CHAPTER VI: SUMMARY AND GENERAL DISCUSSION

1. Summary of the main findings

1.1. General design and aim of research
As the title of this dissertation indicates, the present research investigated whether the differentiation between various memory components (i.e., episodic, semantic, implicit, working memory) contributed to the early assessment of dementia. Thus, whereas clinical neuropsychological assessment primarily employs tests of episodic memory functioning, the present research used a test battery reflecting the different memory components mentioned above. In this way, it was determined which combination of measures (i.e., memory components) was most accurate in predicting dementia, before the diagnosis could officially be made according to DSM-IV criteria. A large group of at baseline nondemented elderly subjects (n=147) was administered this memory test battery at two times of measurement. A first (baseline) measurement took place when these subjects were all clinically nondemented and a second measurement two years later. At the second administration period, a subgroup of elderly subjects was officially diagnosed as demented (i.e., CAMDEX diagnosis ‘mild or moderate dementia’, consistent with the DSM-IV dementia criteria; n=10; these subjects were defined as preclinically demented during the first administration period). In addition, another subgroup of subjects met the CAMDEX criteria of ‘minimal dementia’ (i.e., nondemented according to the official DSM-IV criteria, but symptoms of primarily (episodic) memory deficits are present, while no disturbances in other cognitive domains or occupational or social functioning are observed; n=6). The baseline memory performance of the demented subjects (i.e., two years before they satisfied the DSM-IV criteria) was compared with the baseline performance of the subjects that did not develop dementia. In addition, the performance characteristics of the minimally demented subjects were investigated on an exploratory basis.

1.2. Characteristics of the battery
Whether the battery of memory measures actually reflected several distinctive memory components was analysed by means of factor analysis in Chapter III (section 6). The first factor could be interpreted as reflecting episodic memory processes. The subtests that loaded highest on this factor were, in decreasing order of factor loading values: the ‘Word-recognition test’, the ‘Two-alternative word-recognition test’, the ‘Ten word list-learning test’, the ‘Paired-associate learning test’, and the ‘Visual Association Test’. In addition, a second factor was identified which comprised several cognitive processes, other than episodic memory functioning. The subtests that loaded highest on the second factor were, in decreasing order of factor loading values: the ‘Digit span task’, the ‘semantic memory’ measure of the ‘Perceptual identification task’, the ‘Mirror-reading task’, the ‘Category fluency test’, and the ‘Block span task’. Both priming measures, the ‘Word stem completion task’ and the ‘priming’ measure of the ‘Perceptual identification task’, were not included in the final factor analysis, because of their low level of internal consistency (i.e., no satisfactory factor solution was obtained when these two measures were included).
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subcomponents, such as semantic memory, working memory and visuospatial ability. It may be argued that if the test battery had consisted of more tests reflecting each subcomponent, these subcomponents would have formed distinctive factors. The battery consisted of five subtests that were interpreted as reflecting episodic memory functioning (forming the first factor), while the other subcomponents were represented by only two subtests each. Nonetheless, the second factor could be summarised as a factor sensitive to the executive functions (e.g., working memory, problem solving, initiating ability, mental flexibility, concept formation and reasoning). Overall, it may be concluded that the battery reflected more than episodic memory functioning.

