Module 25.1

Nutritional and Metabolic Consequences of Neurological Diseases

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Learning Objectives

- To identify different factors that may favour malnutrition in patients with neurological diseases, including the effect of drug therapy;
- To know the gastrointestinal consequences of neurological disease, that are relevant for nutritional support;
- To know the main characteristics of dysphagia and its relevance for nutritional support in patients with neurological diseases;
- To understand the effect of neurological disease on energy expenditure;
- To recognize the clinical consequences of malnutrition in patients with neurological diseases.

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Key Messages

- Diet and nutritional factors have been involved in the pathogenesis of neurological diseases;
- Malnutrition is common in neurological patients and can increase the risk of mortality, clinical complications and disability;
- A decreased intake is one of the main factors leading to malnutrition in patients with neurological disease;
- Oropharyngeal dysphagia is common in these patients. Both efficacy and security of swallowing can be impaired, leading to malnutrition, dehydration and aspiration pneumonia;
- Neurological disorders may be associated with alterations in resting energy expenditure, leading to hyper or hypo-metabolism. Nutritional status, body composition and altered neuromuscular function can be responsible for these alterations.
1. Introduction

There is a close relationship between nutrition and neurological diseases. Some nutritional factors may be involved in the pathogenesis of neurological diseases (1). Diet can favours atherosclerosis and neurological ischaemic disease. High saturated fat and salt intake and low fruit and vegetable diet have been related to a higher risk for stroke (2). Vitamin D deficiency and insufficiency have been associated with multiple sclerosis (3). The aetiology of amyotrophic lateral sclerosis (ALS) is far from clear; some dietary factors, including high fruit and vegetable intake, have been reported to decrease the risk of the disease in case-control studies (4). Meta-analyses of cohort studies, comprising more than one million subjects, have shown a protective role of omega-3 fatty acid (5) and carotenoid (6) intake on ALS. Epidemiological studies found that high intake of fruits, vegetables and fish was inversely associated with risk of Parkinson’s disease (PD), and dietary patterns characteristic of a Mediterranean diet are emerging as a potential neuroprotective alternative (7). Higher adherence to the Mediterranean diet may protect from Alzheimer’s Disease in patients with mild cognitive impairment (8). Peripheral neuropathy can be due to vitamin deficiency (thiamine, B6).

Neurological patients are at increased nutritional risk of malnutrition and micronutrient deficiency when intake is low or metabolic rate is high. Alternatively obesity may occur due to immobility and reduced total energy expenditure. Patients with neurological diseases comprise 15 percent of acute care hospital inpatients, over 30 percent of rehabilitation centre inpatients and 50 percent of nursing home patients. Malnutrition can increase mortality, decrease the efficacy of the rehabilitation process and increase the risk of disability in these patients.

In this module we will describe the different factors that may favour malnutrition in neurological patients and the clinical consequences of this common complication.

Acute neurological diseases

Infectious, vascular, or immunological disorders, and also trauma can cause acute neurological disease. The nutritional and metabolic consequences of acute CNS trauma (brain trauma and spinal cord injury) have been studied for many years, as nutritional impairment is a significant prognostic factor in these patients. Traumatic brain injury (TBI) is a major cause of disability, death and economic cost to our society. Brain and spinal cord injury patients are at nutritional risk, and clinical guidelines recommend nutritional screening to identify those patients who require more formal nutritional evaluation and support (9, 10). There is evidence suggesting that malnutrition increases mortality rates in ABT patients. Nutritional support is considered a critical component of care for patients with CNS trauma, and is a factor contributing to survival and optimal rehabilitation (11). Malnutrition is common in patients with acute stroke and is associated with a higher mortality, poor outcome and more disability (12). Nutritional support, with adapted oral diet, oral supplements or enteral nutrition, may be necessary.

