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Multidisciplinary approaches to the understanding of neural control of movement

Program and abstracts

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Program

Integration and learning in the oculomotor system

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The focus of this presentation is on three hindbrain nuclei that appear to be sufficient for processing all the visual and vestibular sensory signals accountable for horizontal oculomotor performance and plasticity in the goldfish. Neural signaling in two of these nuclei is well correlated with **eye velocity**, and in another, with **eye position**. Based on extensive reciprocal connections between these brainstem areas and the cerebellum, each nucleus has been thought to act as a "neural integrator" by way of either single cell or circuit mechanisms. Evidence will be presented suggesting that the proposed neural integration is fundamentally a single cell process for **eye position** and a circuit property for **eye velocity**. In all vertebrates, cerebellar Purkinje cells directly control individual subgroups of vestibuloocular neurons and their firing patterns are well established as essential for oculomotor learning and memory. To clearly distinguish the sites of plasticity, monocular visual stimuli were used to implement separate tracking of the right and left eye during two oculomotor training paradigms; namely, either changes in vestibuloocular reflex gain or retuning of eye position integrator time constants following each saccade/fixation. In both cases, **learning and short-term memory of monocular eye movements** were specially significant in amplitude and direction as well as reversibility. These findings demonstrate that the naturally-occurring conjugate oculomotor behaviors in the goldfish are actually produced by predominantly **monocular visuo-vestibulocerebella**r neurons and circuits. Complementary firing rate analysis of both eye position and velocity (vestibular and precerebellar) neurons clearly distinguished two populations, correlated with either the right or left eye, providing further corroboration that monocular eye movement learning and memory is entrained and relayed through **separate cerebellar Purkinje-vestibular channels**. Together this work supports the hypothesis that all oculomotor plasticity paradigms (e.g., visual, vestibular, fixation) **depend on 'multiple' modifiable sites** in the vestibular nucleus, and that the cerebellar circuitry is used **to initiate and support, but not store**, the behavioral modifications. Finally, based on recording and inactivation of the inferior olive, it will be argued that the two major precerebellar (olivary-climbing and mossy fiber) pathways are operationally independent, employing Purkinje cells to achieve the different, but complementary, motor roles of **'stability' and 'learning'**.

Behavioural and TMS evidence for the estimation of motor state in the cerebellum R.C. Miall

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The cerebellum has been proposed to be a crucial component in the state estimator that combines information from motor efferent and sensory afferent signals to produce a representation of the current state of the motor system. Disruption of this state estimate would lead to errors in movements, and can explain the hypometria and dyscoordination of cerebellar dysfunction.

The state estimate might also be used within an internal negative feedback loop to control action, an idea known as Smith Prediction. In this model, control can be disrupted by imposing additional feedback delays in the sensory-motor loop, as the predicted feedback would be asynchronous with respect to the delayed feedback, until adaptation has occurred. I will first present some recent visuo-motor tracking data testing the Smith Predictor model during adaptation to delays, and show that the model does not predict the observed changes in performance. The cerebellum may act as a state estimator, but the incorporation of this into a high gain, low delay, internal feedback loop does not seem likely.

In contrast, the cerebellar state estimate may be fed to other areas, including motor and parietal cortex, for update of the body schema, for planning and for control of action. I will report the effects of TMS over the ipsilateral cerebellum as healthy subjects interrupted a slow voluntary movement to make a rapid reach towards a visual target. Errors in initial reach direction were made after cerebellar stimulation, and were not seem in control conditions. The average directional errors were consistent with the reaching movement being initiated 140 ms late, and they suggest the intact cerebellum is responsible for estimating the hand position over this time interval. These TMS results support the idea of state estimation within the cerebellum, and provide the first direct evidence for its disruption.

New aspects of visually guided reaching control - Effect of surrounding-world on the arm movement -

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Recent neuroscience studies have been concerned with how aimed movements are generated on the basis of target localization. Sequential processing of trajectory formation, kinematics transformation, and dynamics transformation well explains the computational mechanism of the voluntary movements. However, visual information from the surround as well as from the target can influence arm motor control, in a manner similar to known effects in postural and ocular motor control. In this talk, in comparison with the conventional computational scheme to explain voluntary arm movements, I introduce an ultra-fast manual motor response directly and unintentionally elicited by a large-field visual motion, which we named "manual following response (MFR)".

