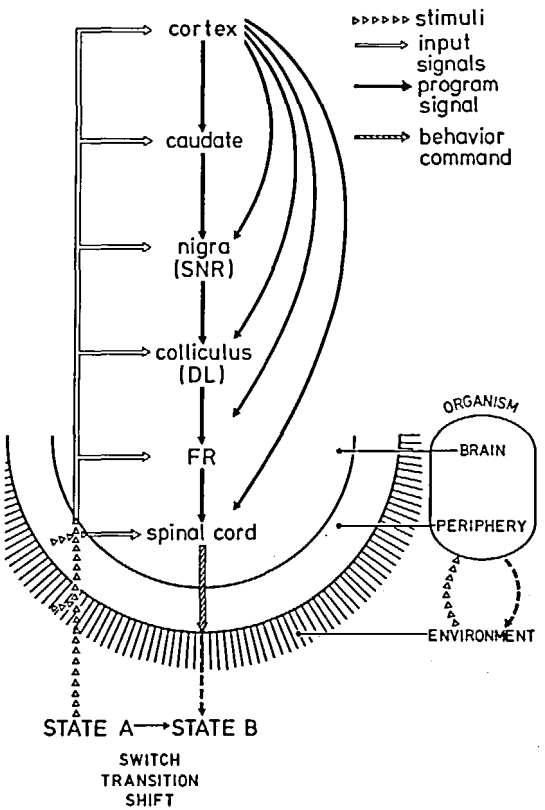

Fig. 8. Oversimplified diagram of the flow of information going downstream in the hierarchy from the cortex. Signals leaving the caudate nucleus (caudate), substantia nigra, pars reticulata (nigra, SNR), deeper layers of the colliculus superior (colliculus, DL), and reticular formation (FR) and bypassing structures inferior to them are omitted. The information carried by the output signals toward successively lower order levels is transformed as follows: *Cortex*: code for arbitrarily programming behavioral states (see Section IX). *Caudate*: code for arbitrarily programming the ordering and sequencing of behavioral states (see Section VI). *Nigra*: code for arbitrarily programming the ordering and sequencing of behavioral states with the help of propriotopic codes (see Section VII). *Colliculus*: code for arbitrarily programming the ordering and sequencing of behavioral states with the help of propriotopic and exteroceptive codes (see Section VIII). *FR*: not yet specified. *Spinal cord*: detailed code for programming the behavioral state to be executed. (Note: This diagram deals with the flow of a particular cortical code that goes downstream in the hierarchy. It will be evident that other cortical codes follow different pathways.)

Table I. Behavioral Consequences of an Increasing Degree of Dysfunction in the Striatum

Effects of increasing corticocaudate input (haloperidol–atropine)	Code programming behavior	Brain structure
	"Arbitrary" code = A	Cortex
		↓
Rigidity, serial ordering	A + Serial code = B	Caudate nucleus
		↓
Rigidity, artificial postures	B + Propriotopic code = C	Substantia nigra (SNR)
		↓
Tactotopic, pressotopic	C + Exterotopic code = D	Colliculus superior (DL)
		↓
		(Intercalated stations)
		↓
Motor deficits	Execution command	Spinal cord
		↓
	Transformation neural current → contractions	Muscles

As a final remark in this context, it is interesting to consider the possibility that the increasing degree of pathology that is produced by increasing doses of haloperidol is not related to the amount of dopamine receptors affected by haloperidol, but is related to the duration of the haloperidol-induced inhibition of dopamine receptors. In a hierarchy of feedback control systems the lowest order system has the fastest response, and the higher in the hierarchy the output of these systems is affected, the more time it takes to send the information downstream in the hierarchy. Consequently the degree to which fixed output signals of the striatal system are able to produce fixed output signals of systems at successively lower order levels is solely determined by the duration of the experimentally induced fixation of the striatal output signals (Vrijmoed-de Vries and Cools, 1983).

X. EPILOGUE

The cornerstone of this chapter is formed by Powers' definition of behavior: behavior is the control of the input of the organism. By definition, behavior is conceived as a process by which the organization inside

the organism (brain) controls the input of the organism. The brain is thereby conceived as an integrated whole of negative feedback systems controlling this input.

Use of Powers' concept of the cerebral organization of behavior allows us to analyze the basic rules of order in programming behavior. It also provides insight into the basic functions of distinct neuronal substrates in programming behavior. It allows us to study how input signals derived from interoceptive, proprioceptive, and exteroceptive sources are transformed into abstract, invariant functions whose degree of abstraction increases at each higher order level in the hierarchy of feedback control systems (Bizzi and Polit, 1979). It also allows us to study how behavioral commands result from behavioral program signals whose degree of freedom in programming behavior decreases at each lower order level in the hierarchy of feedback control systems (Polit and Bizzi, 1979; Terzuolo and Viviani, 1980; Viviani and Terzuolo, 1982).

Concerning the rules of order in programming behavior, Powers' concept offers a well-defined criterion for splitting and lumping behavior, i.e., classifying behavior in terms of terminating the mismatch between actual and desired states of the organism. This criterion is exactly the one used by Kortlandt (1955) in his excellent study of cormorants. Given the fact that using this principle allowed Kortlandt to discover several basic aspects of development and maturation in animals, it becomes evident that Powers' concept may create still more perspectives for ethological studies in this respect. Indeed, Plooy's study on the behavioral development of free-living chimpanzee babies and infants has to be considered as a first successful attempt in this respect (Plooy, 1980).

