BASAL GANGLIA NEURAL CODING OF NATURAL ACTION SEQUENCES

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Abstract: In this study we present evidence that neurones in the basal ganglia code the serial order of syntactic (rule-driven) sequences of natural motor behaviour (rodent grooming). Neuronal activity was recorded from the striatum in freely behaving rats while they spontaneously groomed themselves. Offline, we analysed sequential patterns of movement in a frame-by-frame scan of video taped behaviour and evaluated the correlation of neuronal activity to syntactic and nonsyntactic grooming movements. We found that sequential patterns of grooming movements activated striatal neurones. Neurones were activated preferentially during particular serial patterns (syntactic chains) of grooming and were inactive, weaker or different during the same movements in other sequences. Syntactic chains of grooming were preferentially coded by neurones in a dorsolateral striatum site where lesions disrupt syntactic grooming patterns[1,13]. The timing of neuronal activation, which was generally synchronised with or followed movement onset, suggested a role in the execution of the behavioural sequence rather than one of related to the initiation of phasic elements. We conclude that that neuronal activity in rodent neostriatum codes the serial order of natural actions and not the simple motor properties of constituent actions within a sequence.

1. INTRODUCTION

The idea that the basal ganglia have a role in motor control, first proposed by Magendie[26] more than 150 years ago, is now well accepted. But what exactly do the basal ganglia do for movement? One clue can be obtained from studies of Huntington's and Parkinson's diseases. The devastating impact on movement caused by these degenerative disorders of the basal ganglia strongly supports a motor function. However, close scrutiny suggests that the elemental properties of motor control are less effected by basal ganglia pathology than the organisational aspects of motor control. Parkinson's patients can perform motor tasks that require them to control kinematic and dynamic features of movement such as force and

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direction, however, their difficulty in performing *sequences of movements*[20] suggests that a higher, organisational aspect of motor control is disturbed by this disorder. Huntington's patients have been shown to have special "ideomotor" deficits when asked to make movements of the type, for example that would be involved in using a particular tool[34]. Some have suggested that the neostriatum may even be involved in sequential disorders of human language[11,36]. Marsden[27] suggested that "The *sequencing* of motor action and the *sequencing* of thought could be a uniform function carried out by the basal ganglia." Other evidence supports the idea that injury to the basal ganglia may produce an inability to control behavioural sequences in general. The pathological repetitions of spoken words in Tourette's syndrome[14] and the tormenting habits and thoughts of obsessive compulsive disorder[32], both of which are associated with pathology of the basal ganglia. These disorders suggest that the basal ganglia might even participate in the organisation of the sequential aspects of "cognitive" behaviour. Four decades ago Karl Lashley[25] noted the continuity between serial order at different levels of psychological complexity and the continuity this may imply for the underlying neural substrates of syntax. Several have suggested that behavioural sequencing functions of the basal ganglia might originally have evolved to co-ordinate sequences of instinctive behaviour and later have been modified to control learned behaviour[2,31]. We believe that Marsden may be right; circuitry within the neostriatum may provide a common link for sequencing phenomena as diverse as actions, words, or thoughts and that Lashley's idea of syntax can provide a profitable *formulation offunction* for these structures[12].

2. SYNTACTICAL GROOMING SEQUENCES IN RODENTS

All purposeful behaviour is sequential, so what do we mean by *syntactical sequence?* In the simplest terms, a syntactic sequence is one that follows rules that determine the temporal progression of its elements. These rules impart a mathematical predictability to the sequence. Language has syntax. Given an arbitrary word, it is possible to predict with some level of probability what the next word in a language sequence will be. Other behaviour can be described as having properties of syntax if one can demonstrate lawful sequential dependencies. For example, rodent grooming behaviour has distinct syntactical properties[7,15,16,33]. The most stereotyped serial pattern that occurs in rodent grooming is the 'syntactic chain' pattern shown in the choreograph *(Figure 1).*

