Biomedical Correlates of Voluntary Actions

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We rarely ever give much thought to the processes underlying the commonest voluntary actions, e.g., throwing an object, holding a glass of water, having our meals. It has always intrigued me why it is so. Perhaps it is because there is an implicit assumption that something as common as a muscular contraction is a very complicated process. And in a sense, that certainly is true. The neural mechanisms in the simplest actions performed are unbelievably complex. And even in the first quarter of the twenty-first century, they remain relatively very poorly understood.

The most basic axiom is that the simplest actions are realised through the activation of a large number of muscles. There is hardly any action that can be realised through the activation of just a single muscle. For instance, when we pick up a cup of tea, several muscles of the eye would be initially involved. Then the muscles of the shoulder and upper extremities get activated. A very rough calculation would reveal that at least forty different muscles are brought into action and they do so in coordination with each other. But it is crucial to appreciate that each muscle is made up of muscle fibres and every fibre receives its neural input. Thus, it becomes evident that even the so-called 'simple ' movements are in real terms not so simple when we tend to view them from a neural angle.

We can therefore well imagine the neural conundrum that must be taking place in the brains of the top cricket players where it is crucial for all the actions of different muscles to be adequately coordinated and where there can be no planning in advance.

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Role of Interneurons

A few years ago, neuroscientists at the neurosciences section of MIT conducted researches to look into the process of muscular contractions and coordination by the brain which governs all our voluntary actions. Their basic goal was to determine how the CNS regulates the muscle fibres that are brought into action during our motor activities. They initially focused on the spinal cord and determined that there are a specialised group of cells which they named "interneurons"[1] which play a key role in the process. Interneurons according to them are:

"neurons that transmit impulses between other neurons, and that is interposed between the sensory portion of the spinal cord and its motor output. Interneurons are organized in functional modules, and each module activates a particular set of muscles in distinct proportions. They labelled this entity of patterned muscle activation a muscle synergy. This modular spinal structure is the central piece of a discrete combinatorial system that utilizes a finite number of discrete elements (that is, the muscle synergies) to express a voluntary movement"[1]

Essential Role of the Frontal Cortex

The cerebral cortex in the frontal area usually transmits messages to a specific spinal module. As soon as the cortical command reaches the desired destination, the now activated spinal module fire the nerve cells which constitute a pathway where impulses pass from the spinal cord to a muscle. These nerve cells are known as motor neurons. The muscle fibres are accordingly depolarised and that is followed by muscular contraction leading to movements.[2] The electromyographic activity can be recorded by placing electrodes like an electrocardiogram.

Factoralization algorithm takes into account every data that emerges from the EMG (electromyogram) and which also extrapolates from these a concatenation of generative muscular synergies along with the coefficients of each during particular voluntary motor behaviour. The inference that can be drawn from this is that only a small number of synergies can explain the variation in muscular patterns to a very large degree.[2]

The evidence that we have at present would seem to suggest that peripheral motor systems tend to function in a discrete combinatorial manner. The motor system in many ways is analogous to a language system where very discrete elements and rules that govern their combination can generate a large number of distinct concepts. All this would suggest that the way motor system operates, is a very complex task of controlling so many different muscle systems and motor units through modularization at the spinal cord.[3]

Having dealt with this complex conundrum, we are immediately confronted with another query i.e., how does the human brain work out the exact combination of synergies to perform a particular motor action. The most remarkable feature here is the ability of the motor system to adapt itself to find specific solutions to rapidly changing circumstances. And the evidence at present would suggest that this capacity is almost exclusively dependent upon the neural circuits of the frontal lobe of the cerebral cortex which combines, then selects and finally activates the spinal modules. Although we have been able to uncover many riddles, there remain a large number of questions which as of now remain unanswered and neuroscientists are still lucubrating indefatigably.

