Vivid recollection and emotional re-experiencing of personal past episodes are the key characteristics of autobiographical memory, a subsystem of episodic memory based upon complex interactions between episodic memory, emotion processing, and the senses of self-coherence and -continuity along the time axis of one’s life. The neural correlates underlying autobiographical memory are known to primarily comprise areas of the prefrontal cortex, medial and lateral temporal, as well as posterior cingulate and retrosplenial cortices. By contrast, the effect of encoding and/or storage parameters such as the emotional valence of the memories retrieved or the length of the time-interval between the initial encoding of information and retrieval remains to be clarified. Also, the question of whether there may exist gender differences in the neural substrates subserving autobiographical memory has not been investigated systematically.

In this study which is primarily concerned with the functional neuroanatomy underlying autobiographical memory, functional magnetic resonance imaging (fMRI) was used to assess differences in the distributed networks of brain structures involved in the retrieval of old and new autobiographical memories with positive or negative emotional valence. Also, the issue of whether there are gender specificities in the functional neuroanatomy of autobiographical memory retrieval was addressed. An additional content analysis approach to the autobiographical memories investigated with functional neuroimaging was employed to elucidate the effect of distinct age and emotional valence of memories on the contents of autobiographical recollections.

The theoretical part of this doctoral thesis firstly describes the status of autobiographical memory within broader models of human memory developed in cognitive psychology and neuroscience, thereby especially referring to the multiple memory systems view. Focusing on episodic and semantic memory, studies on the brain structures representing the anatomical basis of specific memory systems and processes are reviewed. As emotional autobiographical memory largely relies on prefrontal and medial temporal brain structures the review is centered upon these regions. Moreover, studies on putative gender differences in the
brain circuits mediating memory and emotion are referred to. Caveats associated with neuropsychological assessment and functional neuroimaging of highly complex emotional autobiographical memory processing are analyzed, and up to date views of the functional neuroanatomy underlying emotional autobiographical memory retrieval are discussed. Thereafter, behavioral aspects of autobiographical remembering are briefly characterized from the point of view of cognitive and behavioral psychology.

The empirical part describes the hypotheses which guided this study and the methods used to accomplish the fMRI experiment and the behavioral measurements. The central hypothesis of this study claimed that the neural substrates of emotional autobiographical memory retrieval vary depending on differential age and emotional valence of the memories retrieved. Given the classic model of a time-limited involvement of the hippocampus in declarative long-term memory processing, it was specifically expected to observe differential activations of the hippocampal region depending on memory age. Additionally, the functional neuroanatomy of autobiographical memory retrieval was assumed to be more lateralized in males compared to females.

Twenty healthy volunteers (age range: 22-35; ten males, ten females) were enrolled in the study. Autobiographical materials were acquired by means of a semi-structured autobiographical interview several weeks prior to the scanning session. Using blocked design fMRI and Statistical Parametric Mapping (SPM), we investigated the impact of remoteness (factor 1: recent, remote) and emotional valence (factor 2: positive, negative) on the neural correlates of autobiographical memory retrieval. To complement the fMRI results, extensive post-scanning debriefing was accomplished, and a content analysis approach was used to investigate time- and emotion-specific aspects of memory contents. For the purpose of the content analysis, memories were coded into a system of categories each representing a specific topic subjects referred to in their autobiographical memory narratives (first level analyses). Subsequently, categories were summarized to achieve a more general categorization of memory contents (second level analyses).

Significant changes in neural activity (p<0.05, corrected across the whole brain volume) related to autobiographical memory retrieval (irrespective of remoteness and emotional tone) relative to baseline were observed bilaterally in medial and lateral temporal, temporal-occipital, posterior cingulate, and frontal cortices. Recent (relative to remote) memories were associated with differentially increased neural activity bilaterally in the retrosplenial cortex and the hippocampal region (p < 0.05, corrected for ROI) whereas remote (relative to recent) memories did not show any statistically significant differential neural
activations. Positive (relative to negative) memories bilaterally activated the orbitofrontal cortex, the temporal pole, as well as medial temporal areas with the activation peak being in the entorhinal region. By contrast, negative (relative to positive) memories differentially increased neural activity in the right middle temporal gyrus only. No differences in behavioral performance were observed across experimental conditions.

Analyses of gender specificities in the neural substrates of emotional autobiographical memory retrieval demonstrated that there were no overall differences in the autobiographical memory network in males and females, respectively. Also, there were no gender differences in behavioral performance. However, analyses of the main effect of TIME revealed statistically significant increases in neural activity in the pons (including the nucleus coeruleus) bilaterally in males. In addition, a ROI analysis demonstrated significantly increased neural activity in the right hippocampal complex. In females, significant activations related to recent memories were observed in the retrosplenial cortex only. Childhood memories (compared to recent ones) did not yield significant activations in either group. However, this contrast demonstrated deactivations of right insula and the left motor cortex related to recent memory retrieval in females.

With regard to the main effect of EMOTION, a hypothesis-driven ROI analysis revealed statistically significant activations of the left hippocampal region related to positive memories in males while females significantly activated the orbitofrontal cortex bilaterally. Moreover, a ROI analysis showed statistically significant activations bilaterally in the females’ entorhinal cortex extending into the amygdala complex. Retrieval of negative memories did not yield any statistically significant increases in neural activity in males. By contrast, females significantly activated the right middle temporal gyrus during negative memory retrieval. Neither in the male nor in the female group, retrieval of negative relative to positive autobiographical memories was associated with activations in meso-limbic regions.