1.3. Impact of cognitive status in nondemented subjects

First, performance on the memory test battery was examined within a group of clinically (i.e., according to DSM-IV) nondemented elderly subjects that varied in their global level of cognitive functioning (indicated by several scores on the MMSE). In this way, a group of ‘cognitively impaired’ elderly subjects (the CI group; MMSE scores < 26) and a group of ‘cognitively healthy’ normal control subjects (the NC group; MMSE scores > 26) was contrasted (see Chapter III, sections 4 and 5). In general, the CI subjects performed significantly worse than their controls, except on the two priming measures. No differences at all were found on the first priming measure, the ‘Word stem completion task’. This subtest showed a low level of internal consistency, which is explained by the finding that the stems were hardly ever completed with target words. The second priming measure, the ‘priming’ measure of the ‘Perceptual identification task’, showed greater priming effects for the CI subjects. This may be explained by the generally slower identification times in the CI subjects, giving them more opportunity to benefit from the repeated presentation of words and improve their reaction times. However, both groups did exhibit effects of priming on this task. Nonetheless, the best discriminating measures between the CI group and their controls were the ‘Paired-associate learning test’, the ‘Mirror-reading task’, and the ‘priming’ measure of the ‘Perceptual identification task’. Thus, the differentiation between two groups of clinically nondemented subjects that differ in global level of cognitive functioning is best characterised by an episodic memory test – which is sensitive to semantic processing capacities – and, furthermore, by two other types of memory tests, which primarily loaded on the second (‘executive functioning’) factor. The evidently worse performance by the CI subjects on the ‘Mirror-reading task’ may be characterised by a greater sensitivity to task complexity. On the other hand, they are indeed able to (implicitly) benefit from the repeated presentation of material to be memorised, as was indicated by their performance on the ‘priming’ measure of the ‘Perceptual identification task’ and, as well, by the normal learning curves on the ‘Paired-associate learning test’ and the ‘Ten word list-learning test’.

1.4. Preclinical assessment of dementia, two years in advance

The baseline memory performance (available from the first administration) of the subjects that were diagnosed as demented two years later was compared with the baseline performance of the nondemented subjects (Chapter IV, section 5). Two sets of analyses were performed: a first set of analyses was performed over the entire group of elderly subjects (thus, including the large group of NC subjects with MMSE scores > 26, in addition to the CI group), and a second set of analyses was performed over a subgroup that only included the subjects that were originally screened for the CI group (with MMSE scores < 26). It may, for that matter, be noted that this latter
subgroup is more relevant to a real-life clinical practice situation. When the cognitive functions of a person are evaluated in clinical practice, first, a cognitive screening test such as the MMSE is administered; only subjects with a relatively low score are further evaluated (in section 3 of this chapter, this discussion will be continued). It may be noted that the two sets of analyses (performed over the group that included vs. excluded the NC subjects) did not show identical results, as will be described below.

First, the entire group of available subjects, including the NC subjects, was examined (see Chapter IV, section 5.1.1). The best predicting variables with respect to dementia, diagnosed two years later, were worse performance on the ‘Visual Association Test’, the ‘Two-alternative word-recognition test’, the ‘priming’ measure of the ‘Perceptual identification task’, and a higher age. This selection of variables was not altered by a different categorisation of the 6 available minimally demented subjects (excluding them or classifying them as ‘demented’), except for the selection of the ‘Paired-associate learning test’, at the expense of age, when the minimal dementia subjects were regarded as ‘demented’. It may be concluded that poor performance on episodic memory tests that are characterised by passive retrieval processes, in combination with poor implicit benefit from the repeated presentation of material and a high age are best at predicting dementia two years before the diagnosis can be made.

The second set of analyses was focused on the cognitively impaired (CI) group. The best predictive variable with respect to dementia two years later was poor performance on the ‘Paired-associate learning test’ (i.e., reflecting cued recall and semantic processing). The strong predictive value of this subtest was not influenced by classifying the minimally demented subjects to the ‘demented’ group or by exclusion of these subjects. In addition, the ‘priming’ measure of the ‘Perceptual identification task’ (i.e., reflecting perceptual repetition priming effects; implicit remembering of previously encountered words) was consistently found to be of good predictive value. Within this group of CI subjects, the ‘Visual Association Test’ and the ‘Two-alternative word-recognition test’ did not significantly contribute to the prediction of dementia. These two measures were only found to be of predictive value within the entire group of subjects, which is more cognitively heterogeneous than the CI group (as was described above). Therefore, it may be concluded that these variables were not sufficiently sensitive to detect demented cases within a dementia-at-risk group of cognitively impaired elderly subjects.

