INTRODUCTION

Owing to recent advances in experimental neurology and physiological psychology, our knowledge and understanding of the role of the brain in the control of memory, learning, emotion and behaviour is steadily increasing (Smythies, 1966). However, in view of the vast amount of research data that has accumulated, particularly in the last ten years, it becomes difficult to discern any over-all pattern that may be hidden by this wealth of detail. This paper presents an attempt to describe such a pattern. Certain facts about the role of specific brain regions in the control of behaviour are presented, together with an hypothesis about the main pattern of information flow in the brain.

The traditional nineteenth century model of cerebral function depended on two main concepts—the idea of cortical “association areas” and Hughlings Jackson’s doctrine of levels. In this scheme (depicted in fig. 1) the incoming sensory information was fed from the primary sensory areas (perhaps via the thalamus) to the association cortex where all higher brain function was effected. The final programme for behaviour was transmitted from here to the motor cortex and behaviour resulted. The subcortical nuclei were either supposed to subsume certain primitive functions (e.g. pain sensation in the thalamus, coarse control of emotional activity in the hypothalamus, etc.), or merely to act as relay stations of tracts going to the all important cortex. The bulk of the limbic system (rhinencephalon) was regarded as concerned in the sense of smell. The influence of the times, a tendency to fall back on Cartesian dualism (Sherrington, 1940) and a relative neglect of subcortical systems, is now apparent.

The next phase was the realization, following the work of Moruzzi and Magoun, of the importance of the reticular formation (RF) in brain function (fig. 2). It appeared that the RF is necessary as a sort of “switching-on” device or power source for the cortex to operate at all: and following Penfield, that it might be the highest integrating centre in the
Fig. 1.—The traditional model of brain function showing flow of information. 
*Abbreviations:* SC sensory cortex; AC association cortex; MC motor cortex; T thalamus; HT hypothalamus; EI external input; II internal input; EO external output; IO internal output.

Fig. 2.—The Moruzzi-Magoun model. RF reticular formation.
brain, receiving messages from the modalities, and integrating them into a final programme which it relays to the motor cortex to control behaviour. It was supposed to function in close liaison with the cortex and thalamus, and thinking on this subject came to be in terms of systems so closely interlocked that nearly the whole brain might be involved in any one piece of thinking or behaviour. Then Gastaut's work suggested that the thalamic reticular formation might be effecting local cortical arousal thus subserving the psychological function of attention.

Now, however much the brain may function as a whole, recent evidence points to the particular roles that certain brain mechanisms play in the control of behaviour and in higher brain functions of all kinds, and it is here that the erstwhile much neglected subcortical nuclei and structures come into their own. It appears that the hippocampus (HC), the amygdala, the septal nuclei, together with the "limbic" cortex, the hypothalamus, certain thalamic nuclei and the RF, may form the central co-ordinating and executive mechanism in the brain controlling such factors as memory formation, motivation, reinforcement, elaboration of emotions, conditioned reflexes, etc. The cardinal anatomical feature of the limbic system is its arrangement into circuits.

The hypothesis to be developed in this paper is that these circuits carry a continual stream of processed schemata that act as a programming "tape" for the brain’s computers. The programme is continually being altered in response to sensory and visceral input, and it acts as the executive "tape" for programming behaviour. It continually interacts with an outer ring of auxiliary neocortical computers, specialized for complex analytical processes, and with an inner core of switching and selecting mechanisms—the RF (fig. 3).

