1. Introduction

In this chapter we provide an overview of the patterns of cerebral cortical and subcortical pathological changes that occur in the various dementias. When viewed in this manner, the dementias can be categorized into five major groups based on the topography of their cerebral cortical involvement. These are: (1) the preferential involvement of the temporal lobes and adjacent parietal, occipital, and frontal lobes in Alzheimer’s disease (AD); (2) the predilection for frontal and parietal lobes in progressive subcortical gliosis (PSG); (3) the combined involvement of the cerebral cortex of frontal and temporal lobes in Pick’s disease (PiD) and dementia of the frontal type (DFT); (4) diffuse Lewy body disease (DLBD) and Huntington’s disease (HD) with prominent cortical and subcortical pathology; and (5) a group characterized predominantly by subcortical pathological changes such as corticobasal degeneration (CBD), multisystem atrophy (MSA) and progressive supranuclear palsy (PSP). Although not strictly a dementia, schizophrenia (SZP) has been included because of its prominent cerebral cortical pathology and the frequent presence of a residual state resembling dementia. First, an overview of each dementia will be presented, followed by discussion of each of the five groups. Schizophrenia will be discussed separately as a developmental disease of subcortical, limbic, and paralimbic systems.
2. Alzheimer’s Disease and the Primary Involvement Pattern of the Temporal Lobe

Of the various pathological changes in AD, the distribution of neurofibrillary tangles (NFTs) and neuronal and synaptic loss have provided the closest correlations with the severity and clinical features of the disease, whereas the deposition of Aβ amyloid as diffuse plaques and the density and distribution of neuritic (senile) plaques (NPs), though prominent features of the neuropathology of AD, have provided less-close clinical correlations (Braak and Braak, 1991a; Terry et al., 1991; Arriagada et al., 1992a; Samuel et al., 1994; Bierer et al., 1995; Blennow et al., 1996; Mann, 1996). Of the pathological changes that correlate strongly with the clinical features of AD, the distribution of the NFTs has been the most thoroughly documented. Although there is a strong relationship between neuronal loss in AD and the development of the neurofibrillary tangle, it does not appear that NFT formation is the sole mechanism for the loss. The presence of high somatodendritic levels of neurofilament protein has been demonstrated in a subset of pyramidal cells in layers III and V and in layers II and IV in the entorhinal cortex that are vulnerable to the development of NFTs and neuronal loss in AD (Morrison et al., 1987; Hof et al., 1990; Hof et al., 1990; see Hof, 1997, and Hof et al., this volume, for reviews), with more than 80% of the large pyramidal cells that are immunoreactive to this protein showing cell loss in the temporal and frontal cortex (Morrison et al., 1987). Recently, Sampson et al. (1997) have identified a similar neuronal type in layer I of the cerebral cortex that is vulnerable to NFT formation. Conversely, the calcium-binding proteins parvalbumin, calbindin, and calretinin have been identified in the nonpyramidal inhibitory neurons in the cerebral cortex that are resistant to both cell death and to the formation of NFTs in AD (Hof et al., 1990, 1992; Sampson et al., 1997). There does not, however, appear to be an obligate relationship between the NFT development of and cell loss, because the lateral vestibular nucleus, which has been shown to develop NFTs in AD, does not show evidence of cell loss. (Ransmayr et al., 1994). Hof et al. (1990) have reported a similar finding in the layer III pyramidal cells in the primary visual cortex. Further, Gomez-Isla et al. (1997) have reported that, although NFTs and neuronal loss increase in parallel to each other in the cerebral cortex in AD, the extent of neuronal loss was seven times greater than the number of accumulated NFTs. Cell loss also occurs in AD in neurons that do not develop NFTs. For example, Lassmann (1996), from an analysis of DNA fragmentation as an index of cell death, thought that neurofibrillary pathology may not directly induce cell death, but that this change and amyloid deposition may increase the risk of cell death in response to additional minor metabolic insults. Bancher et al. (1997), using similar techniques, found that most of the dying cells did not bear NFTs, and further, that most were not located within areas of amyloid deposits. In this later study, and that of Troncoso et al. (1996), there was also evidence of a loss of glial cells, and in the study of Troncoso et al. (1996) of microglial cells as well, cells that do not develop NFTs.

In an early global survey of the regional cerebral cortical distribution of the various pathological changes in AD, Brun and Gustafson (1976) noted that the most marked changes were found in the temporal lobe, where they were most prominent medially, as well as in the adjoining parietal and occipital lobes and in the posterior cingulate gyrus, with less-marked degeneration found in the frontal