Chronic neurological diseases

Patients with chronic neurological disease are at nutritional risk. Several factors may be involved, including decreased intake and increased energy expenditure. Some of these diseases are briefly described:

Dementia is a syndrome of many causes and is defined as an acquired deterioration in cognitive abilities that impairs the successful performance of activities of daily living. Alzheimer’s disease is the most common cause of dementia in western countries and is the cause in more than half of demented patients, followed by
neurological ischaemic disease. Weight loss is a very common finding in advanced dementia and is related to a worse prognosis (13).

Parkinson’s disease is one of the most frequent neurological diseases, affecting 1% of individuals over age 55. Parkinson’s disease results from dopamine depletion in the brain, leading to the characteristic symptoms of the disease: tremor, rigidity and bradykinesia. As the disease progresses, other symptoms become evident, including dysphagia, monotonous speech, impaired gastrointestinal motility, fatigue, depression and cognitive impairment (14).

Amyotrophic lateral sclerosis (ALS) is the most common adult-onset motor neurone disease (15). It has a prevalence of 3-4 cases:100,000 and is a progressive neurodegenerative disorder, involving motor neurons in the cerebral cortex, brainstem and spinal cord, presenting with a combination of upper and lower motor neurone signs (16). It is a purely motor syndrome, without clinically significant visual, sensory, autonomic, sphincter or early cognitive dysfunction. Bladder and bowel function is usually preserved. Bulbar onset is associated with a worse prognosis.

Multiple sclerosis is a demyelinating disorder characterized by inflammation and selective destruction of central nervous system myelin; the course can be relapsing-remitting or progressive. Its prevalence can be 250:100,000 in Northern Europe. It is the second most common cause of neurological disability (after trauma) in young adults. Weight loss in these patients can be due to decreased intake, dysphagia and depression. Some patients experience weight gain and obesity due to immobility and steroid drug therapy.

Peripheral neuropathy, neuromuscular diseases (such as myasthenia gravis), muscular dystrophy, and other muscle diseases complete the spectrum of neurological diseases. All of them can have metabolic and nutritional consequences.

2. Factors Leading to Malnutrition in Chronic Neurological Diseases

2.1 Decreased Intake
The ingestion of food is a complex process. Some patients are not able to handle cutlery properly, or have difficulty in chewing or swallowing. Depression is common in chronic neurological disease, affecting up to 40% of patients and may contribute to malnutrition risk. Patients with impaired cognitive function are also at increased risk of malnutrition, due to their impaired ability to find, buy and prepare food. Apraxia, a common symptom of Alzheimer's disease, can also decrease food intake. Self-imposed or improperly prescribed dietary restriction can also induce malnutrition. Patients with dysarthria can have difficulty in communicating needs. Dyspnoea can get worse in relation to food intake.

Dysphagia
Dysphagia is defined as difficulty or discomfort during swallowing, i.e. the progression of the alimentary bolus from the mouth to the stomach. Dysphagia is classified as oesophageal or oropharyngeal, and from a functional point of view, as organic or functional.
Normal swallowing comprises four stages:
1. The oral preparatory stage is voluntary, i.e. mastication and bolus formation;
2. The oral stage is also voluntary. Bolus is propelled by the tongue;
3. The pharyngeal phase is involuntary. An activation of pharyngeal mechanoreceptors sends information to the CNS and triggers the pharyngeal swallowing motor pattern. An elevation of the soft palate closes the nasopharynx. The airway is then closed by elevation and anterior displacement of the hyoid bone, and by descent of the epiglottis and vocal
cord closure. The upper oesophageal sphincter opens and there is a contraction of the pharyngeal constrictor muscles;

4. The oesophageal phase begins with the opening of the upper oesophageal sphincter, which is followed by oesophageal peristalsis.

The main symptoms of dysphagia are coughing, choking or drooling with swallowing, a characteristically wet-sounding voice, changes in breathing when eating or drinking, frequent respiratory infections and known or suspected aspiration pneumonia. The prevalence of oropharyngeal functional dysphagia in neurological patients is very high: it includes more than 30% of patients with stroke; it affects 40% of patients with myasthenia gravis and up to 84% of patients with Alzheimer’s disease (17). Dysphagia in Parkinson’s disease is a consequence of rigidity and bradykinesia, and can affect 50-82 % of patients, being more prevalent in late-stage disease (18). Dysphagia is a common finding in ALS patients, especially those with bulbar involvement. It is one of the presenting symptoms in 10-30% of ALS patients and affects all patients as the disease progresses; it generally follows a few months after initial speech impairment. Bulbar muscle involvement is associated with labial and lingual dysfunction, palatine incompetence, pharyngeal weakness, difficulty in triggering the swallowing reflex and impairment of laryngeal elevation during swallowing. The tongue is usually involved before the lips or jaw (19).