Every frontal lobe hemisphere has at least four distinct regions which generate signals for voluntary movements -the dorsal region, the ventral pre-motor region, the supplementary motor area and the primary motor cortex. These regions are interconnected and tend to receive inputs from several sources: a) external sensory information, b) internal sensory information (e.g., tendon force or the length of the muscle), (c) attentional system,(d) subcortical areas like the cerebellum (although basal ganglia is also a subcortical structure, its role in motor control has not yet been established). These signals then proceed to the motor cortical areas where they link up with the dendritic cells of cortical areas 5 and 6. It is at this level the signals are integrated and set up neuronal depolarization. This is subsequently relayed to the spinal cord through the long pathway.[4]

Axon Pathways in Voluntary Movements

There are several output pathways of axons that serve to connect the motor and premotor cortical areas with different variety of spinal neurons. One of these descending pathways generates information on any impending movement. Other output pathways are:

a. Corticospinal fibres which terminate at the interneurons involved in the activation of spinal cord modules

b. Coticomotoneural pathway from the most inferior section of the primary motor cortex. Its role in the execution of voluntary motor movements is still incompletely understood

c. A set of fibres connecting the basal ganglia to the motor cortex

d. Fibres connecting cortex to the cerebellum [4]

Initiation of Motor Behaviour by Motor Cortex

Our contemporary state of understanding would lead us to believe that the motor cortex is mainly responsible for initiating motor behaviour but there is no general agreement at all on how neural processing within the frontal cortex can lead to voluntary movements. A leading neuroscience researcher by the name of Edward Evarts attempted to unravel neural activity in the cortex by recording the activity of single cortical neurons in monkeys and correlating them with limb posture and force. Based on his findings, he inferred that the cortical motor neurons probably encoded the muscular force needed for voluntary movement. Nearly forty years ago, another leading neuroscientist Georgopolous and his colleagues were able to demonstrate that cortical neurons were "broadly tuned to the direction of hand movements!" In the last decade, neuroscientists have observed the motor cortex in encoding different types of movements.[5]

There are of course obvious problems in researches based solely on microelectrode recordings. In a recording of this nature that is acute, only a small number of neurons are involved. Likewise in a chronic recording, only about a hundred neurons can be studied. And we are aware that there are millions of neurons within the cortex highly interconnected with each other. The interpretations therefore must be taken with a great deal of caution.

It therefore logically follows that to understand the functioning of the motor cortex, we need different approaches. Recently computational neuroscientists and neurophysiologists have collaborated to produce new models of the motor cortex. One model that has gained some initial popularity suggested optimal feedback control and recurrent neural network. However, as our knowledge of neurons remains limited, these models could not uncover the very complex interactions among different cortical cells and their links with the spinal cord, basal ganglia and the cerebellum.

Recent developments in molecular biology and new techniques in medical technology may assist us in understanding this better. For instance, we are in a position to activate and inhibit neuronal activity utilising different strains of virus-carrying rhodopsin. We are hopeful that we may have answers to some questions in neuroscience that have eluded us thus far.

Neuronal activity in the motor cortex is indeed a complicated issue that involves the coordination of regional and local interactions between the cells, a myriad of sensory inputs and re-entry circuits within the cerebral cortex. Relatively recent researches have indicated that another way to fire the cortical neurons is to imagine an action without producing actual movement. Similar researches have shown that moving from one distinct mental task to another alters the pattern of cortical activation. These results were obtained using the positron emission tomography technique.[6]

What is intriguing here is most of the activity was determined in the premotor and supplementary areas of the brain and less so in the primary cortex in both motor imagery and movement observation. This would suggest that wilful representations of actions involve similar activation as happens during voluntary movements. And these observations indicate a wider scope of the motor system beyond the mere generation of voluntary actions.And it opens the way to record from the cortex and put to use neural signals for the prosthetic devices.