THE ROLE OF DIFFERENT COMPONENTS

(I) The hippocampus.—The major hippocampal connexions are shown in fig. 4. It lies on the limbic ring bestride the main route to and from temporal neocortex and the reticular formation, with important connexions to the septum and hypothalamus. It also forms part of the Papez circuit. The HC–RF connexions run by two routes, a minor route via the fornix and a major direct projection via the subthalamic region. With respect to its function there seems to be general agreement that it is concerned with the retention of recent memories. Stepien et al. (1960) experiments in particular, using Konorski's technique, indicate that the HC is necessary for an animal to remember a stimulus whose meaning or cue-value is not given with it (as in an ordinary conditioned reflex). Its meaning depends on the nature of some later event with which it must be compared and thus it must be remembered per se. Likewise, in humans Penfield has shown that people with bilateral damage to their HC can remember word sequences for as long as their attention is focused on them continuously: as soon as
Fig. 3.—The model suggested in this paper. HC hippocampus; S septum; A amygdala; LC limbic cortex (OF) orbito-frontal (CG) cingulate gyrus (PL) pyriform lobe (T) temporal lobe; SMC sensori-motor cortex; ST specific thalamic nuclei.

Fig. 4.—The main connexions of the hippocampus. TC temporal lobe cortex; OFC orbito-frontal cortex; F fornix; S Te stria terminalis.
their attention wanders, or they are distracted, all is lost. There is evidence that this immediate memory is a function of the primary sensory cortex. Presumably, this can only retain these memories for as long as impulses from the thalamic RF subserving attention are impinging on this part of the cortex. The HC must therefore be a part of the mechanism laying down memories in the permanent store from this effervescent primary attention-dependent store. It is probable that the HC works together with the RF in effecting this function, and there is evidence that the permanent memory store is located in neo-cortex, particularly perhaps in the temporal lobe (fig. 5 illustrates the bare bones of this mechanism).

![Diagram](https://academic.oup.com/brain/article-abstract/90/3/697/339800)

**Fig. 5.—**A possible cerebral mechanism for laying down memories. SC sensory cortex; NC neocortex; TNC temporal lobe neocortex; MRF mid-brain reticular formation; TRF thalamic reticular formation; HC hippocampus. The thin black information flow line indicates the sensory input. The thick black line indicates the circuits responsible for evaluating which experiences to lay down (the amygdala is not shown but appears to play a modulatory role in this). The dotted line indicates pathways to possible permanent memory stores.

The hippocampus has been shown to have some other functions as well. It operates in the control of attention (in particular exerting a mutual inhibitory role over the RF in controlling the alerting response), and has an important neuroendocrine role (maintaining a tonic inhibitory influence over the pituitary/adrenal stress mechanism).

The memories that we retain are determined largely by their importance, and in this context importance often implies what has particular emotional significance or what in the past has been rewarded or punished. There is as yet no evidence that the HC plays any part in such operations, which seem instead to be a role of the amygdala.
(II) Role of the Amygdala. — The amygdala shares much the same circuits as the hippocampus with perhaps more emphasis on a visceral afferent supply and on direct connexions with the hypothalamus and orbito-frontal cortex. Stimulation of the amygdala gives rise to a variety of visceral sensations and to all manner of visceral and autonomic reactions. The experiments of Egger and Flynn (1963) have shown that it exerts higher control of the hypothalamus with respect to many behavioural reactions concerned with aggression, eating, drinking, reproductive behaviour, etc. For example, stimulation of the ventro-medial nucleus of the hypothalamus in a normally placid conscious cat will cause it to make an immediate lethal attack on a mouse it had previously ignored. Simultaneous stimulation of different parts of the amygdala can either inhibit or augment this reaction. Schwartzbaum (1960) has shown that the amygdala modulates behaviour in terms of reinforcement. Normal animals will work harder for large pellets of food than for small; amygdalectomized animals lose this facet of behaviour. Experiments by Brutowski et al. (1960) also suggest that the amygdala is concerned in determining the reinforcing value of stimuli in that animals trained to associate one S with food and another S with shock, lose this power of discrimination following amygdalectomy. Delgado (1964) has shown that stimulation of the amygdala in the freely moving conscious animal will induce such subtle behavioural changes as increasing the rate of chewing or increasing the amount of the day spent in play activity. Weiskrantz (1956) has suggested that the amygdala controls the rate of extinction of conditioned reflexes. Thus the removal of the amygdala may be accompanied by an increased rate of extinction of the conditioned fear response in the animal to human figures. This will appear behaviourally as "placidity"; but this result is not due to any primary effect on an "aggression" centre but to a more general effect on a centre controlling some basic properties of conditioned reflexes.