Overall, it may be argued that in the early (preclinical) assessment of dementia, episodic memory functioning plays an important role, particularly tests requiring passive retrieval processes. However, implicit memory tests significantly improve the accuracy of prediction of dementia, thus emphasising the importance of other memory components than reflecting episodic memory. Furthermore, the importance of age in the differentiation between preclinically demented and nondemented subjects is highly plausible, considering the well-known higher incidence of dementia with increasing age. In addition, when focusing on a dementia-at-risk group of cognitively impaired subjects (the CI group), the disability to benefit from semantic relations within to be learned material may be crucial for the differentiation between cognitively impaired but nondemented elderly subjects and subjects that are in fact in a preclinical stage of dementia. This ‘semantic processing’ deficit may even be sufficiently sensitive to differentiate between cognitively impaired but nondemented elderly subjects and subjects that meet the CAMDEX criteria for minimal dementia two years later (rather than mild or moderate dementia) – see Figure 19 in Chapter IV for an illustration. However, this conclusion is based on
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only a few subjects (n=6). In addition, it is unknown at this stage whether the minimal dementia subjects will indeed develop clinical dementia (consistent with the DSM-IV criteria) in the near future.

1.5. Differential (cross-sectional) assessment of dementia
Finally, analyses were performed over the memory subtest data collected during the second administration period (i.e., the stage at which dementia was diagnosed). Performance in the clinically demented vs. the nondemented subjects was investigated, in order to determine the measures that best assessed dementia at the time of diagnosis (see Chapter IV, section 6).

The search for effective predictors of dementia using the data from the first administration showed the importance of the ‘Visual Association Test’, the ‘Two-alternative word-recognition test’, the ‘priming’ measure of the ‘Perceptual identification task’, the ‘Paired-associate learning test’ and age (as was described above). However, the (cross-sectional) data of the second administration period showed slightly different results. The ‘Visual Association Test’ was again found to be of good discriminative value between demented and nondemented subjects, though (again) only within the entire group of subjects. The ‘Ten word list-learning test’ also differentiated well within the entire group of subjects, while the ‘Word-recognition test’ and the ‘Category fluency test’ discriminated best between demented and nondemented subjects within the CI group.

Thus, it may be concluded that episodic memory measures of more active retrieval processes differentiated best between nondemented and demented subjects, once the diagnosis has been made. Furthermore, an episodic memory test demanding passive retrieval processes (and the inhibition of semantically related distractors), in combination with a category fluency paradigm (i.e., reflecting semantic search ability and the integrity of semantic memory store) discriminated best between cognitively impaired but nondemented elderly subjects and clinically demented subjects (at the time of diagnosis). The impaired category fluency performance in both preclinically demented (i.e., two years before diagnosis) and clinically demented subjects is characterised by a decreased generation level of relatively uncommon (middle-frequency) exemplars (see Chapter V for further details).

Overall, it may be concluded that performance on free recall of unstructured word-lists declines subsequent to decline on cued recall of semantically related words, rather than simultaneously (i.e., the first component only showed clearly impaired performance when dementia was in a clinical stage, while the latter already showed impaired performance in a preclinical stage). Note that traditional (clinical) batteries for assessment of dementia consistently test for free recall of unstructured word-lists.

Finally, it may be argued that differentiating between two nondemented groups of elderly subjects that differ in global cognitive status reflects different cognitive components than differentiating between preclinically demented and nondemented subjects. The only exception may be cued recall tasks demanding semantic processing capacities (i.e., measured by the ‘Paired-associate learning test’), which are found to be useful both in the differentiation within nondemented subjects and in contrasting cognitively impaired but nondemented elderly subjects from subjects that are in a preclinical stage of dementia. However, cognitively impaired but nondemented subjects seem sensitive to semantic relations within material to be learned, but simply process the information less quickly than controls (i.e., they show improvement over trials), whereas preclinically demented subjects seem unable to
benefit from these semantic cues at all (i.e., they show no improvement over trials and their performance level remains close to 0; compare Figure 4 in Chapter III with Figure 17 in Chapter IV).

2. Methodological considerations

As was described in part III of Chapter I, the present research project has several advantages. First of all, in this research it is possible to study preclinically demented subjects (i.e., subjects identified as being demented two years later, thus representing a longitudinal research design), while most experimental and clinical studies merely investigate subjects that already meet the criteria of the clinical diagnosis of dementia (i.e., cross-sectional studies). Secondly, the group of subjects used in this study may be considered as a representative sample of the elderly population, concerning their age and level of education (i.e., around 80 years old and primary school education). Note that the sample of elderly subjects in most experimental studies is restricted to a relatively young age (around 68 years old) and a high educational level (e.g., college education; around 12 years of formal schooling). Thirdly, since in the present research, a battery of various memory tasks was administered, it was possible to investigate the relative contribution of each task to the early assessment of dementia, and to observe how these different memory aspects interacted with one another. In contrast, most experimental and clinical studies focus on merely one aspect of memory functioning. However, several possible disadvantages of the current research should be discussed as well.