Syntactic grooming chains have approximately 25 movements that are linked in a sequence that follows a fixed serial order of four phases[7,9]. Phase 1 consists of 5-9 rapid elliptical strokes over the nose and mystacial vibrissae lasting for about one second. Phase 2 is short (0.25 s) and consists of small asymmetrical strokes of increasing amplitude. Phase 3 consists of large bilateral strokes that take 2-3 s for the animal to complete. The chain concludes with Phase 4, which consists of a postural turn followed by a period (1-3 s) of body licking directed to the flank. Once the pattern begins, each remaining action can be predicted with over 90% accuracy. The four grooming actions that contribute to this sequence also occur in unpredictable order and combination outside of the syntactical chain sequence. The entire syntactical chain occurs with a frequency that is over 13,000 times greater than could be expected by chance (based upon the relative probabilities of the component 25 actions obtained from grooming outside of this syntactic chain[9]).

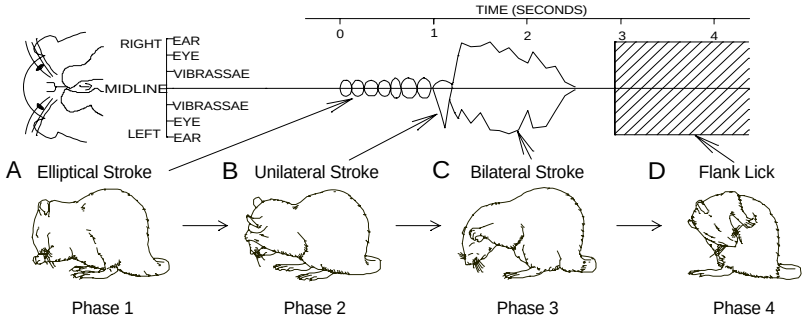

Figure 1. Syntactic grooming chains. The 4 syntactic phases, A) elliptical strokes, B) unilateral strokes, C) bilateral strokes and D) body licking are schematised in the drawings. The top graph, expresses choreographed forepaw movement as distance from the midline (y-axis) as a function of time (x-axis, tics=1 sec) for a typical syntactic chain (left paw represented by line below the axis, right paw represented by line above the axis).

We have exploited this natural sequence as a window into the role of neural systems in sequential co-ordination. The more common approach is to train animals to perform responses in an arbitrary order. That approach allows one to study very complex sequences, but it has the pitfall of confounding neural mechanisms of learning and memory with mechanisms of action syntax or sequential co-ordination per se. Failure on learned tasks can be due either to disruption of memory processes or to disruption of sequencing per se: the two cannot be discriminated. Natural behavioural sequences, on the other hand, do not depend upon explicit training, and provide a way to study neuronal mechanisms of behavioural sequencing independent of memory and explicit training.

3. NEURONAL CORRELATES OF GROOMING MOVEMENTS

3.1 Methods

These studies were based on neuronal recordings from freely moving rats. Briefly, Sprague-Dawley rats (~250g) were anaesthetised with ketamine-xylazine and implanted with a permanent multisite recording electrode in dorsolateral or ventromedial neostriatum. The lightweight implant did not interfere with normal behaviour and caused no discomfort. The electrodes were connected to a preamplifier and a computer through a commutator, which permitted free movement in a circular recording chamber. Spontaneous behaviour was videotaped and neuronal discharge activity was recorded for one or more hours while the animals groomed and moved about freely. A frame-by-frame analysis of the videotaped grooming sequences was conducted off-line[7,8] to find the onset and offset times of movements. Neuronal activity was analysed in relation to grooming actions by the construction of perievent time histograms. At the completion of recording the animals were killed by an overdose of anaesthetic, brains were removed and prepared histologically for verification of recording sites.