Thus, there is evidence to suggest that one role of the amygdala is to modulate behaviour in terms of visceral (in its widest sense) events that play so large a part in determining patterns of reinforcement, extinction, stimulus priority, etc. This function is necessary for the operation of conditioned reflexes of any complexity. Thus it may feed into the limbic circuits information from the viscera and body (e.g. "food in stomach"— "pain in right forepaw"—"thirsty"). The temporal relations between these and the environmental data being simultaneously circulated from the HC may determine which of the latter are to be retained in the permanent memory store as "important" and which allowed to die out as unimportant.

In this section we will be neglecting the small purely olfactory portion of the amygdala.
(III) Integration of hippocampus, amygdala and reticular formation.—To take this argument a step further. There is widespread convergence of all sensory modalities on HC and amygdala neurones, in the latter case particularly from visceral sources. Thus, if we allow that the amygdala exerts control over behaviour by helping to determine reinforcement values, extinction rates and similar essential features of conditioned reflex formation, we can postulate that the joint amygdala-hippocampal system with its very similar circuits impinging on the RF could act as a system correlating environmental data with visceral data as the basis for conditioned reflex formation.

The following scheme is suggested.

(a) Information about the state of the environment is fed continuously in a coded and analysed form to the hippocampus, and then circulated round the limbic circuits in the form of an internal representation of the external world.

(b) At the same time the amygdala is feeding into these same circuits information about visceral events.

(c) The time relations between this visceral data in (b) and the environmental data in (a) may underline conditioned reflex formation. Thus, if a packet of schemata A corresponding to an environmental situation A (e.g. “sound of bell”) circulates from the HC at the same time or shortly before a packet of schemata B originating from the amygdala indicating “food in stomach,” then A will be “strengthened,” will be retained in the programme and laid down in the permanent memory store. If there is no B it would simply die out and be lost. The actual centre computing these relationships may be the RF on which both circuits impinge. The RF is necessary for retention of recent memories as we have seen. Moreover, stimulation of the RF can activate one conditioned reflex and inhibit another. Furthermore, the actual behavioural effect of such stimulation depends on the particular drive present at the time. For example, in Kopa et al. (1962) experiment, if an animal on a grid (data mediated by HC) expecting shock (amygdala) is stimulated in the thalamic RF it will exhibit signs of fear (to hypothalamus), and if a conditioned avoidance response has been previously established, it will move to the safe area (motor cortex). If, however, it is stimulated on a bench (HC) where it has never been shocked (amygdala) it will show signs of general relaxation and sleep (RF). Likewise, an alimentary conditioned reflex can be activated by RF stimulation only if the animal is hungry. Thus, the RF seems to operate in terms of correlated environmental and visceral data, perhaps in the manner suggested.

(d) This “record of experience” is fed to the mid-brain RF and thence may be fed, suitably modulated, to the thalamic RF as a programme for
motor behaviour, and to the hypothalamus as a correlated programme for the visceral concomitants for behaviour ("emotion"). The "tape" produced by the analyses of incoming information can act as the programme for executive behaviour if fed into the appropriate mechanism. The function of the RF can be likened to that of the supervisor of the Atlas computer. This organizes the function of Atlas, integrating its manifold and complex parts as efficiently as possible to deal with a variety of programmes.

