2 The Fundamental Cause of Neural Metabolic Imbalance

2.1 Energy supply issues

The normal functioning of the brain requires sufficient energy, and mitochondria play a crucial role in this process. If the genes responsible for energy production are abnormal, it will interfere with cellular respiration, leading to reduced energy and the accumulation of harmful substances, thereby damaging nerve cells (Makridou et al., 2025; Pokotylo et al., 2025). Studies have found that in the blood of patients with neurological diseases, substances related to energy metabolism change, indicating that the energy regulation function of the body and the brain has become abnormal (Huang et al., 2025).

When mitochondrial function declines, cells will temporarily replenish energy through glycolysis. Although this can temporarily maintain cell survival, in the long term, it will disrupt the metabolic balance and further aggravate nerve damage (Pokotylo et al., 2025). Currently, the academic community believes that these diseases are not only a problem of insufficient energy supply, but also related to abnormal regulation of the entire metabolic network (Huang et al., 2025).

2.2 Abnormalities in amino acid, organic acid and fat metabolism

Many genetic diseases are related to the metabolism of amino acids or organic acids. If a certain enzyme malfunctions during the metabolic process, certain substances will accumulate in the brain, leading to epilepsy or developmental delays. For example, phenylketonuria occurs because the accumulation of metabolic products interferes with the normal transmission of neural signals.

Apart from common metabolic issues, some rare neurological disorders can also affect the metabolism of amino acids and fats. People with muscle disorders, autism, epilepsy and other conditions often have abnormal amino acid and fat metabolism in their blood (Wijekoon et al., 2025). This indicates that metabolic disorders are closely related to the nervous system and may participate in the occurrence of diseases by affecting signal transmission.

2.3 How genetic mutations trigger metabolic disorders

In neuro-metabolic diseases, genetic mutations often disrupt metabolic balance in several ways. Some mutations directly prevent metabolic enzymes from functioning properly, causing toxic substances to accumulate in the body; some damage transport proteins, depriving the brain of sufficient nutrients; and others interfere with the process of cell waste clearance, preventing damaged mitochondria from being removed in time. These different mechanisms ultimately harm the stability of nerve cells.

Genetic research has revealed that many genes related to metabolism can influence the occurrence of neurodegenerative diseases. For instance, patients with Alzheimer's disease typically have abnormal energy and fat metabolism, which is closely related to the progression of their condition (Pokotylo et al., 2025; Huang et al., 2025). These findings can help us understand these diseases and provide ideas for diagnostic methods.

3 Application of Genomics in the Diagnosis of Rare Neurological Disorders

3.1 Application of high-throughput sequencing technology

The new technology of high-throughput sequencing can simultaneously test multiple genes, significantly changing the diagnostic approach for rare neurological disorders. Currently, whole-exome sequencing is a commonly used method for identifying single-gene neurological diseases (such as abnormal development, epilepsy), and most studies show that its diagnostic probability is approximately between 30% and 45% (Gaouzi et al., 2025). Approximately one-third of patients with developmental problems or epilepsy can find the cause of their illness through this method, and it is more convenient than traditional methods (Chang et al., 2025). Therefore, professional guidelines recommend that for many neurological diseases, whole-exome sequencing or whole-genome sequencing should be prioritized (Assadourian and Martinez-Agosto, 2025). Whole-genome sequencing can discover more types of genetic variations and identify some issues that whole-exome sequencing might miss (Zhang et al., 2025a). As costs continue to decrease, these methods are expected to become routine detection methods for neurological genetic diseases.