EDITORIAL

The Investigation and Differential Diagnosis of Dementias

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Editorial to accompany the articles "New Developments in the Diagnosis of Dementia" and "Lewy Body and Parkinsonian Dementia" in this issue of *Deutsches Ärzteblatt International*

Diseases of old age, and dementing diseases in particular, are becoming more common as the population ages. Much progress has been made in research on the etiology and pathogenesis of dementing diseases, but their diagnostic evaluation in clinical practice remains a difficult matter. Classically, it proceeds in two steps: first, the presence of dementia as a syndrome is confirmed, and then a further nosological classification is undertaken (1). The two articles that follow this Editorial, by Eschweiler et al. (2) and Mollenhauer et al. (3), address various problems that arise in each of these two steps.

Early recognition by diagnostic evaluation

The ICD-10 criteria for the dementia syndrome are exclusively clinical and require impairments of memory and other cognitive functions that are severe enough to affect the patient's everyday life, as well as deficits of affect control, motivation, or social behavior. Dementia is thus a classic psychiatric syndrome that should be diagnosed with psychiatric examining methods. Classic screening and testing instruments, such as the Mini-Mental Status Test, the clock test, and the CERAD scales, have long been available to clinicians for this purpose (4). Many newly proposed tests, such as the DemTect, TFDD, Micro-Mental Test, and Mini-Cog, have come about through nothing more than reduction and/or variation of the subdomains of the classic tests. Thus, they cannot improve diagnostic accuracy, and indeed their specificity and sensitivity are nearly identical to those of the earlier tests, namely about 80% in routine clinical practice for any of the tests mentioned above. Conceivably, innovative neuropsychological testing techniques could yet be developed to study newly defined cognitive domains, but none are currently on the horizon.

Instead, recent developments in the diagnostic evaluation of dementing diseases have followed a fundamentally different strategic path, owing to strong clinical interest in the premorbid and early stages of dementia that are known as mild cognitive impairment (MCI). The evaluation now mainly addresses, not the clinical dementia syndrome itself, but rather the neurobiological and neurophysiological changes that are associated with the underlying dementing diseases and which are used as biological markers. This method can be expected to have three main advantages: ideally,

such markers will be examiner-independent, i.e., objectively ascertainable; changes in markers may be detectable much earlier than the dementia syndrome itself; and the use of markers ought to facilitate nosological classification. On the other hand, the risks of this method lie in the lesser clinical importance that it attaches to organic pathology and in the treatment of surrogate parameters.

In the article by Eschweiler et al., the classic diagnostic techniques are presented together with a number of promising newer techniques designed to detect biological markers of the type discussed above. It has long been known that demented patients, particularly those with Alzheimer's disease, have impaired olfactory identification. This function is easily tested, with little stress for the patient. Automated techniques for morphological image analysis can be performed after a classic MR scan of the head with no additional effort. Lumbar puncture (LP), for the detection of amyloid components and tau protein in the cerebrospinal fluid (CSF), is particularly useful for early diagnosis. An LP, however, represents an additional stress for the patient and is not an obligate part of the dementia test battery that the current guidelines recommend. Single photon emission computed tomography (SPECT) and positron emission tomography (PET) require radioactively marked substances and can thus be performed only in specialized centers. The sensitivity and specificity of each of these techniques, considered individually, are no greater than those of the classic methods of diagnostic assessment; thus, the diagnostic yield improves only when all of their findings are considered together.

Differences between dementia syndromes in the first third of the course of disease

The article by Mollenhauer et al. concerns the problem of differential diagnosis, i.e., the second step of the classic diagnostic evaluation of dementia, with respect to two diseases: Lewy-body dementia and Parkinsonian dementia. In general, marked differences in clinical manifestations that enable one type of dementing disease to be distinguished from another are evident only during the first third of the course of disease, if at all. As dementing diseases progress, they resemble one another more and more. The clinical manifestations that are relatively specific to various dementing diseases in their early stages, such as impairment of memory,

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language, or motor function, agitation, and hallucinations, can appear in any type of dementing disease at a later stage. A further difficulty is that, when the brains of demented persons are examined neuropathologically at autopsy, multiple potential causes of dementia are often found, not all of which were necessarily clinically relevant during life (indeed, non-demented persons often have such findings as well). In particular, the neuropathological correlates of Alzheimer's disease and of vascular dementia often appear simultaneously; thus, there is some debate at present over whether these two entities are really distinct or simply represent two opposite, idealized poles of a continuum of diseases (5). Likewise, in the case of Lewy-body dementia and Parkinsonian dementia, one may ask whether these are not simply two different types of clinical course that can arise in patients with one and the same underlying disease.

Academic word games?

It may seem futile to pursue a precise differential diagnosis of dementia when specific, causal treatment is hardly ever available, except for a few rare diseases. Yet correct diagnoses of the underlying diseases that make patients demented will obviously be needed if effective, disease-specific interventions are ever to be developed. Thus, clinical diagnosticians today must do their part to pave the way for better care of demented patients in the future.

Conflict of interest statement

The author declares that he has no conflict of interest as defined by the guidelines of the International Committee of Medical Journal Editors.

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