**FURTHER DEVELOPMENT OF THE MODEL**

The model that we can use in this hypothesis of the basic fore-brain plan is that of Krebs' cycle (fig. 6). In the place of the chemicals circulating around the dicarboxylic acid cycle with smaller packets entering and leaving at all points, we can posit in the brain that there is a stream of complex schemata circulating continuously around the limbic circuits. The primary inputs are (a) from the sensory cortex (perhaps via the frontal cortex (computing contingency) and/or via the temporal cortex (computing familiarity)). It is thus possible that much preliminary analysis and filtering

is carried out at this early stage. This information may travel from the sensory input to the circuit via various possible routes: e.g. (i) to temporal neocortex to HC, (ii) to frontal neocortex to septal nuclei, (iii) from the thalamus, or (iv) from the RF itself. (b) Visceral information may be fed to the hypothalamus, and thence to amygdala (and possibly HC in part as well).

The main outputs are (a) to motor cortex, (b) to the hypothalamus effecting behaviour and its somatic/visceral concomitants and (c) to the permanent memory store. At any point complexes of schemata could be fed by the central switching mechanism to the neocortical outer ring for computation and analysis of problems either too complex for the limbic mechanism to handle, or where specialized functions need to be called on (e.g. spatial analysis, social analysis, language and symbolic function, etc.).

Thus, the central concept is that there is in the limbic circuits a circulating complex of schemata which we can call “programme.” This is being continually modulated by sensory and visceral inputs (to include “feedback” from the motor system). At all points packets of information enter and leave the programme. The nuclei en route and the banks of neocortical ancillary computers at their disposal continually modify the programme, so that the needs of the organism can most effectively be met in response to a complex and ever-changing environment. Direct communication between the neocortical computers themselves would be a necessary part of their “higher function” of dealing with the most complex problems.

Is there then any evidence for such an internal programming circuit? The experiments of John and Killam (1959) may offer some support. A differential response was conditioned to a 10 c/s flash (“food”) and a 6 c/s flash (“no food”). Recordings were taken from different brain loci in the conscious animal. Then a long series of 6 c/s stimuli was presented which was suddenly switched to 10 c/s. At the moment of change the new environmental rhythm at 10 c/s appeared in the mid-brain RF and the visual neocortex, whereas the 6 c/s rhythm still appeared in records from the HC and thalamic RF. As soon as the animal “woke up” and responded correctly to the new situation the rhythm in these loci switched to 10 c/s.2

Thus there is some evidence that the HC-thalamic RF circuits are carrying a programme that corresponds in some sense to the animal’s actual behaviour.

1The distinction between HC (as “environmental”) and amygdala (as “visceral”) need not be absolute, but merely relative.

2This is not necessarily to suggest that the information “S is at 6 c/s” is carried by a wave-train at 6 c/s through different regions of the brain, but merely that the wave-trains carrying this information, however this may be coded, are modulated at 6 c/s. The rhythms may act as tracers of the information path without necessarily carrying the code themselves (vide Deutsch, 1962: Freeman, 1963: Adey, 1966).
This hypothesis does not imply that all brain function is carried out by means of circuit operations. Certainly ECT-resistant memory seems to be effected at the cellular-molecular level and the "switching" functions of the thalamic RF, in part at least, by means of steady DC potentials. Moreover, the greater part of brain function must be carried out by static computers in cortex and subcortical nuclei. The "Krebs' cycle" hypothesis is designed merely as a model for the major routes of information flow in the brain to include what is suggested about the function of certain components of the brain by the clinical and experimental evidence.

SUMMARY

Evidence is presented as to the role of certain limbic structures, in particular the hippocampus, amygdala and reticular formation in the higher control of memory, emotion and behaviour. The fore-brain appears to possess a three-tier arrangement—a central core or "supervisor"—the reticular formation surrounded by the limbic circuits. It is hypothesized that these continually circulate, in the manner of the Krebs' cycle, a stream of processed schemata that represents the external and internal environments in coded form and that acts as a programme for ongoing behaviour. The third tier consists of the neocortex which provides additional computing and analysing potential at the input, the output, and at various intermediate stages of this circuit.

REFERENCES