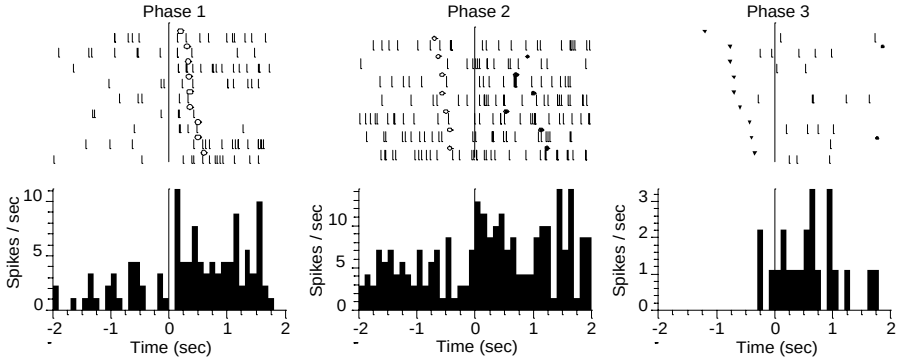

Figure 2. Three neurones responsive to syntactic grooming from dorsolateral (left, middle) and ventromedial (right) neostriatum. The phase onset is at time = 0. The histogram represents the average firing rate (y-axes) in bins 50 ms wide. Rasters of spike trains indicate neuronal activity (one spike train per chain) and the marks in each spike train indicate the time at which the preceding or following Phase began. Neuronal activity generally occurs at about the same time as movement onset.

3.2 Results

Syntactic chain grooming was a potent activator of striatal neurones (41% of tested neurones) in both dorsolateral and ventromedial striatum (Figure 2). Nonsyntactic grooming, in contrast, activated a much smaller proportion of neurones (14%) even though these less stereotyped grooming bouts incorporate the same movements and they occur much more frequently than syntactic chain sequences. Excitatory responses were more common (99%) than inhibitions (20%). All but one instance of inhibitory activity was accompanied by an excitation as well. Each phase of the grooming chain was associated with activity changes. Although the proportion of phasic responses dorsolateral striatum was greater (20%, 14%, 18%, 18%; Phases 1 to 4 respectively) than ventromedial neurones (16%, 11%, 8%, 5%; Phases 1 to 4), the differences were not significant.

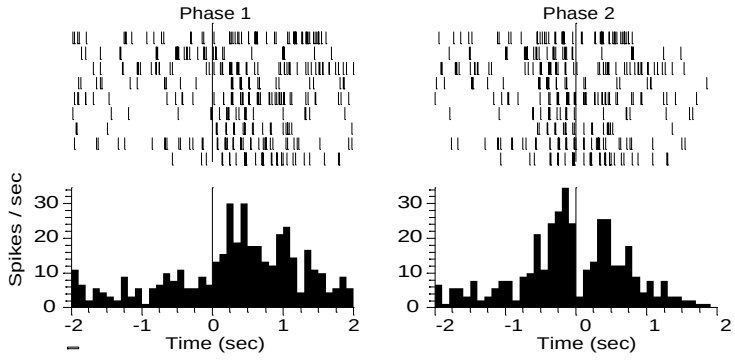

Figure 3. Multiple chain responses from the same cell. This striatal neurone had increases in activity after both Phases 1 and 2.

The dorsolateral region, whose integrity is crucial for chain grooming, had other similarities and differences to the ventromedial striatum. Most neurones were responsive to a single action in the grooming chain (dorsolateral 28% vs. ventromedial 27%), but in the dorsolateral region the proportion responding to 2 or more actions (Figure 3, 18%) was more than 3 times larger than the proportion (5%) in ventromedial striatum. Multiphase responses such as this are consistent with encoding of the sequential pattern as a whole. The predominance of this kind of response in the dorsolateral region suggests a tighter link to syntax properties of the stereotyped pattern.