First of all, though the sample may be considered as representative concerning age and education, it should be noted that the LASA participants that were actually tested may deviate from the elderly population in other respects. The sample of LASA participants tested in the present research may be characterised as relatively well functioning elderly persons (i.e., assertive, active), given their decision to participate in the LASA study and in the present research. In contrast, many other elderly people (or dropped-out subjects) do not want to be bothered by studies like LASA (anymore) (e.g., these persons might be more passive and less socially engaged). This may indicate that the actually tested LASA participants are more socially engaged and, therefore, perhaps more mentally active than other elderly people (non-participants or dropped-out subjects). Furthermore, many of our subjects reported that they solve (crossword) puzzles as a hobby or watch TV quizzes, which may have made them more cognitively healthy and, thus, more inclined to participate in the 'memory section' of the LASA study. Therefore, the present research may have been affected by a certain degree of selection bias: the elderly persons that were actually tested may have performed better than non-participants or dropped-out subjects would have done. It may be argued that this latter group of elderly persons shows more resemblance with patients that are referred for neuropsychological evaluation in clinical practice. However, if this is the case, it may be argued that differences in clinical practice will be greater than the differences found in the present research. Thus, if a broader sample of elderly subjects was tested, the nature of the results described in this dissertation would not have to be different. The results might simply be more powerful.

A second methodological aspect of the present research that may have influenced the nature of the sample are the selection criteria that were applied. The subjects were
screened for depression and residual CVA symptoms by means of self-report questionnaires, as part of the LASA interviews. It is possible that subjects did not answer the questions correctly (either knowingly or unknowingly). However, the effects of a clinically significant depression or a serious and/or recent CVA would be readily apparent to the experimenter, who was instructed to report any observations that might have affected test performance.

A third disadvantage of the present data represents the limited number of demented subjects during the second measurement period. During the first administration period, the sample was screened for dementia by means of the CAMDEX procedure. Subjects that were diagnosed as mildly or more severely demented (i.e., 'demented' according to the DSM-IV criteria) were excluded, while subjects that were classified as minimally demented or nondemented were included. Despite the inclusion of the subjects that were initially diagnosed with minimal dementia (which is supposed to be an intermediate stage between 'no dementia' and 'dementia' according to the CAMDEX procedure; n=18), relatively few subjects developed mild or moderate dementia in the two-year time period (n=10, of whom 6 subjects were initially classified as minimally demented). In addition, the exploratory examination of the subjects that were diagnosed as minimally demented during the second administration period was difficult since this subgroup was even smaller (n=6; see Chapter IV, section 5.2). Naturally, statistically more powerful results regarding the prediction of dementia would have been obtained if a greater sample of demented subjects had been available.

An explanation for the small number of subjects that turned out to be demented during the second administration period may be the reliance on information provided by the GP with respect to the final diagnosis in the dropped-out subjects. This may have led to the missing of an unknown number of actually demented cases. Only 3 out of 44 subjects were diagnosed demented according to the 'GP method'. Most likely, these are subjects that have been diagnosed demented some time ago and in the mean time have progressed to an advanced stage of the disease. The GP indicated a patient as demented not only when the diagnosis was confirmed officially by the physician to whom the patient was referred — if there had been doubts about the cognitive status of a patient to begin with. Thus, this procedure takes a considerable amount of time. In addition, the GP gives a patient 'the benefit of the doubt' (i.e., indicates him as 'nondemented') when this procedure has not been fully completed yet. In contrast, the administration of the CAMDEX during the second administration period may also have identified several demented subjects for whom the CAMDEX diagnosis was the first moment of diagnosis (i.e., subjects that did not yet see a physician; based on personal observation — no official data are available). Such demented subjects must have been missed in the group of dropped-out subjects. In addition, anxiety regarding a memory test administration because of a beginning dementia may well have kept these specific subjects from participating in the second administration period (i.e., an example of selection bias, described previously). Thus, it may be argued that the 'GP method' has a lower sensitivity than the CAMDEX, which may explain the small number of demented subjects in the present research.

