The syndrome of normal-pressure hydrocephalus (NPH) remains a diagnostic and therapeutic challenge, especially as many patients do not display the classical clinical and neuroimaging patterns of NPH, thus questioning the usefulness of a shunt. Gait impairment remains the cardinal symptom, while mental deterioration may be subtle and even unrecognized. NPH is rarely the cause of severe dementia, and substantial improvement in NPH-related mental deterioration is limited to 30–40% of shunted patients. Many ancillary investigations have been described that can increase the probability of selecting the appropriate candidates for a shunt. The reliability and reproducibility of these tests are limited. Unfortunately, the best predictive tests are technically complex and are used only in a few specialized centers. The best management is still to adhere to strict clinical and magnetic resonance imaging criteria and to rely on a positive – but not negative – CSF tap test and the occurrence of B-waves during at least 50% of the continuous intracranial pressure recording time, when this procedure is available.

**Key words** Normal-pressure hydrocephalus · Subcortical dementia · Predictive testing · Gait disorder · Diagnosis

**Pathophysiology**

Experiments in chronic hydrocephalic animals and hydrodynamic studies in humans have shown that at a first stage increased intraventricular CSF pressure due to impaired CSF flow results in increasing ventricular enlargement [8, 9]. Later the disequilibrium between ventricular and convexity CSF pressures progressively disappears, although episodes of slightly elevated intraventricular CSF pressure may remain, especially in patients who improve after a shunt. These episodic CSF pressure elevations mainly consist of so-called B-waves, occurring between 10% and 90% of the pressure recording time [9–13].

Increased transmantle pressure, with slightly higher pressure in the ventricles than in the subdural space of the convexity, is another possible contributing factor [14, 15], although this has not been confirmed by other experiments [16]. Some investigators have suggested that a
“waterhammer effect” due to increased CSF pulse pressure waves on the ventricular walls [17] and altered viscoelastic properties of the ventricular wall [18] may also contribute to maintenance and further progression of NPH. There is now common agreement that, although the CSF pressure is normal at one spinal tap, episodes of slightly increased CSF pressure occur in NPH. Therefore “adult hydrocephalus syndrome” [19, 20] and “adult symptomatic hydrocephalus” [2, 21] are, from a pathophysiological point of view, more appropriate terms than “normal pressure hydrocephalus.”

The clinical triad and a normal pressure at lumbar puncture may be seen in chronic noncommunicating hydrocephalus such as nontumoral aqueduct stenosis [22–24]. In communicating NPH the impairment of CSF flow is distal to the fourth ventricle, almost always at the level of the basal cisterns. In 50% of patients with communicating NPH there is a known cause, such as subarachnoid hemorrhage, meningitis, or cranial trauma [1, 12, 13]. The other 50% of cases are idiopathic. The myth that communicating NPH is due to a CSF absorption deficit across the arachnoid villi remains indestructible. This mechanism would not lead to ventricular enlargement as there would not be a pressure gradient between the intra and extraventricular spaces [25]. Leptomeningeal biopsies have also failed to show [26, 27] an unequivocal association of leptomeningeal “fibrosis” with disturbed CSF flow or shunt responsiveness in presumed NPH patients.

Clinical deterioration in NPH is probably due to slowly progressive impairment of the periventricular blood flow. Compression and stretching of the periventricular arterioles and venules by the dilated ventricles [28–30] may lead to “misery perfusion” especially when there is a pre-disposing narrowing of the periventricular arterioles due to small vessel disease. The latter may explain why the prevalence of arterial hypertension and cerebral atherosclerosis is increased in NPH [31–35].

Epidemiology

Epidemiological data on NPH are limited. NPH is a (very) rare cause of dementia with estimates ranging from 0% to 5% [36–39]. This variable rate may be explained by inconsistent definitions of NPH, including series in which the diagnosis of NPH was based solely on clinical and neuroimaging criteria without confirmation by improvement after a shunt. One study reported the results in 166 patients shunted for presumed NPH in whom the incidence of shunt-responsive NPH was only 2.2 per million persons per year [39].

Although NPH may be seen in children and young adults [40, 41], it occurs generally during the sixth and seventh decades of life [6, 42]. Substantial improvement after shunting occurs in about 30–50% of idiopathic and in 50–70% of secondary NPH cases [7, 42, 53]. The total rate of postsurgical complications is approx. 30–40%, of which some 20% are severe, with death or severe residual morbidity in 6–8% of the shunted patients [39, 53].

Signs and symptoms

Walking difficulties and postural imbalance are usually the first signs of NPH and are also the most likely to improve after a shunt [5, 36, 44–46]. There is no “classical” NPH gait pattern: in a subset of patients with mild NPH the gait may be ataxic and wide-based, whereas in more severe cases the gait becomes short-stepped and shuffling, with difficulties in initiating walking (“magnetic phenomenon”), postural instability and frequent falls [47]. Clinical signs may include hyperreflexia, extensor plantar responses, and extrapyramidal signs such as hypokinesia and freezing during walking. The latter may be improved by visual cueing (placing parallel lines on the walking surface) but almost never by levodopa treatment [48].

The frequently used term of “gait apraxia” [49] is inappropriate in NPH, which is illustrated by the fact that NPH patients may execute walking movements without difficulty when minimally supported or lying down. When trying to start walking the gait may abruptly freeze. It has been suggested that this gait disorder is due to a disconnection between the basal ganglia and the frontal cortex, uninhibited antigravity reflexes, and cocontraction of agonists and antagonists during walking [49, 50].

Dementia is an unfortunate term for designating mental impairment in NPH. Some patients have no clinical evidence of dementia [36], and many with shunt-responsive NPH have only a slight or moderate cognitive deficit [5, 36, 43] which would not fit the criteria of dementia as defined in the Diagnostic and Statistical Manual of Mental Disorders [51]. The mental deficit is of the “subcortical” type, consisting principally of memory impairment, decreased speed of complex information processing, and impaired ability to manipulate acquired knowledge [52, 53]. Few NPH patients are really depressed, but their apathy and bradyphrenia may closely simulate depression. Differentiation between depression and NPH may be difficult because the two conditions may have a very similar profile on neuropsychological assessment [54, 55].

The view that differentiation between Alzheimer’s disease and NPH is diagnostically challenging is no longer tenable. In NPH the mental impairment is of the subcortical type, including absence of aphasia, apraxia and agnosia, and a discrepancy between a severely impaired delayed recall and less affected or even normal delayed recognition on memory tests. This pattern of memory impairment contrasts with that of Alzheimer’s disease, in which encoding deficits and associated impaired recognition are obvious [56]. When mental impairment is the preceding or predominant clinical sign, or when dementia is severe, not NPH but Alzheimer’s disease is the most