Motor Imaging of Voluntary Actions in the Brain

The motor imaging of actions is intimately linked to cerebral representations of motor memories. The logical query here is when we acquire proficiency in a particular skill, how does that find representation in the neuronal circuits. Most of what we do is dictated by what we have learned therefore motor learning automatically acquires a crucial role in our lives. Then we have to work out where these motor memories are stored and how they are represented.[7]

We for instance know that the declarative memory,i.e., factual information of a person's life (for instance events, names and places etc), is stored in the medial temporal lobe of the brain in the region of the cerebral cortex that lies inferior to the lateral fissures bilaterally including the hippocampus, the entorhinal cortex, and the perirhinal cortex. Motor memories by contrast are broadly distributed across the whole motor circuit encompassing the motor cortices, the cerebellum, and the basal ganglia. The process by which motor memories are stored is still unclear and this may provide a very exciting avenue for research for budding neuroscientists. We do have some indications but are not in a position to draw any concrete inferences.[7]

The first indication came to us from the monkey studies. Recordings were made when monkeys made adaptations to their environment. Unsurprisingly when the monkeys had learned to move in a new context, the recordings showed a change in pattern. This finding would afford support to the synaptic trace theory which suggests that memories are embedded in patterns of synaptic connections which ensures that an alteration in an experience dependence such as after the experience, the circuit is capable of initiating a new output. The unexpected problem here was that a proportion of the neurons maintained their altered activity pattern even after the monkeys had stopped indulging in novel tasks. [8,9]

The second clue came to us when two-photon microscopy was used to observe anatomical changes in the synaptic activity of the mouse motor cortex. These studies came up with baffling findings. Even when the animal was not learning anything new, the synaptic spines were still turning over at a very high rate.[9] That of course does not explain how some motor memories persist in an animal for the entire lifetime. Unquestionably this is one of the major mysteries in motor neuroscience begging for a swift resolution. And it is a reasonably safe bet that whosoever comes up with an answer would be a prime candidate for the highest awards.

The final goal of neuroscience is to link the brain with the more abstract phenomena of the mind. That perhaps remains the most complex endeavour of biomedicine. In this case, we do have a model that may explain fluctuating synaptic connections from the sporting world.

We know that to perform at an optimal level an athlete must warm-up for an extensive period before the performance. We operate on the hypothesis that practice is necessary to tone up the athlete's muscles, ligaments and tendons. But the important caveat here is that warm-up must emphasize the skills that the athlete already possesses. A baseball player for instance would not be able to function if asked to perform in a soccer match irrespective of the intensity of the warm-up. The explanatory hypothesis for this could be that there is a need for perpetual neural recalibration for optimal performance. Whenever there is a lapse in the continuity of neural recalibration, we can expect an automatic dip in the performance levels.

We are in the early stages as yet and unsure whether this model would hold. But with the increasing sophistication of modern imaging technology to probe synaptic changes, we can expect some very exciting findings in not too distant a future.

Conclusion

We do not have any answers as yet on how the cortical motor areas of the frontal lobe construct the spatiotemporal patterns of neural activity necessary to activate the spinal cord, enabling it to execute a specific movement. However, we do know that very high-level movement goals are indeed represented in the premotor area. And we also know that signals tend to spread to the primary motor cortex which in most cases had already been influenced by the afferents on postures of the limb. This in turn retrieves the motor memories and a signal is formed which is conveyed to the spinal cord. But the details of this extremely complex process require more research and further elaboration. As does the process of storage of motor memories.

Prima facie, the unanswered questions that have been broadly adumbrated in this column may appear daunting. And they most certainly would require very close collaboration between neurochemists, neurophysiologists, molecular biologist and computational neuroscientists. But any long-term neuroscientist, whether active or retired (like the author of this column!) would attest that more often than not, nature unexpectedly provides us with shortcuts that serve to make our tasks so much simpler and unmentionably enjoyable. And once we have the answers, the benefits that would accrue to the medical profession are beyond imagination.

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