Another disadvantage of the present research is that the CAMDEX administration could not specify the type of dementia (e.g., Alzheimer's Disease, Vascular Dementia), because a physical examination of the subjects was not possible. However, it may be argued that most subjects diagnosed demented suffer from
Alzheimer's Disease since this is by far the most common type of dementia (see Chapter I, part II). In addition, Vascular Dementia is rather unlikely in the current sample of subjects, considering that Vascular Dementia is usually caused by a series of cerebral infarcts, whereas our subjects were screened for residual CVA symptoms. Though some subjects indeed suffered from a CVA at some time in their life – though this was often a single transient ischemic attack (TIA), which is of short duration and has only minor impact – no subjects experienced any current residual effects on cognitive functioning (i.e., subjects that answered LASA questions on this issue affirmatively were excluded; see Chapter II). In fact, none of the subjects that were diagnosed demented reported a CVA, although their reports may not be accurate. However, in most subjects, a hetero-anamnesis was available. Even if a few subjects suffered from Vascular Dementia, the impact on the nature of the results will be minor. Furthermore, the results of the present research concerning the early predictors of dementia correspond very well with relevant literature findings on the performance of Alzheimer's Disease patients (see Chapter I, part II).

Finally, a disadvantage of the current memory measures is that no reliable priming measures were available, which is a frequently reported problem (e.g., Meier & Perrig, 2000). The 'priming' measure derived from the 'Perceptual identification task' repeatedly showed a low level of internal consistency. This was most likely caused by the process of subtraction of reaction times, which leads to a significant reduction of true score variance, while error variance remains. Nonetheless, this priming measure, in combination with a few other measures, was consistently found to be of high predictive value with respect to dementia. However, the 'Word stem completion task' did not induce priming effects at all and may, therefore, be considered as an inadequate measure of implicit memory within the battery (for this population). The discussion of the practicality of this measure will be continued in section 4 of this chapter. In addition, it must be noted that the choice of statistical analysis may also have influenced the results. However, performing a stepwise logistic regression analysis instead of a stepwise discriminant analysis did not change the selection of best predicting variables, except for the significance of the 'Ten word list-learning test', which was not included in the discriminant analysis. The 'Visual Association Test', the ‘Two-alternative word-recognition test’, the ‘priming’ measure of the ‘Perceptual identification task’ and age were consistently found to be of high predictive value.

3. Relevance and implications for clinical practice

The present research was aimed at finding early (preclinical) predictors of dementia since medication may only be effective when the dementia is still in an early stage. However, the current medication has many side effects, which result in relatively many patients abandoning the therapy, while the effects on cognitive functioning are still ambiguous. On the other hand, early detection of dementia has also other benefits, such as early guidance and care of the patient and his family. Nonetheless, the search for early predictors of dementia may, in addition to the advantage of a high sensitivity, also lead to the disadvantage of a lower specificity: elderly persons may be unnecessarily bothered by the concern that they might be in the early stage of dementia while in fact they are not. This causes, in addition to an enormous amount of psychological distress for the patient and his family, a significant pressure on national
health care. Therefore, in addition to a high sensitivity, a high specificity of predictive variables may be equally as important – especially as long as an effective drug therapy with as few side effects as possible is absent.

In order to prevent as many false positive diagnoses as possible, the following diagnostic approach may be appropriate. First, a short screening test (battery) may be administered, in order to investigate the significance of the cognitive complaints with which people visit their GP. Since dementia is a highly prevalent syndrome in the elderly population and because more and more attention is paid to it in the media, many people may be unnecessarily worried that they are becoming demented when they have memory complaints, such as forgetting names (as many LASA participants reported in the present research). The MMSE is a common first screening cognitive instrument, but the addition of, especially, the ‘Paired-associate learning test’ and variables such as age may significantly improve the sensitivity as well the specificity of the prediction of dementia two years before the diagnosis can officially be made. Furthermore, the MMSE and the ‘Paired-associate learning test’ are instruments easily and quickly administered (i.e., a maximum of 10 minutes each). The ‘Visual Association Test’ may be good alternative screening measure for the MMSE, as was described in the present research. If a patient scores in a dubious range on these measures, the GP may suggest a more comprehensive neuro(psychological evaluation. However, the determination of the exact cut-off scores should be in favour of a good specificity as long as an effective (medical) treatment is missing.

