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Neural Assemblies, Corticostriatal Interactions, and the Serial Organisation of Behaviour: Steps toward a Formal Theory

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The cerebral cortex of the brain (see Fig. 1A) is the grey matter that covers its surface. It is composed of nerve cells, the majority of which are pyramidal neurons. Deep in the cerebral cortex lies a large mass of subcortical grey matter known as the striatum. The majority of the nerve cells in the striatum are spiny projection neurons. The nerve cells within the cerebral cortex and the striatum are interconnected with each other by excitatory and inhibitory synaptic connections, respectively, and the two nuclei are connected together to form a re-entrant circuit (Fig. 1B). Although many of the brain's higher functions, such as perception, cognition and language, have been attributed to the cerebral cortex, the functions of the striatum have remained poorly understood. Because diseases of the striatum (such as Parkinson's disease and Huntington's disease) are associated with conspicuous disorders of movement, the striatum has been considered to be a centre for the control of movement, subservient to the cerebral cortex. Recently this view has changed. We now recognise that the striatum is involved in many aspects of behaviour, including but not limited to movement, and extending to higher functions such as thought, language and learning.

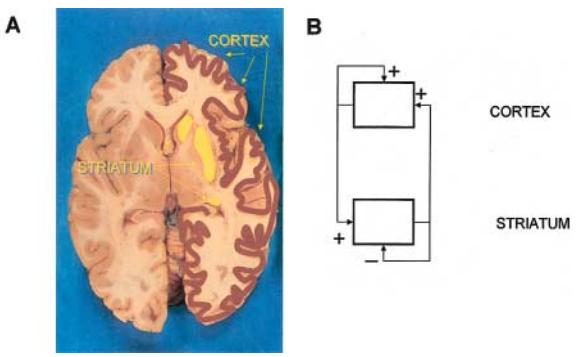

Figure 1. Anatomy of the corticostriatal system. A. Location of the cerebral cortex and striatum in the human brain. Horizontal section. B. Diagram of major excitatory and inhibitory interactions within and between the cerebral cortex and striatum.

The theory of the cerebral cortex is more advanced than the theory of the striatum. In 1949 the psychologist, Donald Hebb, proposed a theory for how things might be represented in the brain. In Hebb's theory, things are represented by assemblies of active nerve cells, each of which individually encodes

specific features of the thing (Hebb 1949). For example, a cell assembly for an equilateral triangle might be composed of nerve cells that represented different corners (with angles of sixty degrees) or edges (of certain orientation). Activation of the nerve cells in an assembly would then correspond to getting the idea of the thing.

Hebb proposed that the nerve cells in an assembly are more strongly connected to each other than to other nerve cells that are not part of the assembly. Activity in some subset of the assembly could spread along the stronger neural connections and lead to ignition of the whole assembly. For example, if we just present the corners of a triangle, without the edges, the cell assembly for the whole triangle can be ignited by spreading activation. The ignition of a cortical cell assembly is a kind of information processing that arises naturally from the dynamics of brain-like networks of nerve cells (Wickens and Miller 1997). This brain-style information processing in the cerebral cortex has useful properties. For example, ignition of cell assemblies is a fast way to perform computations that are quite demanding for digital computers, such as completing a pattern.

Cell assemblies are formed by a process of synaptic modification which strengthens the connections between cells which are repeatedly coactivated. This occurs according to a synaptic modification rule (Hebb 1949), which states that the connection from one neuron to another will be strengthened if the first neuron repeatedly and persistently takes part in firing the second. Synaptic modification according to this rule has been described in many brain areas. Experimentally, Hebbian synaptic modification has been studied in the form of long-term potentiation (LTP). This is a long-lasting increase in synaptic efficacy which follows a conjunction of presynaptic and postsynaptic activity (Bliss and Lomo 1973).

In the past, cell assembly theory has mainly been applied to perception (Braitenberg 1978; Palm 1982). It provides a good model for pattern completion, in which a pattern is recognized despite having missing pieces. After a pattern has been presented many times, the neurons which respond to its presentation become bound together into an assembly by the synaptic modification rule described above. Recognition of an incomplete pattern occurs because the incomplete pattern activates a sufficiently large subset of the elements to bring about rapid spread of activity to all the elements of the cell assembly. In this way the representation of the whole pattern can be recovered from a part of it.

Application of the cell assembly to the question of motor programming began with the proposal (Braitenberg and Schüz 1991) that a cell assembly which included cortical neurons with axonal connections to the motor output organs could represent a motor response in addition to representing the perception that led to it. Assuming that the ignition of a cell assembly occurs in a certain sequence, for example based on the different threshold of the pyramidal cells, this could provide a temporal structure for the activation of muscles involved in a movement (Wickens et al. 1994). However, the time-scale of such a process is probably less than a second. Thus, while it might explain the serial organisation of a sequence of muscle contractions involved in one syllable, it is not a promising explanation for the serial organisation of words in a sentence (Pulvermuller 2002). This requires a mechanism that can orchestrate the sequential activation of different assemblies.

