国际前沿

[编者按] 本期,Daniel 向读者推荐的文章是:在科学研究中充分使用功能原理模型。本文以帕金森氏病为例,向读者解读了:功能原理模型对研究者的重要指导作用。"功能原理模型"貌似一张张卡通画,但实际上是设计和实施一个高质量的研究项目的规划图。作者的原始构思和战略战术,往往就从这些可爱的"功能原理模型"中来。本文将有助于读者和研究人员,保持清醒头脑开展实验设计。

Topics of interest – 'The use of functional models in scientific research – Understanding Parkinson's disease' Edition 3

The use of functional, schematic models in any field of research has proven to be an invaluable tool for developing novel ideas and is often instrumental in taking research ideas in new directions. In this edition, I use the classic functional model of the basal ganglia circuitry, which was originally described in the late 1980's (Albin et al., 1989), as a prime example for what has been used for major developments in the research of neural networks for processing movement, particularly emphasising its use for understanding the pathogenesis of Parkinson's disease (PD).

The now so called 'classic model' of the basal ganglia was based on simple box-arrow circuitry (Alexander and Crutcher, 1990) between subnuclei, which form two main pathways ('direct' and 'indirect') for feed-forward information processing. In PD, the loss of dopamine was described as causing a major imbalance of the direct and indirect pathways of the basal ganglia network (figure 1. A), leading to the hyper-inhibition of the motor thalamic nuclei, subsequently manifesting as parkinsonian motor symptoms (bradykinesia, rigidity and resting tremor) seen in patients. The most common pharmacological treatment for PD remains to be L-3,4-dihydroxyphenylalanine (L-DOPA), the immediate precursor of dopamine, which effectively restores motor function. However, long-term L-DOPA treatment leads to severe motor complications such as abnormal involuntary movements, termed L-DOPA-induced dyskinesia (LID). In the pathophysiology of LID, there is an under activity of the basal ganglia output nuclei, as a result of hyper-inhibition mediated from the direct pathway, leading to increased excitatory input to the motor cortex (figure 1. B).

These original descriptions based on the classic model of the basal ganglia undoubtedly paved the way to a greater understanding of the pathophysiology of PD and LID, allowing the development of therapeutic strategies that are still used in the clinic to date, such as surgical deep brain stimulation. It is therefore important to fully acknowledge the value of such functional models in scientific research that can prove valuable in leading to practical applications, as I have briefly described. In time, such models can be developed into more sophisticated descriptions that, in the case of the basal ganglia model, capture more neural network connections and dynamic non-linear neuronal processing in disease states (Obeso and Lanciego, 2011). The simplicity and accuracy of original functional models are key components that allow for the continuous refinement and addition of new details following collection of research data in each, or across, subject areas. Indeed, recent computational models have been developed for better understanding the basal ganglia in motor control (Guthrie et al., 2013).

References

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(彩图 1 转彩插 1)