As was already mentioned in section 1 of this chapter, the focus on predictive variables of dementia within a cognitively impaired group of elderly subjects (e.g., with lower MMSE scores) is more relevant to the clinical practice situation. Therefore, implementation (in a neuropsychological evaluation) of the ‘Paired-associate learning test’ and the ‘priming’ measure of the ‘Perceptual identification task’ should be emphasised here, rather than the ‘Visual Association Test’ or the ‘Two-alternative word-recognition test’. The latter two measures were found to discriminate between a large group of nondemented elderly subjects (including many cognitively healthy subjects with MMSE scores of 27 and above) and a group of subjects that were diagnosed as mildly or moderately demented two years later. The ‘Paired-associate learning test’ came forward as the best discriminative measure between a group of nondemented subjects that were nonetheless characterised as cognitively impaired (i.e., an average MMSE score of 23) and a group of subjects that were identified as clinically demented during the second administration period. Thus, the ‘Paired-associate learning test’ seems a more sensitive measure that is better able to discriminate between ‘normal’ cognitive impairment and an initial form of dementia. The ‘priming’ measure of the ‘Perceptual identification task’ was found to be of good predictive value in both situations.

In clinical practice, tests of paired-associate learning are already frequently administered (e.g., in versions of the Wechsler Memory Scale or the California Verbal Learning Test). However, clinical neuropsychologists that are responsible for the neuropsychological evaluation of a patient, may not be very well aware of the importance of the aspect of semantic processing, rather than simply cued recall. As was described above, it may also be concluded from the present research that free recall of semantically unrelated words is less useful in the early assessment of dementia (i.e., the ‘Ten word list-learning test’). This type of memory test is, nonetheless, standard procedure in clinical practice regarding the assessment of dementia. It may be argued, however, that free recall of lists of unrelated words
causes deficits in nondemented elderly subjects as well. Only when dementia has progressed to a more advanced stage, differences with normal controls may be sufficiently evident.

The implementation of priming paradigms in clinical practice is more difficult to accomplish. Tests constructed to measure priming effects do not exist within clinical neuropsychological assessment, as was also discussed in Chapter I. A computer is necessary to obtain reliable measures of differences in reaction times. It may be noted that test batteries administered by means of a computer are becoming more and more common practice in clinical neuropsychological assessment (e.g., batteries used to test for attentional functions or computerised versions of the Wisconsin Card Sorting Test). However, it is important to realise that an elderly patient should always be assisted when registering reaction times in a priming task, as was done in the present research. If patients pressed a key themselves to register the reaction time of an answer, reaction times would be strongly influenced by differences in psychomotor speed between patients.

4. Recommendations for future research

First, a few recommendations concerning the content of the test battery should be mentioned here. As was noted above, both priming measures showed a low level of internal consistency. The low level of internal consistency of the ‘priming’ measure of the ‘Perceptual identification task’ was the consequence of the process of subtraction of reaction times. It is difficult to create a different scoring method in order to measure effects of priming, since the priming effect is based on the improvement (difference) of performance relative to performance on previous trials. Nonetheless, the ‘priming’ measure derived from the ‘Perceptual identification task’ may become more solid when it is based on more trials measuring the effect (i.e., only 12 trials were available in the current task). However, since this task was rather tiring for many elderly subjects, it is important to limit the length of the task: the current task consists of a sum of 48 trials, which should not be exceeded. A solution may be to add some middle-frequency words that have a repeated presentation and, instead, to remove low- or high-frequency words, which are only presented once within the task.