In patients with multiple sclerosis, the symptoms of dysphagia can be temporary, for example, during a period of relapse. It may affect 44% of patients.

The clinical evaluation of neurological patients with dysphagia should include:

- A comprehensive clinical and neurological evaluation.
- The use of structured questionnaires, e.g. EAT-10 (20), that is able to differentiate safe and unsafe swallowing in ALS (21), Parkinson’s disease and Alzheimer’s disease (22). It is especially useful in chronic neurological diseases.
- Bed-side clinical evaluation of swallowing (23)
  - Water swallow test (3 ounce = 90ml). Can also be performed using oximetry.
  - Volume-viscosity swallow test (V-VST), that has shown 83.7% sensitivity and 64.7% specificity for bolus penetration into the larynx and 100% sensitivity and 28.8% specificity for aspiration (24).
- Evaluation of the characteristics of voluntary cough can also be useful to identify neurological patients at risk of aspiration (25, 26).
- Videofluoroscopy or radiological examination of swallowing function can also use different consistencies, textures and volumes. It can detect silent aspiration. Patient collaboration is needed.
- FEES: fibre-optic endoscopic evaluation of swallowing, is a bed-side procedure, easy to repeat, and can check the anatomy and function of the pharyngeal and laryngeal structures. Not all of the swallowing phases are visible to this technique.

2.2. Gastrointestinal Dysfunction

Nausea and vomiting

Nausea and vomiting are important symptoms of intracranial hypertension and are more common in acute than in chronic neurological disease. When intracranial hypertension is present, third ventricle floor involvement may further increase vomiting. Some medications used in neurological disease, such as drug therapy for Parkinson’s disease, can also induce vomiting.
Delayed gastric emptying

Delayed gastric emptying in neurological disease can be due to intracranial hypertension, autonomic neuropathy, myopathy and the effect of drug therapy (opioids, anticholinergics). This condition can decrease appetite, induce early satiation, nausea and vomiting, reflux and heartburn, and abdominal bloating. It can also contribute to decreased or irregular drug absorption. Gastroparesis is specially common in Parkinson’s disease (27) and in multiple sclerosis patients (28). Uncontrolled diabetes mellitus can also induce delayed gastric emptying.

Constipation

Constipation is a common condition in patients with chronic neurological diseases and can be a serious, sometimes life-threatening disorder. It can be due to slow gastric and intestinal motility, weakness of abdominal and pelvic muscles, autonomic dysfunction, side effects of medications and immobility. Some dietary factors can also be important, including a decreased intake of fluid and fibre.

2.3 Energy Expenditure Disturbance

Neurological disorders may be associated with alterations in resting energy expenditure, leading to hyper- or hypo-metabolism due to changes in body composition, altered muscle function, paralysis, rigidity, spasticity, fasciculation, tremor and other motility disorders (Table 1). Decreased energy intake and malnutrition themselves cause secondary hypometabolism over and above any effect of the disease itself. Predictive equations may not be accurate in assessing resting energy expenditure in these patients and indirect calorimetry, if available, is advised.