Furthermore, it turns out that Powers' concept opens new perspectives for studies on motivated behavior. According to Powers' concept, for instance, the classical distinction between the concept "voluntary control" and the concept "involuntary control" should be reduced to a quantitative, not qualitative, difference: a quantitative difference in terms of the degree of abstraction of input signals derived from exteroceptive, interoceptive, and proprioceptive sources, but not a qualitative difference in terms of "absence" or "presence" of the latter sources. Consequently, "motivated" and "involuntary controlled" behavior should be studied within the same frame of reference, a principle recognized and used by Teitelbaum *et al.* years ago [for a review see Teitelbaum *et al.* (1983)].

Concerning the basic functions of distinct neuronal substrates in programming behavior, the usefulness of Powers' concept is illustrated by investigating how information arriving at the striatal system is transformed on its way downstream in the hierarchy. The information arriving at the striatum, and possibly derived from the cortex, allows the organism to

arbitrarily program behavior. At the level of the striatal system the degree of freedom in programming behavior is reduced by adding information about the ordering and sequencing of behavioral states. The code resulting from the transformation of the incoming code allows the organism to program arbitrarily the ordering and sequencing of behavior: the striatal code is *inter alia* sent to the substantia nigra, pars reticulata (nigral SNR system). At the nigral SNR system the degree of freedom in programming behavior is further reduced by adding information about the propriotopic coding of behavior, i.e., determining the coordinates of behavioral states in terms of an "egocentric" coordinate system, i.e., a coordinate system with a part of the body as point of reference. This nigral SNR code resulting from the transformation of the incoming striatal code allows the organism to program arbitrarily the ordering and sequencing of behavioral states with the help of input signals derived from proprioceptive sources. The latter, nigral code is *inter alia* sent to the colliculus superior, especially in its deeper layers (collicular DL system). At the collicular DL level the degree of freedom in programming behavior is still further reduced by adding information about the so-called exterotopic coding of behavioral states, i.e., determining how the coordinates of a spatial point to be reached, defined in terms of an "allocentric" coordinates system, i.e., a coordinate system in which the frame of reference is prescribed by the immediate surroundings of the organism, have to be transformed into egocentric coordinates of the movements to be executed. This collicular DL code resulting from the transformation of the incoming, nigral SNR code allows the organism to program arbitrarily the ordering and sequencing of behavioral states with the help of input signals derived from exteroceptive sources.

In general the overall analysis of the transformation of behavioral program signals has revealed several characteristic features of the cerebral organization of behavior: (1) the enormous degree of freedom in programming a single behavioral state, (2) the principal lack of cerebral representation of behavioral states at levels superior to the lowest order system in the hierarchy, and (3) the ability to activate successively higher order levels during ontogeny, maturation, and situations in which the adult organism is unable to produce behavioral consequences delivering input signals that reduce the difference (error) between reference and input signals at a particular level in the hierarchy.

Summarizing, Powers' concept turns out to link Fentress' concept of "hierarchical patterning of behavior," a successful attempt to unify knowledge of ethology in its broadest sense, with Teitelbaum's concept of "hierarchically organized systems inside the brain," a successful at-

tempt to unify knowledge of separate response subsystems inside the central nervous system.

This elucidates why Powers' concept provides a real bridge between different branches of science in which investigators are searching for rules of order in species-specific behavior, including its causal, ontogenetic, phylogenetic, evolutionary, and functional aspects.

XI. POSTSCRIPT AND ACKNOWLEDGMENTS

The reader will notice that only a minor part of the data discussed in this chapter have been published in the usual way. Most of these data have been presented at international congresses (see the list of references). This is mainly due to the fact that the experimental methods we have looked at in this chapter were all aimed at testing or elaborating the model, which is outlined in this chapter for the first time. What was needed to publish our data was a self-consistent description of this model, i.e., the source of the hypothesis to be tested.

Many of the ideas discussed here have emerged from numerous, deeply illuminating discussions about the data collected with the help of the "treadmill" test (Sections VI–IX) during the past 2 years. Most of these experimental data were collected by my colleague and friend Rob Jaspers during the course of joint research programs of varying degrees of formal organization in which we have engaged. Among these are joint research programs with: Dr. K.-H. Sontag, Dr. M. Schwarz, K. Heim, and their colleagues at the Max Planck Institut für Experimentelle Medizin, Göttingen, West Germany; Dr. J. Maj, Dr. S. Wolfarth, and Dr. W. Kolasiewicz at the Department of Pharmacology, Polish Academy of Sciences, Krakow, Poland; Dr. M. Horstink, Dr. H. Berger, Dr. K. van Spaendonck, and Dr. J. van den Bercken at the Department of Neurology, Department of Medical Psychology, and Department of Special Education, respectively, at the University of Nijmegen, Nijmegen, The Netherlands; and my colleagues Dr. J. van Hoof and Dr. M. Vrijmoed-de Vries at the Department of Pharmacology in our Psychoneuropharmacological Research Unit.

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