Several pieces of evidence suggest that the striatum may be important in the serial organisation of complex behaviour. Electrical stimulation of the striatum, conducted in the course of neurosurgery, resulted in disturbances of verbal counting behaviour (Van Buren 1962). Another piece of evidence comes from an inherited speech and language disorder due to a mutation of FOXp2. This gene is associated with abnormalities in the striatum (Watkins et al. 1999). FOXp2 is found highly expressed in the striatum (Takahashi et al. 2003). These observations suggest that abnormalities in the striatum may be associated with impaired sequencing, but do not explain how the striatum normally contributes to this function.

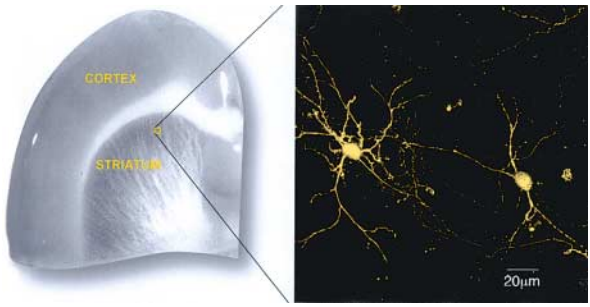

Figure 2. Experimental preparation for measuring inhibitory interactions in the striatum. Rat brain slice, showing region from which simultaneous recordings of pairs of spiny cells were made. Enlargement shows a pair of spiny cells filled with dye in the course of intracellular recording.

What is the mechanism by which the striatum contributes to the organisation of sequences of neural assemblies? One possibility is that inhibitory interactions among the spiny projection neurons bias these neurons to respond in a certain order. We have recently demonstrated inhibitory interactions between the spiny projection neurons (Tunstall et al. 2002). This was done by making simultaneous measurements from inside two spiny neurons, of the effect that the firing of one spiny neuron had on the other (Fig. 2). These interactions were asymmetrical, in that they were not reciprocal. Computer simulations (Wickens et al. 1995) have shown that a network of spiny neurons interconnected by asymmetrical inhibitory connections will exhibit slow travelling wave activity in response to a constant, uniform input (Fig. 3).

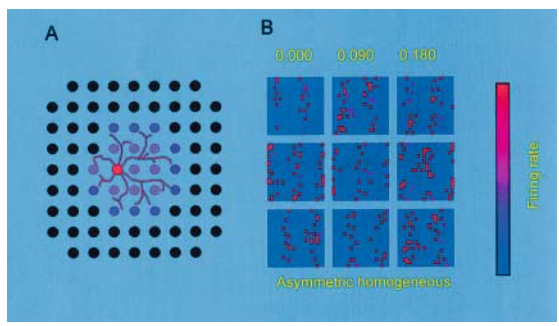

Figure 3. Simulation of network activity of the striatum. A. Connectivity of individual nerve cells in the model network. The edges of the network are connected to their opposite sides to form a 2D torus, in order to avoid edge effects. Asymmetric connectivity is assumed in this model. B. Slow travelling waves arising in response to uniform synaptic input. Panels in the vertical direction are 30 msec apart.

In the context of corticostriatal interactions, this bias to respond in a certain order may help to ensure that certain sequences of neural assembly activation are permitted, while others are prevented from occurring. To illustrate this idea with an example from language, if we assume that each neural assembly represented a word, the striatum may ensure

that only certain sequences are possible (Fig. 4). In the example, for instance, "the man with the tie" is allowed, but a sequence such as "the with" or "the the" would be prevented by the inhibitory connections between the corresponding striatal cells.

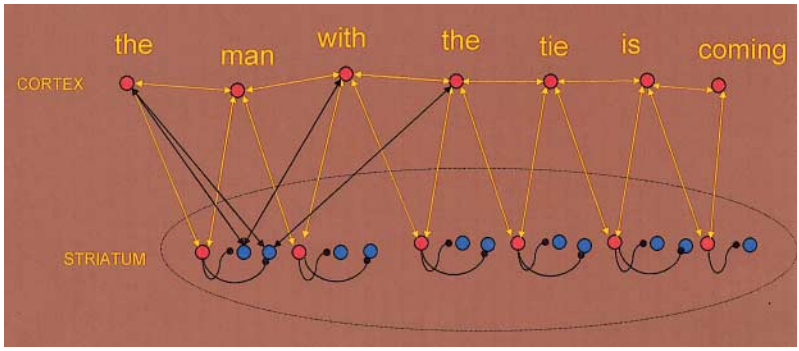

Figure 4. Conjecture about the contribution of the striatum to serial activation of neural assemblies. Inhibitory connections in the striatum create a bias towards certain sequences of neural assembly activations that are supported by corticostriatal interactions. Arrows represent excitatory connections. Black dots represent inhibitory connections. Yellow connections are active. Black connections are inactive.