Table 1

<table>
<thead>
<tr>
<th>Neurological condition</th>
<th>Energy expenditure (EE) alterations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tremor, fasciculation's, spasticity, dyskinesia, myoclonia</td>
<td>Increase EE</td>
</tr>
<tr>
<td>Paralysis, paresis</td>
<td>Decrease EE</td>
</tr>
<tr>
<td><strong>Nutritional status</strong></td>
<td></td>
</tr>
<tr>
<td>Malnutrition, loss of lean body mass</td>
<td>Decrease EE</td>
</tr>
<tr>
<td>Refeeding</td>
<td>Increase EE</td>
</tr>
<tr>
<td><strong>Physical activity</strong></td>
<td></td>
</tr>
<tr>
<td>Decrease in leisure physical activity</td>
<td>Decrease EE</td>
</tr>
<tr>
<td>Rehabilitation</td>
<td>Increase EE</td>
</tr>
<tr>
<td><strong>Ventilatory function</strong></td>
<td></td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>Increase EE</td>
</tr>
<tr>
<td><strong>Infections</strong></td>
<td></td>
</tr>
<tr>
<td>Drug therapy: sedatives, baclofen</td>
<td>Decrease EE</td>
</tr>
</tbody>
</table>

Huntington’s disease is associated with increase in resting energy expenditure (29), even in early stages of the disease (30). Energy expenditure in Parkinson’s disease...
may vary according to disease stage and the severity of symptoms. Increased total energy expenditure can contribute to weight loss in late-stage disease (31). Some patients with dyskinesias may expend as much energy at rest as people undertaking moderate physical activity. Subthalamic stimulation decreases EE and can favor weight gain and obesity.

Some clinical studies have observed increased resting energy expenditure in patients with ALS, and this can contribute to malnutrition (32). Resting energy expenditure in ALS patients may depend on many different factors, including nutritional status (malnutrition decreases REE), the main clinical neurological manifestations (predominant upper or lower motor neurone signs) and the need for ventilation. Kasarskis attributed hypermetabolism to increased respiratory effort (33). Desport (34) evaluated 62 patients and found that measured energy expenditure was 10% higher than that of control subjects. Multivariate analysis, however, did not reveal a relationship between hypermetabolism and ventilatory function. Sherman studied ventilated and non-ventilated patients with ALS. Patients who were receiving mechanical ventilation had higher energy expenditure than that predicted by Harris-Benedict equations, whereas those patients who were not receiving mechanical ventilation had a lower-than-predicted energy expenditure. Both over- and underestimation of REE have been observed in these patients using standard equations (35). REE in relation to fat-free mass tends to increase during the course of the disease (36).

2.4 Effect of Drug Therapy

Drug therapy can decrease food intake due to dysgeusia, nausea and vomiting, dry mouth, decrease in gastric emptying, etc (Table 2). Interactions with micronutrients have also been described.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Side effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interferon</td>
<td>Weight loss, anorexia, fever, depression, dysgeusia</td>
</tr>
<tr>
<td>Atypical antipsychotics</td>
<td>Weight gain, central obesity, metabolic syndrome</td>
</tr>
<tr>
<td>Dopaminergic agents</td>
<td>Nausea, vomiting, anorexia, psychosis</td>
</tr>
<tr>
<td>Levodopa</td>
<td>Nausea, vomiting, constipation</td>
</tr>
<tr>
<td>Steroids</td>
<td>Decrease in muscle mass</td>
</tr>
<tr>
<td>Anticholinergics</td>
<td>Dry mouth, dehydration, delayed gastric emptying, constipation</td>
</tr>
</tbody>
</table>
Table 3
Micronutrient-related side effects of drugs commonly used in neurological patients

<table>
<thead>
<tr>
<th>Drug</th>
<th>Micronutrient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steroids</td>
<td>Negative calcium balance. Osteoporosis</td>
</tr>
<tr>
<td>Phenytion</td>
<td>Vit D, K, folate, and B6 deficiency</td>
</tr>
<tr>
<td>Levodopa</td>
<td>Increased homocysteine, vitamin B6, B12 deficiency</td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>Folate and vit D deficiency</td>
</tr>
<tr>
<td>Omeprazole, ranitidine</td>
<td>Vitamin B12, calcium, iron deficiency</td>
</tr>
<tr>
<td>Antacids</td>
<td>Phosphate deficiency</td>
</tr>
<tr>
<td>Diuretics</td>
<td>Thiamine deficiency</td>
</tr>
</tbody>
</table>