Other factors also point to the much more potent influence of syntactic chain grooming. Most chain-related neurones were not activated during nonchain grooming. Even highly similar movements evoked different responses from most neurones depending on whether they occurred inside or outside a syntactic chain sequence. For some of these neurones, the pattern of neuronal activation related to equivalent strokes was radically different (Figure 4). In a few neurones there were some similarities between chain and nonchain responses, however, even in these cases the equivalent nonchain grooming actions were associated with much weaker activation than their chain counterparts. Overall, our findings suggest that information processing in the striatum is concerned preferentially with syntactic grooming sequences. Activation by nonchain grooming is not only less common, but the patterns of responses also differ and they are weaker than activation related to syntactic chain sequences. The ability of sequential context to gate neuronal firing to equivalent movements in an all-or-none fashion provides one of the strongest indications that these neurones coded *action syntax* or sequential properties of behaviour rather than the mere component movements.

Does striatal activity *initiate* grooming movements in a chain? The answer may generally be no. In our sample of neurones responsive to Phase 1 onset, which was the most reliable activator of striatal activity, not a single neurone in dorsolateral striatum had a change in neuronal activity and only one ventromedial neurone had activity before Phase 1. This timing relationship also appeared to be true for other movements in the sequence with a general pattern of movement bout onset contiguous with or followed by neuronal activation. Neuronal activity following the onset of a movement could be initiating subsequent

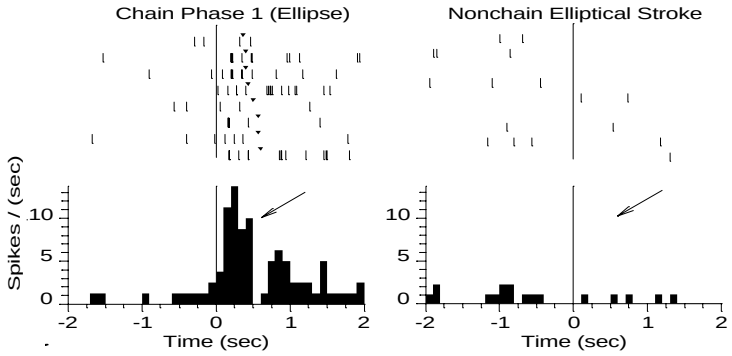

Figure 4. Chain versus nonchain activity. This dorsolateral striatal neurone had an increase of activity associated with the onset of Phase 1 (elliptical strokes) during chain grooming (left panel, arrow). The same neurone had no change associated with the onset of elliptical strokes during nonchain grooming (right panel, arrow).

movements in the grooming chain, however, the variability between the onset of neuronal activity and the onset of movement was usually less to the preceding than the following phase. This timing of neuronal activation suggests that these neurones may in fact be contributing in some manner to the initiation of the next action in the sequence, or else to coding of the sequential pattern as a whole. Such a role in movement control is in keeping with our idea that the basal ganglia are facilitating the execution of syntactic action sequences. In general it seems that striatal neurones do not play a direct role in movement *initiation so* much as in movement pattern. This functional relationship to the movement sequence is important since previous work has shown that dorsolateral striatal damage does not impair the animals' ability to initiate syntactic chains, but the ability to complete the sequential pattern is severely disrupted.

3.3 Rate Coding

Besides the phasic changes in neuronal activity noted above, the neuronal code may be distributed over assemblies of neurones in a manner not easily detectable as phasic changes in perievent time histograms. Target structures, in the pallidum for example, could retrieve this information by combining input from many striatal neurones. We searched for possible rate codes[3] across periods of chain grooming, nonchain grooming (i.e., grooming movements in other patterns of serial order) and quiescent behaviour (i.e., quiet resting). Median rates differed significantly with these 3 categories behaviour (Figure 5, ANOVA, $p = 0.032$) in dorsolateral striatum but not in ventromedial striatum ($p > 0.05$). Syntactic grooming chains were associated with higher spike rates than either resting or nonchain grooming (Figure 5). Faster firing during syntactic grooming reinforces the unique relation of this sequentially stereotyped behavioural sequence to activity in the dorsolateral neostriatum.

