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Basal forebrain and memory

The cholinergic cells of the basal forebrain have long been known to be amongst the first to die in early stage Alzheimer's disease. However, many studies into the function of these cells have indicated they have a role in attentional mechanisms rather than learning or memory per se. By extending a hypothesis on the cause of medial temporal lobe amnesia put forward by Horel in 1978 we examined the anterior temporal stem white matter (white matter of the temporal lobe) as a cause of global anterograde amnesia. We furthered his proposal by hypothesising that the cause of the amnesia was the isolation of the inferior temporal cortex and medial temporal lobe from their afferents from the cholinergic basal forebrain. We found that disrupting ALL the cholinergic communication (by section of the anterior temporal stem white matter, fornix and amygdala) resulted in a global anterograde amnesia, but minimal retrograde amnesia (similar to patients such as H.M. (Scoville & Milner, 1957). Use of IGg-Saporin (an immunotoxin specific for the cholinergic cells of the basal forebrain) also results in this severe anterograde amnesia. We have interpreted these findings as indicitive of a circuit between frontal and inferior temporal cortices, via the basal forebrain, being crucial for normal learning. Any disruption of this circuit will result in severe anterograde learning impairments. **PUBLICATIONS**

Frontal control of learning and memory formation

Developing from the work on the role of the cholinergic basal forebrain in learning was the notion of a circuit for memory formation where the frontal cortex indicates the current goals of the subject. In line with this we have proposed a model in which the frontal cortex interacts with the inferior temporal cortex, either directly or indirectly via posterior cortical areas. This interaction serves to activate the object representation in the inferior temporal cortex, and this representation is then reinforced by the cholinergic input to it from the basal forebrain. This model developed from a series of studies that investigated the role of the interactions between frontal and inferior temporal cortex in a variety of learning tasks.

PUBLICATIONS

Reward learning

One of the crucial experiments in determining the model outlined above on the role of frontal cortex in memory formation was a study on the unexpected role of the frontal cortex in a modified conditional learning task. Frontal cortex is known to be involved in conditional tasks (if A choose X, if B choose Y) but we found that if condition A was rewarded with one type of reward and condition B another (a biconditional learning task) then the frontal cortex was no longer required. We have also used novel transfer tasks within this paradigm to show a learning advantage in a conditional task, given these differential outcomes, in normal adults. **PUBLICATIONS**

Behavioural control by social modulation

The goals that are deemed to be so important in the frontal cortex's role in learning (see above) can be numerous things. For example, one particular behaviour can be appropriate or inappropriate given certain contexts. Laughing at a joke is normal, but the laughter may be enhanced in a situation where you are attempting to impress the person telling the joke, or the laughter may be suppressed in a solemn situation. Spatial and temporal contexts can control learning (this is the basis of episodic memory where the memory is specific to a time and place) but also social contexts can control learning. Peer pressure may influence your goals, for example not wanting to stand out as being too intelligent, or too slow for fear of being picked on. The origin and cause of this type of social modulation is the basis for my current research in the laboratory.

PUBLICATIONS