

GUEST EDITORIAL

Cholinergic treatment across the spectrum: therapeutic trends in mild to severe dementia

The field of Alzheimer's disease (AD) research is in transition. Advances in our knowledge of AD pathology are translating into improved understanding of pharmacological agents that may have benefits across the spectrum of the illness. A major focus of current research is the potential ability of cholinergic therapy to enhance function and quality of life in all patients affected by AD, from the mildest to the most advanced stages.

The Eisai- and Pfizer-sponsored satellite symposium *Cholinergic Treatment Across the Spectrum: Therapeutic Trends in Mild to Severe Dementia* was held on September 23, 2005, during the 12th Congress of the International Psychogeriatric Association in Stockholm, Sweden. This meeting highlighted the role and utility of cholinesterase inhibitors across the spectrum of AD and facilitated the exchange of knowledge and experience in this rapidly evolving clinical arena.

As explained by Professor Agneta Nordberg, the pathogenesis of AD may begin many years before clinical symptoms become apparent. Recent years have witnessed dramatic improvements in our ability to visualize these early changes using *in vivo* imaging techniques, and these methods have allowed us to observe amyloid deposition and metabolic deficits in patients with mild cognitive impairment (MCI) many months before Alzheimer's dementia develops. Professor Nordberg also described the changes that occur within the cholinergic system across the continuum of dementia. These observations reflect the diagnostic dilemmas that we all face: although it is not difficult to diagnose the dementia phase of AD, it is a much greater challenge to identify and differentiate those overlapping areas between normal functioning, mild impairment, and dementia. Our goal as physicians is to preserve functional and cognitive ability not only in patients with diagnosed AD, but also in those who present with milder impairments at earlier stages of the disease spectrum, thereby maintaining patients at the highest level of function for the longest period of time, and within the community for as long as possible. As a consequence, there is currently a great deal of interest in the early initiation of therapeutic interventions. The second paper in this supplement describes how the efficacy of donepezil in AD has provided the rationale for investigation of its use in MCI; preliminary studies suggest that the agent may provide benefits for this patient population in terms of improved cognitive function and delayed progression to AD. Although further

research in this area is required to provide appropriate evidence of therapeutic benefit, these early results provide signals supporting the potential efficacy of donepezil in MCI.

At the other end of the spectrum, our efforts must focus on alleviating the symptoms and improving the quality of life of those patients affected by severe dementia. Professor Bengt Winblad presented new data from a randomized, controlled trial in which donepezil was found to have significant benefit over placebo in improving cognition and the ability to perform activities relating to daily life in patients with severe AD. These data suggest that donepezil may be effective not only in mild to moderate dementia, but also in more severe stages of AD.

These presentations all highlighted the vital role played by cholinesterase inhibitors in the comprehensive treatment strategies used in AD. New and emerging data suggest that these agents are effective across the entire spectrum of the disease and not solely in the mild to moderate stages for which they are currently licensed. Furthermore, ongoing studies of AD pathology have led to an increased awareness that cholinesterase inhibitors may have effects beyond enhanced cholinergic transmission. Our aim must now be to slow progression of AD, prolong the time spent in the milder stages of cognitive impairment and protect the autonomy of affected patients. Cholinesterase inhibitor therapy is clearly central to achieving these goals.

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