The latency of muscle activity generating MFR was as short as that of the ocular following responses (OFR) to the visual motion. The degrees of motion coherence of the visual stimulus modulated this arm response. This visuomotor behaviour was still observed when the visual motion was confined to the "follow-through" phase of a hitting movement, in which no target existed. The series of experimental evidence suggest this visuomotor response is generated in a manner similar to the reflexive somatomotor response.

To explore the sensorimotor processing involved in the MFR, we next examined the MFR specificities to the image stimulus contrast and spatiotemporal frequency. The high sensitive feature in the low contrast range and the spatiotemporal tuning of MFR were surprisingly similar to those of the OFR, while that spatiotemporal tuning was clearly different from that of perceptual effects caused by visual motion. These observations suggest that two different reflexive visuomotor responses, MFR and OFR, share a common visual motion analysis despite of completely different motor coordination. Based on the above results and new findings in the recent experiments, I will discuss the computational mechanisms of online visuomotor control.

Conversion of sensory signals into perceptual decisions

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Most perceptual tasks require sequential steps to be carried out. This must be the case, for example, when subjects discriminate the difference in frequency between two mechanical vibrations applied sequentially to their fingertips. This perceptual task can be understood as a chain of neural operations: encoding the two consecutive stimulus frequencies, maintaining the first stimulus in working memory, comparing the second stimulus to the memory trace left by the first stimulus, and communicating the result of the comparison to the motor apparatus. Where and how in the brain are these cognitive operations executed? We addressed this problem by recording single neurons from several cortical areas while trained monkeys executed the vibrotactile discrimination task. We found that primary somatosensory cortex (S1) drives higher cortical areas where past and current sensory information are combined, such that a comparison of the two evolves into a decision. Consistent with this result, direct activation of the S1 can trigger quantifiable percepts in this task. These findings provide a fairly complete panorama of the neural dynamics that underlies the transformation of sensory information into an action and emphasize the importance of studying multiple cortical areas during the same behavioral task.

Thalamic control of oculomotor decisions

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Preparing and generating a goal-directed movement is a fairly complex process. Even a simple saccadic eye movement to an object may invoke a number of neural processes that are related to attention, working memory, coordinate transformation, timing adjustment, decision-making, and reward expectation. Although most studies of oculomotor control have emphasized the role of fronto-parietal networks in performing the relevant computations and relaying the results of these computations downward to the basal ganglia and brainstem, more recent studies suggest that the bi-directional communication through cortical-subcortical loops is equally important.

 To provide evidence for the importance, I will show that the ascending half of these loops via the central thalamus plays a crucial role in saccade generation. In recording from single neurons within the ventrolateral thalamus, we found a strong correlation between the timing of buildup activity and the timing of self-initiated saccades. Inactivation of these neurons did not alter externally triggered, visually-guided saccades, but delayed the initiation of self-timed, memory-guided saccades. The results indicated that the central thalamus played a role in saccade generation, in particular, when both goals and timing of saccades were internally determined. Neuronal signals through the thalamus that increase over time might assist preparatory processes in the cerebral cortex, thereby regulating the timing of self-initiated saccades. I will suggest a possible role of thalamic signals in self-timing in general.

Representation of decisions in a free choice task by prefrontal neurons

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For the better survival in a dynamic environment, the brain must perform active selections of behavioral options, rather than just making passive reflexive responses. In order to investigate this active selection process in the brain, which is often referred to as 'decision making', free-choice task has been recently introduced to the field of neuroscience. Although it has been suggested that parietal, prefrontal, and striatum neurons show activities relevant for the decision-making process, there is yet much to be known for the full description of the whole decision-making mechanisms in the brain. Here we show that prefrontal neurons, during the performance of a free-choice task, change activities depending on the stimulus selection in the upcoming choice period. By examining the activity of these neurons by the receiver-operated-curve (ROC) analysis, it was indicated that an ideal observer could predict the future stimulus selection of a subject with sufficient accuracy by observing the activity of only one of these neurons. Existence of such a clear representation of decision in the prefrontal cortex suggests its deep involvement in the process of decision-making, as well as the process of action execution based on decision. We anticipate that this study would be the starting point of the investigation of the decision representation in the prefrontal cortex. Possibly in the near future, complete predictions of a subject's choice behavior based on the prefrontal multiunit recording will be possible.