The Principles of Humane Experimental Technique

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CHAPTER 1

INTRODUCTION

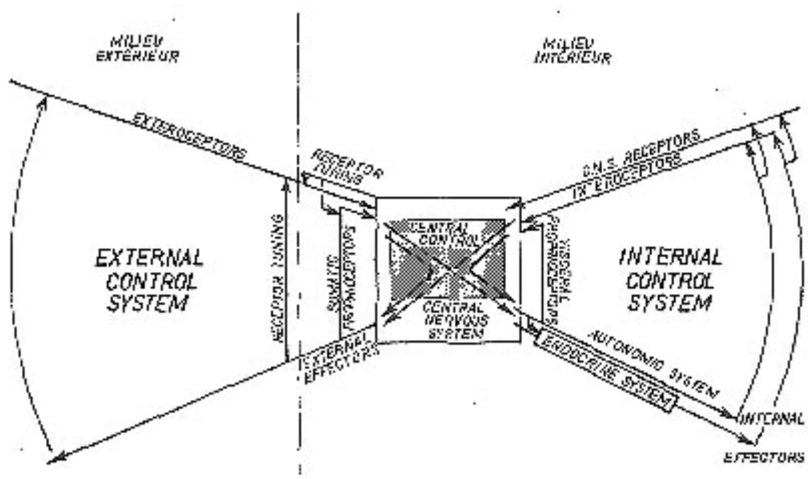
Under any excitement there will be much mutual action and reaction between these ... organs of the body.

Integration in the Vertebrate Organism

Before starting on this program, it is convenient briefly to notice certain aspects of the integration of vertebrate organisms (reviewed elsewhere on a more ample scale--Russell, in press, c), which need to be singled out for special mention here if this introductory chapter is to be complete; for these mechanisms underlie much that we shall discuss in the pages that follow, and from one ground for the close relation between humanity and efficiency in experiments on vertebrate animals.

Three major control systems are responsible for integrating the functions of the adult vertebrate organism: the somatic nervous system, the autonomic nervous system, and the endocrine system. Others there may well be (cf. Medawar, 1956), but of these virtually nothing is known at present. Of these three, the somatic nervous system, the organ of behavior, is mainly concerned with what is within (despite extensive overlaps that deter too nice a use of these time-honored categories). But the major discovery of anatomy and physiology in the last half-century has been that of the subtle, comprehensive, and intimate linkages and interactions between these three systems. The somatic and autonomic systems are closely connected at all levels of the central nervous system, from the spinal segment to the mammalian frontal neocortex (cf. e.g. Hess, 1948; Fulton, 1950, 1951). With the doubtful exception of the parathyroids (themselves influenced by peripheral changes on endocrine origin), the endocrine units are all influenced from the brain, either by direct autonomic innervation (adrenal medulla and neurohypophysis) or through the mediation of the adenohypophysis (cf. e.g. the reviews of Harris, 1948, 1950, 1955; Harris and Woods, 1956; the CIBA Colloquium, 1952a). Many hormones react back upon the somatic central or peripheral nervous system (cf. e.g. Beach, 1948; Harris, 1955; the CIBA Colloquium, 1952; Russell, 1952, 1954; Bonvallet, Dell, and Hiebel, 1954; Bonvallet, Dell, and Hugelin, 1954; Loewenstein, 1956; Loewenstein and Altamirano-Orrego, 1956). All these feedbacks and interactions have been most studied in mammals, but autonomic (Nicol, 1952) and endocrine (Bretschneider and De Wit, 1947; Russell, 1949) systems of comparable complexity with those of mammals have apparently been evolved independently in teleosts, and evidence for the relations between all three systems can be obtained in all vertebrate groups (see Fig. 2).