4. CONCLUSIONS

We have shown that neuronal activity in the neostriatum of rodents is preferentially correlated to specific syntactic sequences of grooming movements. It appears that the serial

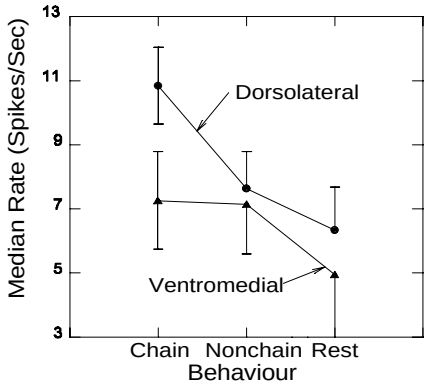

Figure 5. Rate coding. Median firing rates (y-axis) were greater for chain than nonchain or rest in dorsolateral striatum (top line). There were no significant differences in the sample of ventromedial neurones.

order of the movements and not the grooming movements per se was the critical factor in determining neuronal activation. In other words, it was the action syntax that was crucial for the activation of these neurones.

Our findings also demonstrate that the dorsolateral region of the neostriatum may be especially important in coding the serial order of grooming movements, in comparison to ventromedial neostriatum. Both regions had neurones that were sensitive to syntactic grooming chains, but dorsolateral neurones were more vigorously activated than ventromedial neurones during syntactic chains. Dorsolateral neurones were also more likely to respond during multiple phases of a syntactic grooming chain. This suggests that dorsolateral neurones may code syntactic patterns of movement serial order as a higher-order property, distributed over the duration of the chain. By contrast, activity of neurones in the ventromedial region actually declined during some phases of syntactic grooming chains, and ventromedial neurones were less likely to code either multiple phases or terminal phases of the chain pattern. These findings suggest that the dorsolateral region may be concerned with syntactic phase to phase transitions, or overall sequential structure, while ventromedial activity is concerned more simply with the onset of the chain pattern.

The timing of striatal neuronal activity with respect to movement suggests that it likely does not *initiate* or *generate* the syntactic sequence. Instead, we believe it is more likely to have a role in the *implementation* of the sequence that is initiated and programmed elsewhere in the brain. This role is consistent with the results of lesion and transection studies of the neural basis of behavioural grooming syntax[6,10]. Elementary generation of the basic 4-phase syntactic pattern in rats can be carried out by the isolated pontine brainstem. Even when the brain has been transected above the superior colliculus or pons and cerebellum the rat can still generate occasional syntactic chain patterns of grooming more often than chance even though they have marked deficits in sequence implementation[6]. However, the neostriatum is needed for the implementation of the pattern into normal streams of behaviour. Rather than a role in generating the syntactic sequence, these findings support an executive function for the striatum regarding serial co-ordination in which brainstem-generated syntactic patterns are incorporated into behaviour. This is consistent with suggestions that the basal ganglia may serve a role to focus selection and inhibit competing motor programs[28] and a specific role in sequence control 5. This role is also compatible with recent models of the neostriatum[17-19,21]. A recent review points out that several computational models of basal ganglia "have emphasised pattern recognition or mutual competition, or a combination of the two, to form pattern classification networks"[4].

How does this proposed role for the basal ganglia in facilitating stereotyped sequences in rats relate to basal ganglia function in humans? One possibility is that striatal circuitry preadapted for coordinating innate sequences of movements may now also participate in coordinating sequences of learned movement, and even of language and thought. The basal ganglia are activated by learned including sequential patterns of movements[22], and deficits in humans with basal ganglia disease have been suggested to include linguistic grammar errors as well as habit learning[24,29,35,23,30]. Thus serial coordination of action syntax by basal ganglia may provide a window into normal human behavior and into pathologies related to complex behavioral sequences.

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