The content analysis data showed significant differences in memory contents depending on both the age and the emotional valence of recollections. This was not only the case for categories pertaining per se to a specific memory type (e.g. accidents to negative memories and kindergarten to childhood memories). Analyses referring to the factor TIME demonstrated that memory contents relating to the extended categories Social contact and Education were significantly more referred to in the narratives of recent memories while the category Family had a significantly higher representation in the childhood memory conditions. With regard to the factor EMOTION, the content analysis indicated that topics included in the categories Education, Leisure, and Festivities and social events were
statistically significant more frequently represented in positive memories compared to negative ones. By contrast, the categories *Impairment of health* and *Anxiety and shock experiences* were (by nature) significantly more referred to in the negative memory conditions. Based on the system of summarized categories (second level analyses), there were no gender differences in the contents of the autobiographical memories investigated in the present study. At the more specific level of analysis, however, a highly punctual gender differences was observed in that males remembered *Christmas* significantly more often as a negative event than did females.

The neuroimaging data suggest differential functional roles for temporal, prefrontal and retrosplenial regions during autobiographical memory retrieval depending on the remoteness and the emotional valence of the memories retrieved. In particular, our findings support the "classic" model of long-term memory processing which suggests a time-limited differential involvement of the hippocampus in memory consolidation. Interestingly, the observation of such a time-dependent involvement of the hippocampal region in memory consolidation corresponds to the course of retrograde amnesia observed in demented patients, with the loss of recent memories appearing during early stages of the disease when conspicuous neurofibrillary changes are restricted mainly to the hippocampal and parahippocampal regions. Only during later stages, as the neurofibrillary changes spread out to neocortical association areas, remote memories become impaired, too. With regard to the effect of differential emotional valence of the memories retrieved, our data suggest that the entorhinal cortex and adjacent medial temporal areas (including the amygdala) are relatively more engaged in the processing of positive compared to negative emotion. Interestingly, this finding is in good accordance with recent research on emotion processing in patients with Alzheimer's disease (AD) indicating that early brain pathology within the entorhinal region specifically yields a deficit in the processing of positive information.

Moreover, our results indicate that the neural substrates supporting emotional autobiographical memory retrieval are highly similar in males and females. This finding is consistent with the observation that there were not any significant gender differences in memory task performance. Nonetheless, the current study revealed a relatively stronger lateralization of activations related to autobiographical memory retrieval in posterior visual and cerebellar areas in males relative to females. Similar gender-specific laterality effects have been reported previously by studies on gender differences in visuospatial abilities and language. Analyses of gender effects in the main effect of TIME demonstrate the nucleus coeruleus, the midbrain, and the hippocampal regions to be more engaged in the retrieval of
recent (relative to remote) memories in males compared to females, thus suggesting that gender differences in the mechanisms of memory consolidation have to be taken into account. Regarding the main effect of EMOTION, neuroimaging data indicate that females (right orbitofrontal cortex and entorhinal cortex bilaterally, with activations extending into the amygdala complex) may have had more intense emotional memories of their positively valenced past experiences than males (left hippocampal region). However, behavioral data do not support such an hypothesis. Post-scanning debriefing demonstrated that females (compared to males) did not rate any type of memories significantly higher on items describing typical emotion-related qualities of autobiographical recollections. It is thus more likely that males and females differed from each other with regard to their preferential retrieval strategies used to access positively valenced memories, and their ways of generating appropriate retrieval cues from the verbal stimuli.

The content analysis data show differences as well as similarities in autobiographical memory contents across the experimental memory conditions suggesting that the topics referred to in autobiographical recollections vary with differential age and emotional valence of memories. However, this finding also demonstrates that some topics may play an overall significant role across an individual’s whole life history. We observed one highly specific gender difference in the contents of emotional autobiographical memory only (males remembered significantly more negative Christmas memories than did females), indicating that there were no overall differences in the contents of males’ and females’ positive and negative autobiographical memories of childhood and recent past. The punctual gender effect observed is likely to reflect aspects of social learning yielding differential social roles for males and females.

The neuroimaging data demonstrate that the brain regions involved in autobiographical memory retrieval are influenced by the triggered memories’ emotional significance and their relationship to the individual time axis. Importantly, the findings support the view that the hippocampal formation functions as a distributor during memory consolidation, but becomes largely obsolete once the information has firmly been integrated in (primarily) neocortical networks. The amygdala complex was more involved in the retrieval of positive (relative to negative) memories. Although unexpected, this finding is in accordance with both recent research on patients with AD and several neuroimaging studies which also implicated the amygdala in positive emotion processing. However, the issue of amygdala engagement in positive and negative emotion remains to be clarified.
The analyses of gender differences in the functional neuroanatomy of autobiographical memory retrieval corroborated the hypothesis that the neural circuits underlying cognitive functions are more lateralized in males compared to females.

The content analysis results clearly demonstrate that the contents of autobiographical recollections are modulated by differential age and emotional valence of memories. It should be noted that knowledge of the topics typically referred to in positive and negative autobiographical memories of childhood and early adulthood allows for the development of more standardized study designs and memory cueing methods in functional neuroimaging research on different types of autobiographical memory. The question of whether there are more specific content-related differences in the neural substrates of autobiographical memory beyond the four memory types investigated in the present study warrants further investigation. It may be less difficult to address this issue when studying simpler forms of episodic memory than highly complex autobiographical recollections.