3. Nutritional Consequences of Chronic Neurological Diseases

The consequences of malnutrition are well known and are described in other LLL modules. In neurological patients, it will exacerbate atrophy, and dysfunction of limb and respiratory muscles. This further impairs mobility, weakens the respiratory muscles and increases the risk of pneumonia. The increase in demand for gas exchange associated with diet-induced thermogenesis during feeding may induce dyspnoea in patients with respiratory muscle weakness and therefore necessitate a reduced feeding rate. In addition, malnutrition leads to immunodeficiency and increases the risk of infection, a common cause of death in these patients. Malnutrition also impairs muscle function (type II fibres) and the recovery of swallowing ability. Malnutrition and micronutrient deficiency (zinc or iron) increase the susceptibility to pressure sores (37). Nutritional status and body weight are important predictors of survival in ALS (38, 39, 40).

Dysphagia is associated with a decrease in both the efficacy and safety of swallowing (Fig. 1). Because of this, the patient can develop malnutrition, dehydration, oropharyngeal aspiration and aspiration pneumonia. Aspiration may be silent in patients with chronic neurological disease.

![Fig. 1 Clinical Consequences of dysphagia (18)](image)
Dehydration is common in patients with neurological diseases and dysphagia, causing confusion and impaired renal function. Salivary production decreases and respiratory secretions become thicker. This may further impair swallowing and increase dyspnoea. Dehydration can also exacerbate orthostatic hypotension in patients with autonomic dysfunction. Elderly patients are especially prone to dehydration, due to their decrease in total body water and the relative insensitivity of the osmo-receptors. Frequent assessment of fluid status is mandatory in patients with neurological diseases, in order to prevent these complications. It should include a clinical evaluation, diuresis and body weight recording, and evaluation of fluid intake. Some laboratory parameters can help, such as haemoglobin, plasma/urine osmolality or urea-BUN/ creatinine, but there is no gold standard. Dehydration cannot be diagnosed using simple laboratory variables. Dehydration is usually under-diagnosed in chronic neurological patients (41). An adequate fluid intake can decrease stroke recurrence (42).

Aspiration pneumonia is a complex process in which pathogenic bacteria colonize the oropharynx, and are aspirated into the airway; the patient is unable to clear the material by coughing and subsequently, respiratory infection can develop (Fig. 2). In patients with dysphagia, there is a 93% increase in hospitalization because of aspiration pneumonia (43). Aspiration pneumonia has the highest rate of mortality of all causes of pneumonia.

Dysphagia can decrease quality of life in neurological patients (44). Osteoporosis is common in patients with chronic neurological disease, due to immobilization, lack of weight-bearing exercise, decreased food intake and malnutrition (45). Bone mass density correlates with severity of disease in patients with Parkinson’s disease (46). Osteoporosis is also common in multiple sclerosis (47), even in men (48). The risk of osteoporosis in MS patients is related to disability and disease duration; the effect of high dose pulse corticosteroid therapy is controversial. Bone mineral density and calcium and vitamin D status need to be assessed in order to prevent or limit osteoporosis in these patients.
4. Summary

Neurological patients are at nutritional risk. Several factors may be responsible for malnutrition in these patients, including decreased intake (dysphagia, gastrointestinal disturbances, depression, etc), the effects of drug therapy, and disease-related changes in energy expenditure. A structured nutritional evaluation is mandatory. Nutritional support is considered a major component of care in patients with acute and chronic neurological disorders. Changes in energy expenditure have been described in these patients. Standard equations may be inaccurate and indirect calorimetry, if available, should be used to assess energy requirements. Malnutrition in neurological patients is related to a worse prognosis, being an independent factor for mortality in amyotrophic lateral sclerosis and other neurological diseases. It exacerbates muscle atrophy and function and impairs the recovery of swallowing ability. Malnutrition also impairs immune function and increases the risk of pneumonia and the susceptibility of pressure sores. Dysphagia increases the risk of malnutrition, dehydration and aspiration. Osteoporosis and high fracture risk are common in patients with chronic neurological disease.
5. References