In order to make flexible use of the sequencing potential of the striatal network some plasticity is required. This probably occurs at the level of the corticostriatal synapses. These synapses are modifiable by a mechanism that is similar to LTP in some ways, but different in others. Potentiation of corticostriatal synapses requires, in addition to a conjunction of presynaptic and postsynaptic activity, the release of dopamine (Reynolds et al. 2001; Wickens et al. 1996). Dopamine is a neurochemical released in response to rewarding events, and required for certain types of learning. Thus, the corticostriatal system can be thought of as an adaptive sequencing device.

In attention-deficit hyperactivity disorder (ADHD) there is thought to be a dysfunction of some corticostriatal circuits, particularly those involving projections to the striatum from the prefrontal cortex. These circuits are not primarily associated with speech and language, but play an important role in planning action and maintaining a working memory during task performance. There is also thought to be a dysfunction of the dopamine system in ADHD. One aspect of ADHD to which the foregoing may be especially relevant, is the difficulty that children with ADHD have in integrating the consequences of their past actions into the organisation of their future actions. The foregoing suggests that this difficulty may reflect an impairment of the adaptive sequencing capabilities of the corticostriatal system.

Summary

Hebb (1949) proposed that neural assemblies may constitute the neural substrate of representation in the brain. This is a powerful idea which is consonant with many results of experimental research. The theory of neural assemblies was originally developed to explain perceptual phenomena, such as pattern recognition. Recently, the theory has been extended to the representation of movements and complex behaviour. Such behaviour is generally governed by rules. The serial ordering of actions involved in speech provides an excellent example, where the rules

constitute a grammar. Interactions between the cerebral cortex and the striatum, a subcortical nucleus in the basal ganglia of the brain, may be necessary to account for rule-governed progression of neural assembly activity. Anatomical details of the microcircuitry of the striatum and its interconnections with the cerebral cortex suggest a plausible mechanism for the serial organisation of behaviour. Dysfunction of the corticostriatal interactions may contribute to problems in the serial organisation of behaviour in children with ADHD.

References

Bliss, T.V.P. and Lomo, T. Long-lasting potentiation of synaptic transmission in the dentate area of the unanaesthetized rabbit following stimulation of the perforant path. *J Physiol* 232: 331–356, 1973.

Braitenberg, V. Cell assemblies in the cerebral cortex. In: Heim R, Palm G (eds), *Theoretical approaches to complex systems*, Springer: Berlin, 1978, p. 171–188.

Braitenberg, V. and Schüz, A. Anatomy of the cortex: Statistics and geometry. Berlin: Springer, 1991.

Hebb, D.O. The organization of behaviour: A neuropsychological theory. New York: Wiley, 1949.

Palm, G. Neural Assemblies. Berlin, Heidelberg and New York: Springer, 1982.

Pulvermuller, F. A brain perspective on language mechanisms: from discrete neuronal ensembles to serial order. *Prog Neurobiol* 67: 85–111, 2002.

Reynolds, J.N.J., Hyland, B.I. and Wickens, J.R. A cellular mechanism of reward–related learning. *Nature* 413: 67–70, 2001.

Takahashi, K., Liu, F.C., Hirokawa, K. and Takahashi, H. Expression of Foxp2, a gene involved in speech and language, in the developing and adult striatum. *J Neurosci Res* 73: 61–72, 2003.

Tunstall, M.J., Oorschot, D.E., Kean, A. and Wickens, J.R. Inhibitory interactions between spiny projection neurons in the rat striatum. *J Neurophysiol* 88: 1263–1269, 2002.

Van Buren, J.M. Confusion and disturbance of speech from stimulation in vicinity of the head of the caudate nucleus *J. Neurosurg* 20: 148–157, 1962.

Watkins, K.E., Gadian, D.G. and Vargha-Khadem, F. Functional and structural brain abnormalities associated with a genetic disorder of speech and language. *Am J Hum Genet* 65: 1215–21, 1999.

Wickens, J.R., Begg, A.J. and Arbuthnott, G.W. Dopamine reverses the depression of rat cortico-striatal synapses which normally follows high frequency stimulation of cortex in vitro. *Neuroscience* 70: 1–5, 1996.

Wickens, J.R., Hyland, B. and Anson, G. Cortical cell assemblies: A possible mechanism for motor programs. *J. Mot Behav* 26: 66–82, 1994.

Wickens, J.R., Kotter, R. and Alexander, M.E. Effects of local connectivity on striatal function: Simulation and analysis of a model. *Synapse* 20: 281–298, 1995.

Wickens, J.R. and Miller, R. A formalisation of the neural assembly concept: 1. Constraints on neural assembly size. *Biol Cybern* 77: 351–358, 1997.