Furthermore, the low level of internal consistency of the ‘Word stem completion task’ was due to the fact that the subjects hardly ever completed the stems with target words. This may be explained by the number of tasks that was administered between the study phase (the ‘Ten word list-learning test’) and the test phase (the ‘Word stem completion task’). The ‘Digit span task’, the ‘Word-recognition test’, the ‘Paired-associate learning test’ and the ‘Block span task’ were administered between the study and the test phase, which may have been a too large degree of interference. When a word stem completion paradigm is used in experimental studies of implicit memory, it is usually the sole object of investigation rather than as part of a whole battery of tests. In addition, the processing capacity of elderly subjects is diminished, relative to younger subjects, which makes them more vulnerable to interference between two tasks. Therefore, it may be recommended to decrease the number of tasks administered between the study and the test phase when testing priming effects by means of a word stem completion paradigm.

In addition, the number of tasks should be reduced anyhow, because of the frequently reported feelings of fatigue in our elderly subjects. Because of the presence of relatively many episodic memory tests, it may be best to delete some of these
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measures (e.g., the ‘Word-recognition test’, the ‘Ten word list-learning test’). In addition, both working memory measures (the ‘Digit span task’ and the ‘Block span task’) demonstrated to be of only modest predictive value regarding dementia.

Furthermore, more attention should be paid to aspects of semantic processing, considering the good predictive value of the ‘Paired-associate learning test’. The importance of components of semantic memory was also demonstrated by the various scores derived from the ‘Category fluency test’ (see Chapter V; the ability to switch between subcategories and the availability of less common exemplars of a category). However, it was highly laborious to obtain these exact fluency measures and, therefore, a more easily obtainable and direct measure should be designed in order to test for these aspects of semantic processing. It might also be interesting to investigate semantic processing capacities within tasks of implicit memory, considering the promising predictive value of both the ‘Paired-associate learning test’ (sensitive to semantic processing) and the ‘priming’ measure of the ‘Perceptual identification task’ (a measure of implicit memory). In addition, tasks of ‘conceptual priming’ have been found to differentiate well between AD patients and healthy controls (see Chapter I).

Secondly, more early stage demented patients should be tested in order to obtain more reliable results. A serious limitation of the present research was the limited number of demented subjects after two years. Therefore, it is important to keep on following the LASA participants that were tested in the present research (e.g., by means of a repeated diagnostic procedure after another two years). For the subjects that turn out to be demented, memory test data will be available at two times of measurement (i.e., two and four years before diagnosis). Furthermore, it may be interesting to administer the most promising memory measures in patients that are suspected to develop dementia and first enter an outpatients’ department for a neuropsychological evaluation. In this way, the accuracy of the measures, which are described in this dissertation as best predictors of dementia, might be improved.

5. Conclusions

It may be concluded that, in addition to the differentiating value of tests of episodic memory functioning, the investigation of other memory components has proven to be useful in the early assessment of dementia. First of all, deficient implicit remembering of words that were previously presented, which may be characterised as a typically non-episodic aspect of memory functioning, consistently demonstrated to be of good predictive value.

Furthermore, the addition of other memory components than reflecting episodic memory has improved the understanding of which specific aspects of so-called episodic memory tests have the best discriminative value. It may be argued that the semantic processing (encoding) of to be learned material is functioning normally in nondemented elderly people, even if they are characterised by an impaired global cognitive status. In contrast, elderly people who are in a preclinical stage of dementia (diagnosed two years later) show hardly any benefit of inherent semantic structure of material to be learned (even if the material is repeatedly presented). These results are in correspondence with several studies reviewed in Chapter I, which suggest that semantic memory disorders occur in a very early stage of Alzheimer’s Disease (e.g., Hodges, Salmon & Butters, 1990; Weingartner, Kawas, Rawlings & Shapiro, 1993; Rosser & Hodges, 1994; Hodges & Patterson, 1995). It may be argued that the
explanation by Sailor, Bramwell and Griesing (1998) that Alzheimer’s Disease patients have a specific deficit in the ability to evaluate semantic relations, is also relevant for subjects in the preclinical stage of their disease.

In sum, future research into the early assessment of dementia should be focused on the aspects of memory functioning described above. This will hopefully lead to an improvement of neuropsychological assessment methods in the early identification of dementia.