Figure 2. Integration in the Vertebrate Organism (click illustration for larger version)



This is a purely schematic and obviously simplified plan of the major functional control systems of a vertebrate. The vertical dashed line divides, roughly, the outside of the animal (milieu extérieur) *from the inside* (milieu intérieur). *The central nervous system is represented (without any pretensions to anatomical accuracy!) as a simple box in the middle of the diagram. Two great arcs stand out from the figure, and represent the two major control systems, external and internal. All the arrows in the diagram indicate causal functional relations, which can be classified as outputs from and inputs into the central box. That part of the nervous system controlling external outputs is usually called somatic; that part of the nervous system controlling internal outputs is called visceral. The internal outputs are mediated by the autonomic and endocrine systems. On both sides of the diagram, the effects of the outputs are liable to change the input system, via changes in the external environment on one side and in the blood and other tissue fluids on the other. Besides these two broad loops, the system is richly supplied with feedback. Within the central box, four arrows are drawn, representing four kinds of pathway linking input and output. It is seen that both internal and external inputs can control both internal and external outputs. In addition to these simple pathways, there remain the intricate control mechanisms of the central nervous system itself. These are represented (again, obviously, only* *formally) as concentrated in an inner box, labelled 'central control.' All four pathways linking input and output are represented as passing through this inner box, and thus as interacting with the central control mechanisms.*

Every arrow in the diagram (i.e. every causal relationship) can be substantiated in mammals. Most of the arrows, including all those discussed in the text, can be substantiated in all vertebrate groups.

Among the endocrine units influenced by the central nervous system via several different routes, the adrenal cortex wields perhaps the wider range of functions (Sayers, 1950). Its regulating action can alter, as it were, the whole mood of the body, and its activity, if prolonged over certain parts of its range, can bring about a variety of states of ill-health and physiological malfunction, in a desperate attempt to adjust the deployment of metabolic resources to a wide variety of stressful conditions (cf. Selye, 1949; Zuckerman, 1952). Of particular interest is the implication of adrenal cortical (and other) steroids in the control of activity levels of the immunological and phagocytic defenses of the body (cf. e.g. Snell and Nicol, 1956, 1957; Nicol and Snell, 1957; Berglund and Fagraeus, 1956; MacKinnon and MacKinnon, 1956; and the interesting case of tissue transplantation immunity, Medawar, 1953). All the links seem to be present in the chain required for the control of almost all physiological processes, general health, and even resistance to infection, by the central nervous via the autonomic and endocrine systems. As a central connecting link between exteroceptors and internal control, interoceptors and external action, in general between behavior and internal physiology, the hypothalamus seems to play a fundamental role in all vertebrates--even down to lampreys (Young, 1938); and with the development of the neocortex in mammals a wealth of new connections have insured the continued integration, and older cortical structures have been pressed into service as relays, assuming such importance in this role that they have been christened by one worker the "visceral brain" (MacLean, 1954).

Against this background of anatomical and physiological knowledge, and indeed often considerably in advance of it, the partly empirical discipline of *psychosomatic medicine* has assumed the proportions of a major branch of science, with several journals and an abundant literature (see especially Wittkower and Cleghorn, ed., 1954). It is now almost undisputed ground that any aspect of a man's physiology and health is to a varying extent at the mercy of what goes on in his brain. Behavioral factors are thus assuming their proper status in human medicine. The terms "organic" and "functional" are still used, quite properly, in describing the present state of a patient, and in predicting the amount of interference (dietary, pharmacological, surgical, etc.) necessary to alter his condition. But when we consider the *origin* of diseased states, we are always concerned with the interaction of a set of casual factors, among which central nervous mechanisms and their conditions loom large. At one end of the scale they may have to be quite exceptionally adaptive and active to save their possessor from, say, an epidemic pathogen to which he is not specially resistant on genetic or nutritional grounds; at the other, they can take advantage of the slightest environmental stimulus to prostrate him with almost any kind of illness. The specificity of a diseased state may, in turn, be determined by central nervous and other factors in any proportions along a similar scale (cf. Kubie, 1954). This sort of causal situation is found in many biological contexts, and has been the subject of various kinds of formal treatment (Quastler, 1953; Russell *et al*, 1954).

