Neurodegenerative dementias are linked to severe damage to various brain structures and interconnecting fibres. These structural abnormalities are accompanied by additional functional brain changes. Both structural and functional alterations are found extensively in various brain regions including cortical and sub-cortical areas. However, dementia-type specific changes were described in the last years. For instance, dementia of the Alzheimer type is primarily associated with damage in the hippocampal region while brain pathology in fronto-temporal dementia is centred around the prefrontal cortex and the lateral temporal lobe. In recent years, investigations using structural and functional imaging techniques expanded our knowledge on brain correlates of dementia-type specific behavioural changes. These findings are also relevant for the diagnosis and differential diagnosis of dementias. In this chapter, we will summarise common findings concerning structural and functional brain abnormalities in patients with dementias of different aetiology. We will focus on the most prominent type of dementia, the Alzheimer's disease (AD). In addition, we will briefly describe the neural correlates of dementia with Lewy bodies (DLB), fronto-temporal lobe degeneration (FTLD) including fronto-temporal dementia, semantic dementia and primary progressive aphasia as well as the most common findings in vascular dementias (VD).

Alzheimer's disease (AD) is often seen as a “hippocampal dementia” (Ball et al., 1985; see also the review by Mosconi, 2005). Indeed, there is convincing evidence that structures of the medial temporal lobes are primarily affected in patients with AD, including the hippocampal formation, the entorhinal and the perirhinal cortices as well as the parahippocampal gyrus (e.g., Kantarci and Jack, 2003; Ezekiel et al., 2004; a meta-analysis of studies that used structural and functional brain imaging techniques in AD can be found in Zakzanis et al., 2003). As a result of the critical function of the hippocampus and surrounding structures of the medial temporal lobe in memory processes (see Markowitsch, 1995; Markowitsch, 2000; Brand and Markowitsch, 2003; Piefke et al., 2003) damage to these structures in AD is considered to be the neural correlate of the cardinal symptom of memory impairments (e.g., Mortimer et al., 2004). Within the structures of the medial temporal lobe mentioned, the typical neuropathological changes associated with AD can be found even in the absence of clinical symptoms (Braak and Braak, 1991). The histopathological signs are neurofibrillary tangles (NFT) and beta-amyloid plaques (AP) accompanied by reductions of synaptic connections and neural loss leading to a general brain volume loss (atrophy). NFTs are believed to interfere with cytoskeleton integrity and probably result in neural dysfunction and neuronal death. NFTs can also be found in healthy
aging brains, however, their density is significantly higher in patients with AD (Braak and Braak, 1996). NFTs are primarily located in limbic and paralimbic regions, such as the hippocampus, the nucleus basalis of Meynert within the basal forebrain, the amygdala and entorhinal cortex, and are linked to memory dysfunctions in both patients with AD (e.g., Mortimer et al., 2004) as well as individuals with mild cognitive impairment (Petersen et al., 2006). In the course of AD, high densities of NFTs are also found in neocortical areas, such as the parietal and the frontal lobes, and are related to severity of dementia (Braak and Braak, 1991; Braak and Braak, 1996). The distribution of APs shows a high inter-individual variability. In addition, the density of APs is less intensively associated with cognitive decline than that of NFTs (Mesulam, 1999). Recent review articles also emphasise additional pathological signs in AD, such as changes of the density and the excitatory level of glutaminergic NMDA-receptors (Wenk, 2006) and a higher level of oxidative stress (Harman, 2006). Some authors also propose that the appearance of NFTs and APs is not closely related to developing dementia and that they are rather the consequence than the causation of the neurodegenerative process in AD. In addition, NFTs and APs can be present relatively independently from each other (Armstrong, 2006).

Medial temporal volume loss is found consistently in patients with AD and a disease duration of less than four years (since clinical diagnosis) indicating that these changes occur at an early stage in the course of symptom progression. Beyond these characteristic lesions, patients with AD also suffer from frontal lobe damage primarily affecting the dorsolateral and orbitofrontal section, the basal forebrain (Teipel et al., 2005) and the temporo-frontal junction area (Salamon et al., 2004). The neocortical lesions are considered the primary correlates of cognitive impairment beyond memory disturbances, such as language problems, deficits in problem solving and other executive functions which can severely affect activities of everyday life and also co-vary with symptoms of anosognosia (Kalbe et al., 2005; Marshall et al., 2006; Salmon et al., 2006). Frontal lobe damage can also occur at the early stages, but is less prominent compared to the medial temporal lobe abnormalities mentioned (Zakzanis et al., 2003). In addition, there is consistent evidence that the amygdala and the superior temporal gyrus are severely affected at an early stage of AD (e.g., Galton et al., 2001; Basso et al., 2006).

In the course of the disease, volume loss can be found in widespread brain regions including various sub-cortical structures beyond the characteristic cortical atrophy. Concerning sub-cortical lesions, parts of the basal ganglia (i.e., putamen, globus pallidus and caudate nucleus) are affected (Zakzanis et al., 2003). However, effects on basal ganglia are less severe than the volume loss of neocortical regions. Tissue loss in parts of the thalamus was also found in patients with Alzheimer’s disease, although this pathology is not very specific as it is also found in other neurodegenerative disorders.

The volume loss of the medial temporal lobe, especially damage to the hippocampal formation as mentioned above, is the most reliable measure in differentiating between patients with AD at an early stage and healthy individuals (e.g., Wang et al., 2003). However, a recent study by van de Pol et al. (2005) principally confirmed smaller hippocampal volume in patients with AD compared to control subjects, although the authors reported no differences between patients with AD and patients with fronto-temporal dementia (FTD). Comparable results concerning hippocampal atrophy in patients with FTD were reported previously (Frisoni et al., 1999; Boccardi et al., 2003; but see also the study by Ibach et al., 2004, mentioned in Sect. 2.3). In addition, there is also evidence for hippocampal damage in patients with semantic dementia comparable with that found in AD (Galton et al., 2001). Therefore, hippocampal volume loss is less specific for AD than previously assumed, however, it is still the most prominent and most frequently described pathology which is correlated with memory decline in patients with AD. In addition, a recent study by Apostolova et al. (2006) indicated that those patients with mild cognitive impairment and smaller hippocampal volume have a higher risk to convert to AD than patients with mild cognitive impairment and