The term 'psychosomatics' is among the most inept and confusing ever introduced into science. What it means in actual usage is the relation between central nervous states (partly determined by events in the external environment) and internal physiology or pathology. The prefix 'psycho' is unsatisfactory in itself, and until telepathy ceases to be a subject, and becomes a *technique* of scientific study, there is no justification for preferring this prefix to that of 'etho', now regularly used in the sense of 'behavioral' (Russell, in press, c). The suffix 'somatics' is even worse, for it is used in the exactly contrary sense to that traditional in anatomy and physiology since the nineteenth century. The proper term for the matter in hand would be the unattractive hybrid 'ethoviscerals'. 'Psychosomatics' is, however, far too firmly fixed in the literature to be dislodged at this stage.

The point is not academic in our present context. 'Psychosomatics' literally means the relation between 'soul' or 'mind' and 'bodily' affairs. The mind-body dichotomy is an entirely pathological fantasy, whose casual origin has been analyzed elsewhere (Russell and Russell, in press). It was first thrust upon science by Descartes. (No doubt the same factors which compelled him to rationalize in this way *permitted* him to make his really valuable scientific invention of Cartesian coordinates.) It is relevant in this book because it led at once to the notion that nonhuman animals, being 'mindless' or 'soulless', have no feelings and can be hurt with complete abandon, a principle Malebranche is said to have made the subject of practical demonstrations (cf., on this important byway of human pathological thought, Hume, 1956). We retain the term 'psychosomatics', but we must keep in mind that it simply concerns the relationship between what goes on in our brains (our feelings, or moods--see next chapter) and what goes on in our viscera. In this sense, there can be no doubt that for lower animals (the source for much of our knowledge of all the physiological cross-connections), psychosomatics is just as important a relationship as it is for ourselves.

It is regrettable alike on humane and scientific grounds that so large a proportion of the study of psychosomatics in animals has so far been carried out with the bludgeon of 'stress' of the more severe kinds. Everything about the rich physiological network suggests the possibility of much more refined effects of behavior upon internal states. Nevertheless, the more subtle interactions are beginning to be studied. In 1952, Beach published a thoughtful review of animal psychosomatics (in which, incidentally, he exposed with a clean and sharp scalpel the disease of thought underlying the term itself). It is not surprising that more than 90% of his review concerned reproductive physiology (the remainder being devoted to gastrointestinal responses to behavioral states). For it is in the former field that we know most about the complex effects of the physical *and social* environment on endocrine control units (via the central nervous system)--alike in pathological and adaptive function. There is indeed here a very considerable literature (cf. especially Beach, 1948). One of the most recently analyzed problems is that of behavioral effects on mammalian milk ejection (Cross, 1953, 1955a, b). Still more recently, a case of special interest has been reported. It is well known that vertebrates have in general adopted two distinct modes of synchronizing ovulation with mating: (a) estrous cycles, such that the female will only mate (or is only attractive) at a period suitable timed with her own spontaneous ovulation; and (b) the method found (e.g.) in rabbits and cats, which ovulate under the stimulus of mating (for review, cf. Russell, 1952). It has now been shown that females of the vole *Microtus agrestis* may--specifically, whether or not they are caged in groups with unrelated animals of the same species (Chitty and Austin, 1957). Here is a radical change produced by what might appear very trivial circumstances.

The more general aspects of animal psychosomatics, apart from the normal adaptive control and timing of reproduction, have so far been exploited chiefly in two contexts. The principle has been applied with success to the study of natural population control in wild animals (Chitty, 1952, 1954; Clarke, 1953a, b, 1955). In a study more directly relevant to animal welfare, Hediger (1950) has examined the effect of subtle behavioral factors on the health and physiological functions of captive animals in zoos.

The experimental biologist almost always requires animals in a stable and known physiological state; he commonly requires a number of animals in as nearly as possible the same physiological state. It is even more surprising that until very recently (see Chapter 6) little or no systematic work has been done on psychosomatics in the commoner laboratory animals, and indeed that all too little is known of their behavior in general (see especially Lane-Petter, 1953a; Chance, 1957a). This is a striking and challenging example of knowledge acquired in one context not being employed in another. We shall return frequently to this problem; suffice it here to say that the psychosomatics of experimental animals are perhaps the most important single subject for the development of humane and efficient technique in animal experiments. If we may by this time use the tag without fear of Cartesian implications, the motto of the experimenter in his dealings with his subjects must be mens sana in corpore sano, and he will not get the one without the other.